Thyroid-related Hormone Levels in Clinical Patients with Moderately Severe-to-Profound Sudden Sensorineural Hearing Loss: A Prospective Study

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Research

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Abstract

Background and Purpose

SSNHL is a common otology emergency, that may lead to hearing loss and impact quality of life. This study aims to investigate the association of thyroid-related hormone levels with moderately severe-to-profound sudden sensorineural hearing loss (SSNHL) that may contribute to treatment optimization.

Methods

The study included 70 patients with moderately severe-to-profound SSNHL and 100 age- and sex-matched healthy controls. Peripheral venous blood samples were taken from the participants, and their thyroid-related hormone levels were measured at admission and one week after treatment.

Results

Thyroid-related hormone levels of total triiodothyronine (TT3), total thyroxine (TT4), free triiodothyronine (FT3), and thyroid stimulating hormone (TSH) (all $P < 0.05$) were found to be at significantly lower levels in moderately severe-to-profound SSNHL patients to that of the control group. The increases of TT3, TT4, FT3, and TSH levels were significantly higher in the effective group than that in the ineffective group (all $P < 0.05$). Through receiver operating characteristic curve analyses, areas under the curve were 0.737, 0.636, 0.837, 0.458, and 0.903 for TT3, TT4, FT3, FT4, and TSH, respectively. Linear correlation analysis revealed that TSH level ($R = 0.707$, $P < 0.05$) elevation after treatment successfully predicted a favorable outcome of hearing recovery. Logistic regression analyses suggest low FT3 and TSH levels to be independent occurrence predictors while the increase of TSH level may be an independent favorable outcome predictor.

Conclusions

The results suggest low FT3 and TSH levels are risk factors for moderately severe-to-profound SSNHL. By discovering the positive association between TSH elevation and hearing recovery, along with the potential novel predictors of FT3 and TSH, our study may contribute valuable insights to the study and treatment of moderately severe-to-profound SSNHL.

Trial Registration

Chinese Clinical Trial Registry; ChiCTR1800017072. Registered 10 July 2017, http://www.chictr.org.cn/showproj.aspx?proj=29023

1. Background

Sudden sensorineural hearing loss (SSNHL) is defined as the rapid onset of hearing impairment with a more than 30 dB decreases in at least 3 continuous frequencies within 72 hours [1]. The incidence of

SSNHL in the United States ranges from 5 to 27 per 100,000 population, with about 66,000 new cases per year [2–4]. The morbidity rate of SSNHL in China has been increasing in recent years, but large-scale epidemiological data are still lacking. SSNHL usually occurs unilaterally and is sometimes accompanied by tinnitus, vertigo, ear fullness, and nausea. However, the inaccurate interpretation of its causes, the delay in seeking care or referral to medical specialists, and the limited treatment options have made SSNHL a particularly devastating disease [5]. The degree and frequencies of hearing loss, age, presence of vertigo, and the initial time of therapy are all factors that influence the prognosis of SSNHL [6]. Among these factors, the degree of hearing loss plays the most important role in determining the prognosis of SSNHL[7]. Sheehy et al. [8] reported that primary hearing loss with a decrease in intensity of 45 dB or lower presented a satisfactory recovery prognosis. In contrast, Enache et al. [9] reported that hearing loss with a decrease in frequency of more than 50–60 dB, even with adequate treatment, leads to the recovery of no more than 20–30 dB. Moreover, steroids have no effect when the initial hearing loss is 90 dB or higher [10]. Generally, high hearing loss severity translates to a worse prognosis. According to the latest World Health Organization hearing classification, hearing loss of more than 50dB is classified as moderate to severe deafness, where patients experience difficulty in hearing conversational speech [11]. Thus, our research was focused on moderately severe-to-profound SSNHL at all frequencies.

The guidelines of China (2015) [6] emphasize that moderately severe-to-profound SSNHL at all frequencies may be caused by vasospasms or endothelial dysfunction and inner ear embolism or thrombosis. Thyroid disorders are risk factors for cardiovascular and cerebrovascular disease, including acute ischemic stroke, atherosclerosis, and myocardial infarction [12–14]. Hypothyroidism has a significant causal association with a worse profile of atherosclerotic risk factors and may play a role in atherothrombotic myocardial infarction [15]. Given the similar pathogenesis between cardiovascular disease, cerebrovascular disease, and moderately severe-to-profound SSNHL, we hypothesize that comparing the thyroid function test upon admission and after treatment covering measurements of total triiodothyronine (TT3), total thyroxine (TT4), free triiodothyronine (FT3), free thyroxine (FT4), and thyroid stimulating hormone (TSH), may assist with the diagnosis and prognosis of moderately severe-to-profound SSNHL. This is based on previous studies that have established the vital role that thyroid hormones play in cochlear development and in the maintenance of hearing in adulthood [16, 17]. Ng et al. [18] and Forrest et al. [19] have demonstrated that thyroid hormones and their receptors are required for the development of hearing, while Richter et al. [20] and Ng et al. [21] supports the same concept reporting that T3 is essential for normal cochlear function and morphology in mice, where a lack of T3 could lead to important alterations in cochlear morphology and loss of cochlear function. T3 regulates not only the development of auditory function but also the maturation of auditory sensitivity which is evident through reports from Li et al. [22] who reported hypothyroidism to be associated with sensorineural hearing loss.

To investigate the potential roles that thyroid-related hormone may play in the development of moderately severe-to-profound SSNHL, we designed this prospective study to compare the thyroid hormone levels before and after treatment for the first time. A regression analysis was done to determine the occurrence

and prognosis, and linear regression was performed between thyroid-related hormone versus the severity of hearing loss, and the elevation of thyroid-related hormone versus hearing recovery. Receiver operating characteristic (ROC) curve analysis was used to assess the predictive value of thyroid-related hormone for SSNHL.

2. Methods

2.1 Study population

A total of 70 consecutive patients with moderately severe-to-profound SSNHL diagnosed at our Hospital between July 2018 and December 2020 were prospectively enrolled. All participants provided written informed consent for their inclusion in the database and the use of their data for research purposes. The study protocol was approved and implemented according to the ethical standards of our Hospital ethics committee [2018-KY-036(K)]. The progress was conducted in accordance with the spirit of the Helsinki Declaration. Patients included in the study visited the hospital for the first time within 7 days after the onset of moderately severe-to-profound SSNHL. All participants underwent standard laboratory tests and audiological diagnostic procedures. Included patients were those with hearing loss at all frequencies and mean pure tone audiometry (PTA) across 0.25 to 8 kHz ≥ 50 dB, while those excluded had acute inflammatory conditions, obstructive sleep apnoea, connective tissue diseases, abnormal ear examination findings, a previous history of thyroid disorder, chronic otitis media, a history of acoustic trauma or otologic surgery, conductive hearing loss, or had used ototoxic medications. Patients with malignant disease, psychiatric conditions, dementia, hepatitis B or C, or other major comorbidities (heart failure; stroke; and severe hepatic, pulmonary, or renal dysfunction) were also excluded. A group of 100 sex- and age-matched controls without any disease at regular health check-ups was used for comparison. The exclusion criteria were the same as those for the SSNHL group.

2.2 Data collection

The baseline characteristics included age, sex, height, weight, body mass index (BMI), and blood pressure on admission (systolic blood pressure and diastolic blood pressure). The clinical characteristics included affected side, accompanying symptoms (including tinnitus, vertigo, ear fullness), history of hypertension and diabetes, time to treatment, and hearing level on admission. All hearing assessments were performed in standard shielding rooms and PTA was performed for both air and bone conduction at 0.125, 0.25, 0.5, 1, 2, 4, and 8 kHz before and after 7 days course of systemic treatment. The hearing loss of each individual was calculated by averaging the PTA value of damaged frequencies after onset. The extent of hearing recovery is calculated using PTA after onset minus PTA after treatment. All patients underwent temporal bone computed tomography or inner ear magnetic resonance imaging, and no ear structural abnormality and tumors were found. Upon admission, thyroid function tests of TT3, TT4, FT3, FT4, and TSH levels were performed using blood samples obtained from the antecubital veins of all patients between 6 and 7 a.m. after an overnight fast. The thyroid function test was performed again post-

treatment and its difference (post minus pre) to the first test was used to evaluate the changes in thyroid-related hormone.

2.3 Treatment procedure

Once SSNHL was diagnosed, patients were hospitalized for one week. All the patients underwent comprehensive treatment, including treatment with steroids and batroxobin following the 2015 China guideline for the diagnosis and treatment of sudden deafness [6]. The comprehensive treatment consisted of intravenous injection of Prednisone (1mg/kg/day) for 3–5 days, followed by a reduced dosage for the remaining days according to the hearing improvement, and intravenous batroxobin (10U batroxobin for the first time and then reduced to 5U batroxobin, once every other day, 1 to 3 times in total according to the level of fibrinogen). Patients that experienced hearing recovery were divided into the effective group (PTA of impaired frequencies which improved more than or equal to 15 dB, or back to normal/ unaffected ear) and the ineffective group (PTA of impaired frequencies which improved less than 15 dB).

2.4 Statistical analyses

Statistical analyses were performed using SPSS for Windows version 22.0 (IBM Corp., Armonk, NY, USA). Data on quantitative variables are presented as mean ± standard deviation and qualitative variables as numbers (percentage). The Chi-squared test was used for categorical variables. The independent samples t-test was used to compare continuous variables. Linear correlation was performed to assess the association between thyroid-related hormone, hearing loss and hearing recovery. ROC curve analysis was used to assess the relationship between thyroid-related hormone and the occurrence of moderately severe-to-profound SSNHL. Binary logistic regression models were used to estimate the odds ratios (OR) and 95% confidence intervals (CI) for the correlation between thyroid-related hormone and the occurrence and outcome of moderately severe-to-profound SSNHL. $P < 0.05$ was considered significant for all tests. The figures were generated using GraphPad Prism 7.0 for Windows (GraphPad Software Inc., CA, USA).

3. Results

3.1 Baseline and clinical characteristics of participants

The baseline characteristics of participants are summarised in Table 1. About half of the patients (n = 38, 54.29%) were male and the mean age of the patients was 51.00 ± 15.89 years. There were no differences in age, sex distribution, height, weight, BMI, and blood pressure on admission between the two groups. From the results, the thyroid-related hormone levels of the moderately severe-to-profound SSNHL group were significantly lower than those of the control group (TT3, TT4, FT3, and TSH; all $P < 0.05$) as shown in Table 1.

Table 1
Baseline characteristics of participants in the moderately severe-to-profound SSNHL and control groups

	Moderately severe-to-profound SSNHL (n = 70)	Control (n = 100)	P value
Baseline characteristics			
Age (years)	51.00 ± 15.89	49.73 ± 9.75	0.553
Sex (male, %)	38 (54.29)	51 (51.00)	0.673
Hight (cm)	167.49 ± 8.76	168.09 ± 7.52	0.631
Weight (kg)	68.25 ± 12.64	67.84 ± 11.39	0.826
BMI (kg/m^2)	24.27 ± 3.69	23.92 ± 3.14	0.519
Systolic blood pressure (mmHg)	120.71 ± 16.93	123.69 ± 10.66	0.196
Diastolic blood pressure (mmHg)	76.01 ± 9.98	77.18 ± 9.73	0.448
Laboratory variables			
TT3 level (nmol/L)	1.27 ± 0.21	1.43 ± 0.20	< 0.001*
TT4 level (nmol/L)	88.36 ± 14.56	96.67 ± 16.67	0.001*
FT3 level (pmol/L)	3.74 ± 0.64	4.58 ± 0.58	< 0.001*
FT4 level (pmol/L)	16.41 ± 2.45	16.00 ± 2.15	0.249
TSH level (mIU/L)	1.46 ± 0.79	6.04 ± 4.87	< 0.001*

Data are expressed as a number with percentage for qualitative variables or mean ± standard deviation for quantitative variables. BMI, body mass index; TT3, total triiodothyronine; TT4, total thyroxine; FT3, free triiodothyronine; FT4, free thyroxine; TSH, thyroid stimulating hormone

* The correlation was significant at the 0.05 level (P < 0.05).

Patients that experienced hearing recovered were divided into the effective group (n = 30) and the ineffective group (n = 40), as shown in Table 2, the baseline characteristics of the two groups had no significant difference (all P > 0.05). There are no significant differences between the two groups in terms of the affected side, accompanying symptoms like tinnitus and ear fullness, and history of hypertension and diabetes (all P > 0.05). However, the number of patients with vertigo in the ineffective group was significantly higher than that in the effective group (P < 0.05). The time to treatment and the hearing loss level of the ineffective group were 4.95 ± 1.54 days and 82.11 ± 12.50 dBHL, respectively, and both were significantly higher than that (3.57 ± 1.98 days and 75.43 ± 12.40dBHL) in the effective group (P < 0.05).

There were no significant differences in thyroid-related hormone levels (all $P > 0.05$), however changes in TT3, TT4, FT3, and TSH levels were significantly higher in the effective group than that in the ineffective group (all $P < 0.05$).

Table 2
Demographics and laboratory variables in the moderately severe-to-profound SSNHL with different outcomes.

	Effective (n = 30)	Ineffective (n = 40)	P value
Baseline characteristics			
Age (years)	50.10 ± 16.97	51.68 ± 15.22	0.685
Sex (male, %)	15 (50.00)	23 (57.50)	0.533
Hight (cm)	168.13 ± 9.27	167.00 ± 8.45	0.596
Weight (kg)	69.12 ± 13.59	67.60 ± 12.00	0.629
BMI (kg/m^2)	24.36 ± 3.73	24.20 ± 3.71	0.860
Systolic blood pressure (mmHg)	121.70 ± 16.15	119.98 ± 17.65	0.676
Diastolic blood pressure (mmHg)	77.07 ± 9.66	75.23 ± 10.26	0.445
Clinical characteristics			
Affected side (left, %)	20 (66.67)	19 (47.50)	0.110
Tinnitus (%)	13 (43.33)	18 (45.00)	0.890
Vertigo (%)	3 (10.00)	15 (37.50)	0.009*
Ear fullness (%)	3 (10.00)	6 (15.00)	0.536
Hypertension (%)	4 (13.33)	8 (20.00)	0.464
Diabetes (%)	4 (13.33)	6 (15.00)	0.844
Time to treatment (days)	3.57 ± 1.98	4.95 ± 1.54	0.002*
Hearing level (dBHL)	75.43 ± 12.40	82.11 ± 12.50	0.030*
Laboratory variables			
TT3 level (nmol/L)	1.26 ± 0.19	1.28 ± 0.22	0.697
TT4 level (nmol/L)	89.08 ± 14.21	87.81 ± 14.98	0.722
FT3 level (pmol/L)	3.66 ± 0.60	3.79 ± 0.67	0.393
FT4 level (pmol/L)	16.48 ± 2.75	16.36 ± 2.22	0.844

Data are expressed as a number with percentage for qualitative variables or mean ± standard deviation for quantitative variables. BMI, body mass index; TT3, total triiodothyronine; TT4, total thyroxine; FT3, free triiodothyronine; FT4, free thyroxine; TSH, thyroid stimulating hormone; △, the difference of thyroid-related hormone after treatment minus that before treatment.

* The correlation was significant at the 0.05 level ($P < 0.05$).

	Effective (n = 30)	Ineffective (n = 40)	P value
TSH level (mIU/L)	1.50 ± 0.74	1.42 ± 0.83	0.653
△TT3 level (nmol/L)	0.29 ± 0.16	0.10 ± 0.39	0.006*
△TT4 level (nmol/L)	15.21 ± 18.85	5.71 ± 19.87	0.047*
△FT3 level (pmol/L)	1.00 ± 0.58	0.40 ± 0.94	0.002*
△FT4 level (pmol/L)	0.35 ± 3.13	-0.65 ± 2.93	0.174
△TSH level (mIU/L)	4.94 ± 3.21	1.92 ± 1.62	< 0.001*

Data are expressed as a number with percentage for qualitative variables or mean ± standard deviation for quantitative variables. BMI, body mass index; TT3, total triiodothyronine; TT4, total thyroxine; FT3, free triiodothyronine; FT4, free thyroxine; TSH, thyroid stimulating hormone; △, the difference of thyroid-related hormone after treatment minus that before treatment.

* The correlation was significant at the 0.05 level (P < 0.05).

3.2 Thyroid-related hormone and the occurrence of moderately severe-to-profound SSNHL

The ROC curve analysis (Fig. 1) revealed that a serum TT3 level ≤ 1.27 nmol/L (sensitivity, 84.00%; specificity, 57.14%), TT4 level ≤ 96.89 nmol/L (sensitivity, 50.001%; specificity, 75.71%), FT3 level ≤ 4.00 pmol/L (sensitivity, 86.00%; specificity, 65.71%), FT4 level ≤ 13.18 pmol/L (sensitivity, 93.00%; specificity, 12.86%), and TSH level ≤ 2.37 mIU/L (sensitivity, 80.00%; specificity, 88.57%) were the most powerful predictors of moderately severe-to-profound SSNHL. The areas under the curve were 0.737 (95% CI, 0.658–0.817), 0.636 (95% CI, 0.553–0.719), 0.837 (95% CI, 0.777–0.897), 0.458 (95% CI, 0.368–0.548), and 0.903 (95% CI, 0.858–0.948) for TT3, TT4, FT3, FT4, and TSH, respectively. FT3 and TSH levels showed good predictive efficacies for the occurrence of moderately severe-to-profound SSNHL. In the univariate logistic regression analysis, the ORs for occurrence outcome of disease with parameters are presented in Table 3. With unadjusted ORs of 0.093 (95% CI, 0.044–0.195, P < 0.05) and 0.245 (95% CI, 0.155–0.389, P < 0.05), FT3 and TSH level showed a strong association with the occurrence of moderately severe-to-profound SSNHL. After adjusting for all other significant outcome predictors, FT3 and TSH level remained independent occurrence predictors with adjusted ORs of 0.064 (95% CI, 0.016–0.255, P < 0.05) and 0.270 (95% CI, 0.157–0.462, P < 0.05).

Table 3
Binary logistic regression analysis of the relationship between thyroid-related hormone levels and the occurrence of moderately severe-to-profound SSNHL

Parameter	Univariate analysis			Multivariate analysis		
	OR	95% CI	P value	OR	95% CI	P value
Predictor: occurrence of disease						
Age	1.008	0.984–1.033	0.518			
Sex	1.142	0.618–2.105	0.673			
BMI	1.031	0.941–1.129	0.517			
Systolic blood pressure	0.984	0.962–1.007	0.162			
Diastolic blood pressure	0.988	0.958–1.019	0.446			
TT3 level	0.133	0.020–0.892	< 0.001*	5.262	0.174-158.842	0.339
TT4 level	0.966	0.946–0.987	0.002*	0.974	0.934–1.015	0.211
FT3 level	0.093	0.044–0.195	< 0.001*	0.064	0.016–0.255	< 0.001*
FT4 level	1.083	0.946–1.241	0.248			
TSH level	0.245	0.155–0.389	< 0.001*	0.270	0.157–0.462	< 0.001*

OR, odds ratio; CI, confidence interval; BMI, body mass index; TT3, total triiodothyronine; TT4, total thyroxine; FT3, free triiodothyronine; FT4, free thyroxine; TSH, thyroid stimulating hormone

* The correlation was significant at the 0.05 level (P < 0.05).

3.3 Thyroid-related hormone and the functional outcome of moderately severe-to-profound SSNHL

In the linear correlation analysis and scatterplots of the elevation of thyroid-related hormone levels versus hearing recovery (Fig. 2), an association was found between moderately severe-to-profound SSNHL and TSH when hearing loss was treated as a continuous variable. The elevation of TSH level (R = 0.707, P < 0.05) after treatment predicted a favorable outcome of hearing recovery. In the univariate logistic regression analysis, the ORs for the outcome of moderately severe-to-profound SSNHL with parameters

are presented in Table 4. With an unadjusted OR of 1.656 (95% CI, 1.267–2.165, P < 0.05), the change in TSH level showed a strong association with the treatment outcome. After adjusting for all other significant outcome predictors, the change in TSH level remained an independent outcome predictor with an adjusted OR of 1. 473 (95% CI, 1.094–1.983, P < 0.05).

Table 4 Binary logistic regression analysis of the relationship between thyroid-related hormone levels and the outcome of moderately severe-to-profound SSNHL

Parameter	Univariate analysis			Multivariate analysis		
	OR	95% CI	P value	OR	95% CI	P value
Predictor: outcome of disease						
Age	0.994	0.964-1.024	0.680			
Sex (male)	0.739	0.285-1.914	0.533			
BMI	1.012	0.889-1.151	0.858			
Systolic blood pressure	1.006	0.978-1.035	0.671			
Diastolic blood pressure	1.019	0.971-1.070	0.443			
Affected side (left)	2.211	0.829-5.893	0.113			
Tinnitus	1.070	0.412-2.777	0.890			
Vertigo	5.400	1.395-20.907	0.015*	2.850	0.607-13.392	0.185
Ear fullness	1.588	0.363-6.943	0.539			
Hypertension	1.625	0.440-6.005	0.467			
Diabetes	1.147	0.293-4.488	0.844			
Time to treatment	0.641	0.477-0.861	0.003*	0.720	0.501-1.035	0.076
Hearing level	0.958	0.921-0.997	0.034*	0.959	0.911-1.010	0.113
TT3 level	0.629	0.063-6.253	0.692			
TT4 level	1.006	0.974-1.040	0.717			
FT3 level	0.717	0.336-1.527	0.388			
FT4 level	1.021	0.840-1.241	0.836			
TSH level	1.151	0.630-2.103	0.648			
△TT3 level	7.605	1.428-40.504	0.017*	1.286	0.060-27.440	0.872
△TT4 level	1.026	1.000-1.053	0.052			
△FT3 level	2.533	1.300-4.937	0.006*	1.718	0.524-5.630	0.372
△FT4 level	1.119	0.951-1.317	0.175			
△TSH level	1.656	1.267-2.165	<0.001*	1.473	1.094-1.983	0.011*

OR, odds ratio; CI, confidence interval; BMI, body mass index; TT3, total triiodothyronine; TT4, total thyroxine; FT3, free triiodothyronine; FT4, free thyroxine; TSH, thyroid stimulating hormone

* The correlation was significant at the 0.05 level (P < 0.05).

4. Discussion

SSNHL is a common otological emergency with an increasing incidence rate worldwide. It can cause long-term hearing loss, irreversible hearing loss, and tinnitus [23, 24], which severely affect the quality of life of patients. Recently, many studies have found that hematological indices, such as routine blood parameters, serum lipid level, and coagulation function, predicted a favorable prognosis in patients with SSNHL [24–26]. Kim et al. [27] studied a large, representative population cohort found that SSNHL patients are more likely to have goiter and hypothyroidism than normal people. In addition, a large case-control study in Taiwan reported that pre-existing hypothyroidism and hyperthyroidism are associated with SSNHL susceptibility [28]. Investigating the potential relationship between hypothyroidism and SSNHL, this study is the first to show an association between thyroid-related hormone before and after treatment in patients with moderately severe-to-profound SSNHL.

4.1 Lower Thyroid-related Hormone Levels Reflects Higher Risk of Moderately severe-to-profound SSNHL

In this study, although still within normal ranges, we found that the levels of thyroid-related hormones were significantly lower in patients with moderately severe-to-profound SSNHL than those of the control group (Table 1). Analyzing the relationship between thyroid-related hormones and SSNHL through ROC curve suggests that the AUC for FT3 diagnosis of SSNHL is 0.837, with cut-off point at 4.00 pmol/L (sensitivity, 86.00%; specificity, 65.71%). In terms of TSH, diagnosis for SSNHL is 0.903, with cut-off point at 2.37 mIU/L (sensitivity, 80.00%; specificity, 88.57%). This shows that early detection of FT3 and TSH are valuable for the diagnosis of SSNHL (Fig. 1). Lower FT3 and TSH levels in the early stages of moderately severe-to-profound SSNHL were independent predictors of the occurrence of moderately severe-to-profound SSNHL (Table 3).

4.2 Ischemia and Lower Neuroprotection Contributes to the Higher Risk of Moderately severe-to-profound SSNHL

The mechanisms behind our findings may be understood from several established researches. Hypothyroidism is related to the severity of atherosclerosis risk factors (hypertension, hyperlipemia, hyperhomocysteinemia) and may be a risk factor of atherothrombotic myocardial infarction [15]. Low triiodothyronine (T3) level also plays a role in vascular diseases, including complications after brain tumor surgery, respiratory failure, and acute cardiovascular events [29–31]. Given that the blood supply of the inner ear is mainly dependent on end arterioles, the function of inner ear is greatly affected by

ischemia, and ischemia may lead to hearing loss at all frequencies when thrombosis occurs in the peripheral arterioles [32].

In regards to the association of poor outcomes of moderately severe-to-profound SSNHL with low serum thyroid hormone levels in patients, one possible mechanism is secondary neuronal damage after moderately severe-to-profound SSNHL. Wang et al. [33] reported that a decrease in TSH levels and an increase in the basal metabolic rate may lead to a higher risk of post-stroke fatigue; this could lead to the production of excess reactive oxygen species and free radicals, resulting in neurotoxicity [34]. In addition, thyroid-related hormones and their derivatives have a great influence on the repair of injured neurons [35, 36]. Sadana et al. [37] reported that T3 can reduce the infarct and oedema in a focal ischemia model. Therefore, we speculate that patients with hypothyroidism may experience lower neuroprotection and worsened secondary damage, leading to a poor outcome.

Furthermore, a growing body of research found that thyroid-related hormone levels are greatly associated with the secretion of many neurotrophic factors, including nerve growth factors [38, 39]. Therefore, we can infer that patients with hypothyroidism may experience inhibition of endogenous neuron repair systems, leading to poorer functional outcomes. The elevation of TSH levels after treatment predicted a favorable outcome of hearing recovery (Fig. 2). The increases of TT3, TT4, FT3, and TSH levels in the effective group were much higher than that in the ineffective group (Table 2) and the change of TSH level remained an independent outcome predictor (Table 4). Tamura M et al. [40] found that replacement of maintenance dose of steroid can not only improve thyroid function but also lead to a transient decrease in thyroid hormone and an increase in reverse thyroid hormone. Most patients showed an upward trend of thyroid-related hormone levels after glucocorticoid treatment. This may explain why some patients had thyroid hormone increase after glucocorticoid treatment and thus a better prognosis.

Our study has some limitations. First, being a preliminary study, the repeatability of the results needs to be verified in more prospective studies to determine their stability and effectiveness. Second, the sample size of this study was small, and the follow-up time was short. Larger studies are needed to verify our conclusion.

5. Conclusion

In summary, our study indicated that thyroid-related hormones play an important role in the clinical characteristics and outcome of moderately severe-to-profound SSNHL. During in-hospital monitoring, thyroid function testing may be important as higher levels of thyroid-related hormones have been associated with better functional outcomes. Therefore, treatment to normalize and/or elevate thyroid-related hormone levels among patients with moderately severe-to-profound SSNHL could be beneficial to their recovery. Further prospective studies with longer-term follow-up are needed to confirm our findings.

6. Abbreviations

SSNHL, sudden sensorineural hearing loss; TT3, total triiodothyronine; TT4, total thyroxine; FT3, free triiodothyronine; FT4, free thyroxine; TSH, thyroid stimulating hormone; ROC receiver operating characteristic; PTA, pure tone audiometry; body mass index (BMI); OR, odds ratio; CI, confidence intervals.

7. Declarations

7.1 Ethics approval and consent to participate

The study protocol was approved and implemented according to the ethical standards of our Hospital ethics committee [2018-KY-036(K)]. Information of patients was anonymized and deidentified prior to analysis. The progress was conducted in accordance with the spirit of the Helsinki Declaration.

7.2 Consent for publication

Written informed consent for publication was obtained from all participants.

7.3 Availability of data and materials

All of data and materials are available from the corresponding author upon reasonable ask.

7.4 Competing interests

The authors have no conflict of interest.

7.5 Funding

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7.6 Authors' contributions

Zhong Zheng, Ying Shen, Yanmei Feng, and Shankai Yin designed and supervised the research. Ying Shen, Liang Xia, Lili Xiao, Yuanyuan Sun analysed data. Hui Wang, Zhengnong Chen, Yaqin Wu, Haibo Shi, Jingchun He, Yanmei Feng, and Shankai Yin gave suggestions on the data acquisition and analysis. Zhong Zheng and Ying Shen wrote the manuscript. Yanmei Feng and Shankai Yin participated in manuscript editing. All authors reviewed the manuscript.

7.7 Acknowledgements

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Figures

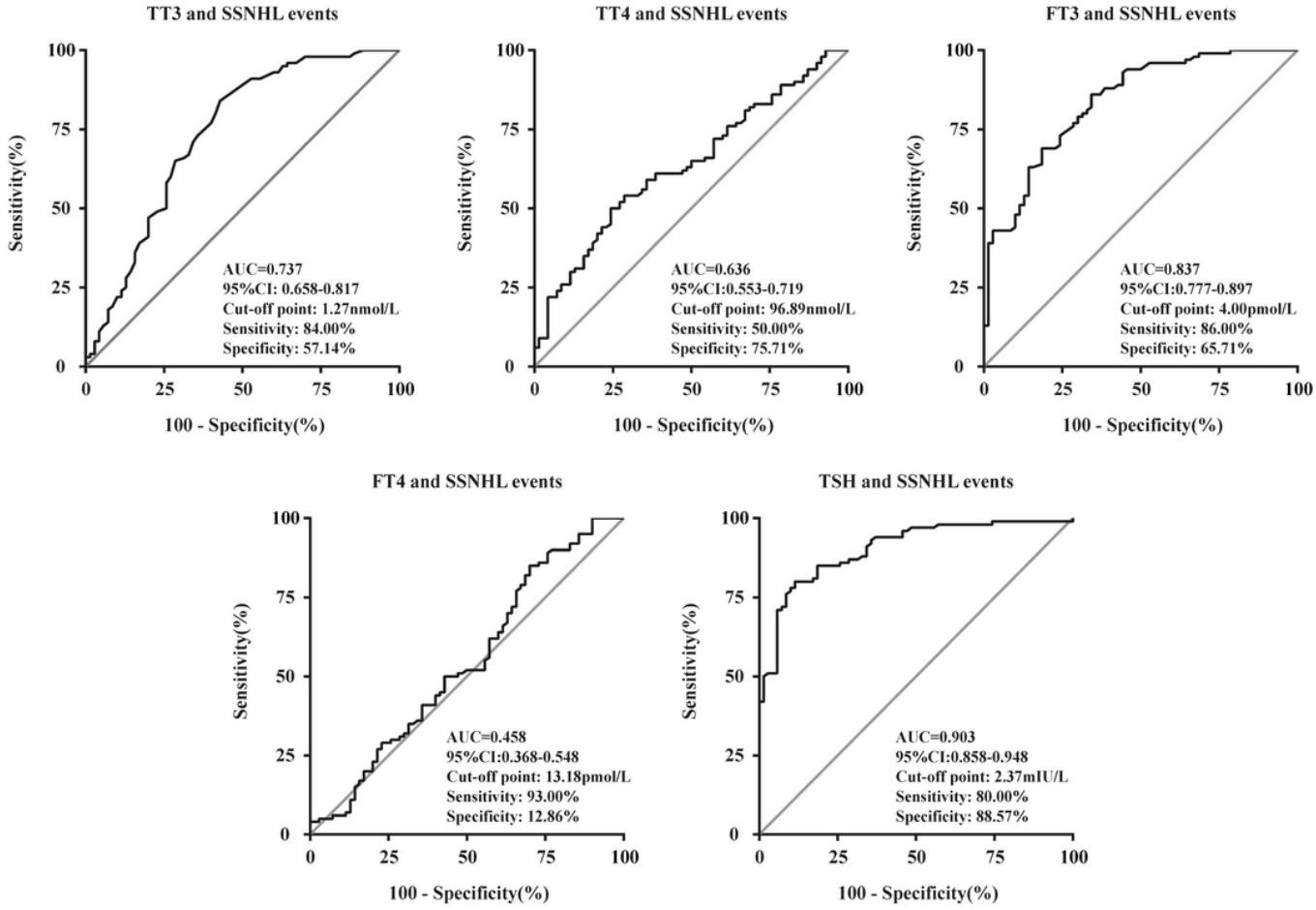

Figure 1

Receiver operating characteristic curve analysis of thyroid-related hormone levels for the prediction of the occurrence of moderately severe-to-profound SSNHL AUC, area under the curve; TT3, total triiodothyronine; TT4, total thyroxine; FT3, free triiodothyronine; FT4, free thyroxine; TSH, thyroid stimulating hormone; CI, confidence interval; SSNHL, sudden sensorineural hearing loss

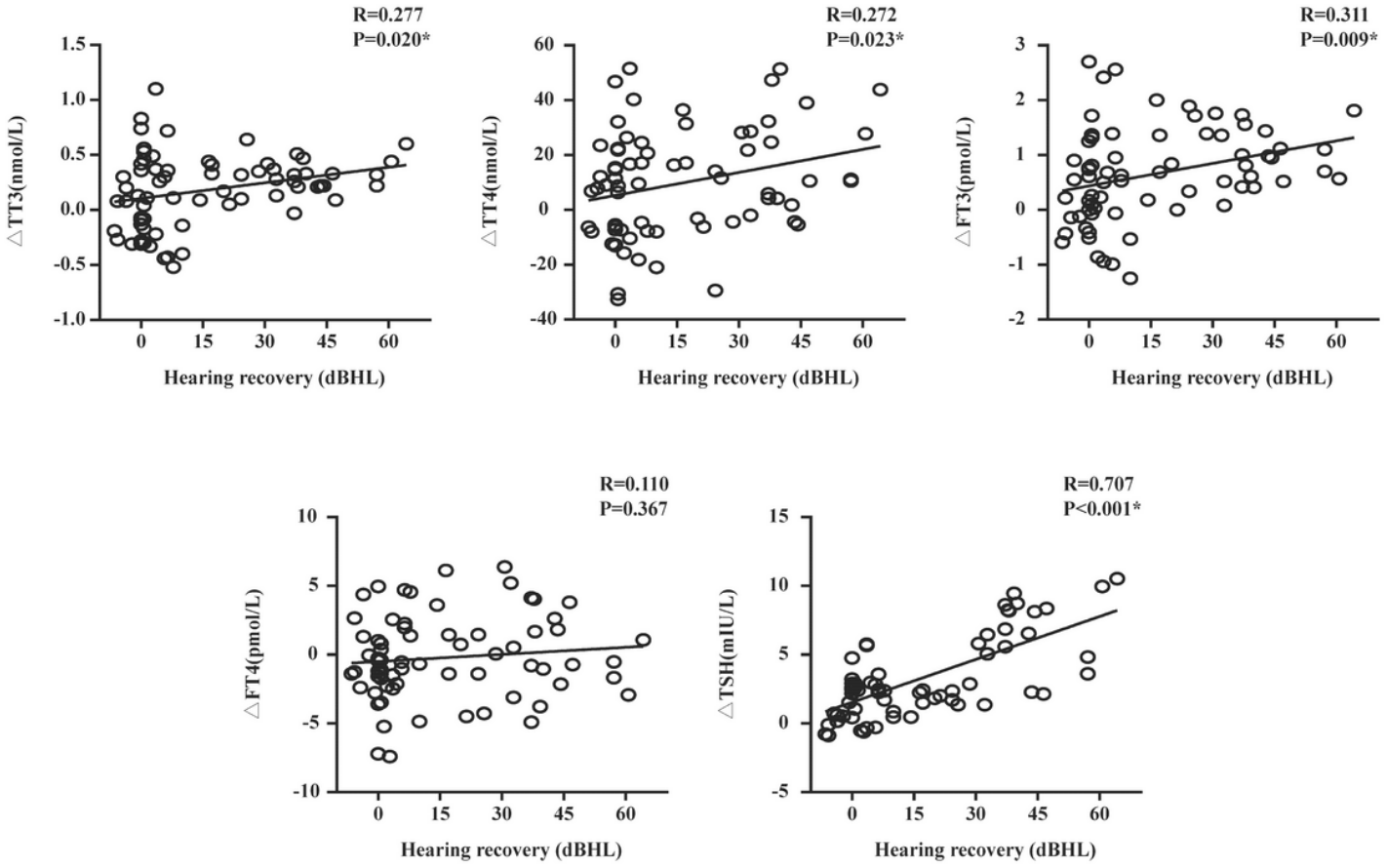

Figure 2

Plots of the change in thyroid-related hormone levels against the recovery of hearing TT3, total triiodothyronine; TT4, total thyroxine; FT3, free triiodothyronine; FT4, free thyroxine; TSH, thyroid stimulating hormone; R, correlation coefficient; △, the difference of thyroid-related hormone after treatment minus that before treatment. Data are presented as correlation coefficients and P values. * The correlation was significant at the 0.05 level ($P < 0.05$). Hearing recovery was positively correlated with the elevation of TSH levels ($R = 0.707$, $P < 0.05$)

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