Received: 27 April 2023 | Revised: 5 August 2023 | Accepted: 6 October 2023

DOI: 10.1002/lio2.1170

ORIGINAL RESEARCH

Laryngoscope Investigative Otolaryngology

Effect of statins on hearing outcome in patients with idiopathic sudden sensorineural hearing loss

Yoshihiro Nitta MD[1] | Takaomi Kurioka PhD[2] | Shogo Furuki MD[1] | Hajime Sano PhD[3] | Taku Yamashita PhD[1]

[1]Department of Otorhinolaryngology, Head and Neck Surgery, Kitasato University School of Medicine, Kanagawa, Japan

[2]Department of Otorhinolaryngology, National Defense Medical College, Saitama, Japan

[3]School of Allied Health Sciences, Kitasato University, Kanagawa, Japan

Correspondence
Yoshihiro Nitta, Department of Otorhinolaryngology, Head and Neck Surgery, Kitasato University School of Medicine, 1-15-1 Kitasato, Minami-ku, Sagamihara, Kanagawa 252-0374, Japan.
Email: n-yoshihiro@med.kitasato-u.ac.jp

Abstract

Objective: Statins have been reported to improve vascular endothelial function and microcirculation, reduce oxidative stress, and exert anti-inflammatory and protective effects against inner ear damage. Therefore, this study aimed to investigate the effect of statins on hearing prognosis in patients with idiopathic sudden sensorineural hearing loss (ISSNHL).

Methods: We reviewed the medical records of 149 patients diagnosed with ISSNHL. Clinical characteristics, hearing thresholds, statin medications, and hematological findings were investigated. First, patients with ISSNHL were assigned to the good and poor outcome groups, and factors influencing their prognosis were analyzed. Furthermore, patients with dyslipidemia were investigated to determine whether statins have therapeutic effects on ISSNHL.

Results: Significant differences in age ($p = .011$), days from the onset of ISSNHL to the initiation of treatment ($p = .04$), and hematological total cholesterol (TC; $p = .015$) between the good and poor outcome groups were observed. Furthermore, when hearing outcomes were investigated in patients with dyslipidemia, TC was significantly lower in the good outcome group ($p = .03$). Although no significant therapeutic effects of statins were observed in participants with dyslipidemia, patients in the statin-treated group were significantly older and experienced more diabetic complications than those in the non-statin-treated group.

Conclusion: Although our study showed that dyslipidemia is a poor prognostic factor for ISSNHL, statins had no significant therapeutic effects on hearing recovery in ISSNHL patients with dyslipidemia. The patients that received statin medications were significantly older and experienced more diabetic complications, which may have affected their hearing prognosis.

Level of Evidence: Level 4.

KEYWORDS

dyslipidemia, idiopathic sudden sensorineural hearing loss, prognosis, statins

1 | INTRODUCTION

Sudden sensorineural hearing loss is a sudden onset (within 72 h) hearing loss (HL) that affects 5–27 people per 100,000 in the United States annually.[1] The etiology of idiopathic sudden sensorineural HL (ISSNHL) remains unknown, and various etiologies have been proposed, including microcirculation disorders, viral infections, and autoimmunity. Approximately 1% of sudden sensorineural HL cases are reportedly caused by central intracranial lesions, 10% to 15% are caused by trauma, autoimmune diseases, and infection, whereas others are idiopathic.[2] The American Academy of Otolaryngology-Head and Neck Surgery guidelines recommend systemic corticosteroids as an adjunctive therapy within 2 weeks of ISSNHL onset, followed by intratympanic steroid therapy (ITS) as salvage treatment within 2–6 weeks of ISSNHL onset.[3] However, there is insufficient evidence for the effectiveness of using both systemic corticosteroids and ITS. To date, no effective treatment for ISSNHL exists, and there is a need to establish new promising treatments.

Statins were originally developed as 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors, and are administered in clinical practice to reduce the risk of complications, such as myocardial infarction and cerebrovascular disease in patients with dyslipidemia. Statins improve vascular endothelial function and microcirculation, have anti-inflammatory effects, and reduce oxidative stress, in addition to their inhibitory effects on HMG-CoA reductase.[4] Recently, statins were reported to exert neuroprotective effects against cerebral ischemia and stroke by targeting cell signaling pathways that control cell proliferation, adhesion, and migration; cytokine production; and reactive oxygen species generation.[5] Since various etiologies, including circulatory disturbances, inflammation, oxidative stress, and apoptosis, are involved in inner ear damage, statins may be potentially useful in treating inner ear dysfunction. Several animal studies have reported that statins protect against inner ear damage by inhibiting apoptosis and via the generation of reactive oxygen species, both of which cause inner ear damage.[6,7] However, reports on the effects of statins on human inner ear function are few, and it remains unclear whether statins are effective in treating HL due to inner ear damage. In this study, we hypothesized that statins would improve hearing in patients with ISSNHL, where inner ear damage is the main pathophysiology. This study aimed to investigate the effect of statins on hearing prognosis in patients with ISSNHL.

2 | MATERIALS AND METHODS

2.1 | Study design and materials

The Institutional Review Board of Kitasato University Hospital approved this observational retrospective study (B22-077). The need for informed consent was waived owing to the retrospective nature of the study. The clinical records of the patients who visited the outpatient clinic of the Department of Otorhinolaryngology and Head and Neck Surgery at Kitasato University Hospital between January 2015 and December 2019, and were diagnosed with ISSNHL, were examined. The inclusion criteria were patients with (1) unknown etiologies, (2) sudden onset of the disease, (3) sensorineural HL of ≥30 dB after at least three consecutive frequencies, and (4) follow-up duration longer than 3 months.[8] The exclusion criteria were as follows: (1) middle ear or retrocochlear pathology, (2) low-tone sensorineural HL, and (3) history of genetic HL or otologic surgery. The survey variables were as follows: age at onset, affected side, sex, mean hearing threshold, grade of HL, presence or absence of vertigo, history of hypertension, presence or absence of statin medication, body mass index, initiation of treatment, presence or absence of ITS, and hematological findings (HbA1c, Glucose [Glu], total cholesterol [TC], and high-density lipoprotein). Patients with TC ≥220 mg/dL or taking statins were classified as having dyslipidemia.

2.2 | Assessment of hearing function

Pure-tone audiometry was performed in a soundproof room using an audiometer (AA-78; Rion, Tokyo, Japan). Hearing thresholds were obtained through air and bone conduction measurements at frequencies of 0.25, 0.5, 1, 2, and 4 kHz. To prevent cross-hearing, sound masking was used for the non-test ear, while the other ear was tested as required. The HL grade, defined according to the Japanese Ministry of Health and Welfare guidelines,[9] was determined using the initial audiogram data (Table 1). Treatment outcome based on the criteria of the Japanese Ministry of Health and Welfare Research Group[10] was determined using audiogram data 3 months after the commencement of treatment (Table 2). A good outcome was defined as complete

TABLE 1 Criteria for the grading of HL in ISSHL.

Grade	Criteria
1	PTA <40 dB
2	40 dB ≤PTA <60 dB
3	60 dB ≤PTA <90 dB
4	90 dB ≤PTA

Note: PTA: arithmetic mean of the five frequencies. The five frequencies used were 250, 500, 1000, 2000, and 4000 Hz.
Abbreviations: HL, hearing loss; ISSHL, idiopathic sudden sensorineural hearing loss.

TABLE 2 Hearing improvement as defined by the Ministry of Health and Welfare in Japan.

Complete recovery	All five frequencies of the final audiogram were ≤20 dB or an improvement to the same degree of hearing as in the unaffected ear
Marked improvement	PTA improvement > 30 dB
Slight improvement	10 dB < PTA improvement < 30 dB
No change	PTA improvement < 10 dB

Note: PTA: arithmetic mean of the five frequencies. The five frequencies used were 250, 500, 1000, 2000, and 4000 Hz.

recovery or marked improvement, whereas a poor outcome was defined as slight improvement or no change (Table 2).

2.3 | Treatment

Patients were treated with systemic corticosteroids for 10 days (betamethasone 8 mg via intramuscular injection on the first day followed by betamethasone 4 mg via oral administration for the first 3 days, tapered to 2 mg for another 3 days, and finally to 1 mg for the last 3 days). Oral administration of vitamin B12 (1.5 mg daily) and adenosine triphosphate (300 mg daily) was initiated concurrently with the corticosteroids on the first day of treatment. Forty one patients underwent ITS as salvage therapy after systemic corticosteroids. Patients with HL of ≥grade 3 underwent ITS as salvage therapy for the initial steroid therapy. Local xylocaine (lidocaine hydrochloride, 40 mg/mL; Sandoz, Japan) was administered as local anesthesia after observing the tympanic membrane of the participant's ear at a sitting position. One puncture was made in the anterior tympanic membrane using a 26-gauge needle, and 0.3–0.4 mL of dexamethasone disodium phosphate (3.3 mg/mL, Sandoz, Japan) was injected while the participant was in the sitting position. After the injection, the patients were instructed not to make swallowing movements, and their heads were tilted 45° to the healthy side for 30 min in the supine position. ITS was administered once daily for three consecutive days.

2.4 | Statistical analyses

For statistical analysis of the prognostic factors, univariate analysis was performed using Fisher's exact test or Mann–Whitney *U* test. We used the chi-squared test to evaluate the clinical characteristics and possible prognostic factors. Parameters that were statistically significant in the univariate analysis were entered into a binary logistic regression model for multivariate analysis. All statistical analyses were performed using the JMP PRO 16 software (SAS Institute, Cary, NC, USA). All data are presented as standard errors, and the significance level was set at $p < .05$.

3 | RESULTS

3.1 | Prognostic factors for ISSNHL

Overall, 149 participants (83 men and 66 women) were enrolled in this study, of which 41 underwent ITS as salvage therapy after systemic corticosteroids. The mean age of the participants was 57.5 ± 16.4 years, and none of the patients discontinued corticosteroid treatment owing to serious complications. Of the 149 patients, 29 (19.5%) were taking statins, including atorvastatin, rosuvastatin, pitavastatin, and pravastatin, as shown in the Table S1. Statin type did not significantly affect therapeutic outcomes ($p = .028$).

First, to investigate the prognostic factors for ISSNHL, the patients were assigned to good (65 patients) and poor (84 patients) outcome groups, and univariate analyses were performed for each variable (Table 3). Univariate analysis showed that age ($p = .0068$), days from onset to start of treatment ($p = .028$), and TC ($p = .0054$) were significantly different between the two groups; however, no significant difference in the statin medication ($p = .84$) was observed between the two groups. Multivariate analysis showed significant differences in age ($p = .011$) and TC ($p = .015$), suggesting that being older and having dyslipidemia with high TC were independent poor prognostic factors for ISSNHL.

TABLE 3 Prognostic factors for ISSHL.

	Good outcomes ($n = 65$)	Poor outcomes ($n = 84$)	*p*	
			Univariate	Multivariate
Age (years)	53.4 ± 16.7	60.7 ± 15.5	.0068	.011
Affected side (right/left)	31/34	48/36	.32	
Sex (male/female)	27/38	39/45	.62	
Initial grade of HL (1,2,3/4)	42/23	57/27	.73	
Vertigo (+/−)	29/36	35/49	0.74	
Hypertension (+/−)	18/47	29/55	.48	
Statin use (+/−)	12/53	17/67	.84	
BMI (kg/m^2)	24.3 ± 4.5	23.4 ± 4.1	.28	
ITS (+/−)	20/45	21/63	.46	
Initiation of treatment (days)	3.6 ± 2.3	5.4 ± 7.0	.028	.26
Hematological findings				
HbA1c (%)	6.01 ± 0.93	5.94 ± 0.77	.36	
Glu (mg/dL)	130 ± 50.6	120 ± 26.4	.13	
TC (mg/dL)	203 ± 32.4	222 ± 42.4	.0054	.015
HDL (mg/dL)	63.9 ± 18.1	66.0 ± 18.6	.53	

Abbreviations: BMI: body mass index; Glu: glucose; HDL: high-density lipoprotein; ISSHL, idiopathic sudden sensorineural hearing loss; ITS: intratympanic steroid therapy; TC: total cholesterol.

TABLE 4 Prognostic factors for ISSHL in patients with dyslipidemia.

	Good outcomes ($n = 26$)	Poor outcomes ($n = 42$)	p
Age (years)	58.5 ± 12.7	63.1 ± 12.5	.15
Affected side (Right/Left)	16/10	17/25	.13
Sex (male/female)	14/12	14/28	.13
Initial grade of HL (1,2,3/4)	20/6	30/12	.78
Vertigo (+/−)	10/16	15/27	1.00
Hypertension (+/−)	8/18	17/25	.45
Statin use (+/−)	12/14	17/25	.80
BMI (kg/m^2)	24.5 ± 4.7	24.4 ± 4.8	.91
ITS (+/−)	6/20	12/30	.78
Hematological findings			
HbA1c (%)	5.95 ± 0.83	6.15 ± 0.82	.32
Glu (mg/dL)	124 ± 23.5	123 ± 26.8	.90
TC (mg/dL)	222.9 ± 35.7	243.5 ± 39.0	.029
HDL (mg/dL)	65.1 ± 18.7	70.0 ± 16.1	.25

Abbreviations: BMI: body mass index; Glu: glucose; HDL: high-density lipoprotein; ISSHL, idiopathic sudden sensorineural hearing loss; ITS: intratympanic steroid therapy; TC: total cholesterol.

3.2 | Prognostic factors for ISSNHL in patients with dyslipidemia

As our results indicate that dyslipidemia may be a poor prognostic factor for ISSNHL, the hearing outcome in the statin-treated group may be poorer than that in the non-statin-treated group due to the effect of dyslipidemia. Sixty eight patients with dyslipidemia, including those with TC ≥220 mg/dL or those taking statin medication, were assigned to good (26 patients) and poor (42 patients) outcome groups, and univariate analysis was performed for each variable (Table 4). Only TC differed significantly between the two groups ($p = .029$), suggesting that high TC may be a poor prognostic factor for ISSNHL in patients with dyslipidemia. However, no significant difference in statin medication was observed between the two groups.

3.3 | Effect of statins on hearing outcomes in patients with ISSNHL

The 68 patients with dyslipidemia were further assigned to the statin-treated (29 patients) and non-statin-treated (39 patients) groups, and univariate analyses were performed for each variable. Although there were significant differences in age ($p = .0010$), HbA1c ($p = .0045$), Glu ($p = .0033$), and TC ($p < .0001$), no significant difference was observed in hearing outcome ($p = .80$) between the two groups (Table 5).

4 | DISCUSSION

In this study, we investigated the effect of statins on hearing prognosis in patients with ISSNHL. Summarily, dyslipidemia may be a poor prognostic factor for ISSNHL. However, no significant therapeutic effect of statins was observed. If dyslipidemia can be improved by statin therapy, it may indirectly improve hearing prognosis.

The cause and pathophysiology of ISSNHL remain unknown, and no standard treatment has been established. Impaired blood circulation is an important pathophysiological feature of ISSNHL. This is because the cochlea is supplied with blood from the labyrinthine artery, which does not have a collateral blood supply,[11] and any interruption of blood supply due to thrombosis or bleeding may easily cause inner ear ischemic damage, resulting in irreversible sensorineural HL. Diabetes, hyperlipidemia, and aging are well-known factors contributing to microvascular and circulatory disturbances, and contribute to the incidence and prognosis of ISSNHL.[12] In addition, inflammatory cytokines may be involved in the pathophysiology of ISSNHL, indicating that corticosteroid therapy could inhibit the inflammatory-induced cell death cascade in the cochlea.[13] Drug therapy with vasodilators, steroids, plasma expanders, and anticoagulants improves blood circulation, increases oxygen supply to the inner ear, and controls inner ear inflammation.[14] Steroid therapy is a standard treatment used worldwide, and there are increasing reports on the effectiveness of ITS as a salvage treatment.[15,16] The therapeutic effects of steroids are limited in clinical settings, and there is a need to develop new treatment methods.

In this study, the analysis of prognostic factors for ISSNHL showed that age, treatment initiation time, and TC level were potentially useful prognostic factors. Consistent with our results, prognostic factors for ISSNHL have been previously reported to include age, concomitant dizziness, degree of HL, diabetic complications, and time from the onset of ISSNHL to treatment initiation.[17]

Regarding age, a study comparing 55 elderly and 55 younger patients with ISSNHL reported that the recovery rate among elderly patients was significantly lower than that among younger patients.[18] Furthermore, elderly patients with normal hearing in the healthy ear had a higher recovery rate than those with HL. Elderly patients are

TABLE 5 Effect of statins on hearing prognosis in ISSHL.

	Statin user group ($n = 29$)	No statin user group ($n = 39$)	p
Age (years)	67.0 ± 10.5	57.2 ± 12.6	.0010
Affected side (Right/Left)	15/14	18/21	.81
Sex (male/female)	11/18	17/22	.81
Initial grade of HL (1,2,3/4)	21/8	29/10	1.00
Vertigo (+/−)	13/16	12/27	.31
Initiation of treatment (days)	4.4 ± 3.9	4.4 ± 6.9	.98
Hearing prognosis (good/poor)	12/17	14/25	.80
BMI (kg/m^2)	24 ± 5.1	24.9 ± 4.4	.52
ITS (+/−)	9/20	9/30	.58
Healthy hearing level (dB)	26.0 ± 20.0	19.6 ± 12.6	.10
Hematological findings			
HbA1c (%)	6.4 ± 1.0	5.8 ± 0.57	.0045
Glu (mg/dL)	134.0 ± 32.4	116.2 ± 15.4	.0033
TC (mg/dL)	210.2 ± 35.6	253.7 ± 30.2	<.0001
HDL (mg/dL)	68.1 ± 14.1	68.1 ± 19.3	.10

Abbreviations: BMI, body mass index; Glu, glucose; HDL, high-density lipoprotein; HL, hearing loss; ISSNHL, idiopathic sudden sensorineural hearing loss; ITS, intratympanic steroid therapy; TC, total cholesterol.

more likely to have systemic diseases, such as diabetes, hypertension, and dyslipidemia, than younger patients,[19,20] and microcirculatory disturbances may worsen the recovery rate of ISSNHL.

Regarding TC, plasma cholesterol and low-density lipoprotein (LDL) levels were significantly higher in patients with ISSNHL than in participants with normal hearing.[21] In addition, a study that compared 39 patients with ISSNHL to 44 healthy individuals reported that patients with metabolic syndrome were more likely to have ISSNHL and that the recovery rate of ISSNHL correlated negatively with metabolic syndrome.[22] Furthermore, a study comparing fibrinogen/LDL apheresis to standard therapy in patients with ISSNHL and high plasma fibrinogen levels reported a significant improvement in speech discrimination in the fibrinogen/LDL apheresis group.[23] Endothelial function is impaired in the peripheral arteries in patients with dyslipidemia, which may result in impaired blood perfusion in the cochlea. In the cochlea without a collateral blood supply, impaired blood circulation may worsen ISSNHL prognosis by preventing oxygenation to the inner ear and therapeutic agents from reaching the damaged tissue.

In animal and human models, statins exert therapeutic effects on cerebral and heart ischemic diseases by improving vascular endothelial function, microcirculation, and inflammation, and reducing oxidative stress. In addition, an animal study reported that aminoglycoside-induced cochlear hair cell death was prevented by treatment with statins, which enhanced the phosphorylation of the phosphatidylinositol 3-kinase/Akt signal pathway, an intracellular signal that promotes cell survival.[24] In addition, statins protect against cochlear damage, including cochlear hair cells and spiral ganglion neurons, by inhibiting the generation of poly ADP-ribose polymerase, poly ADP-ribose, caspase 3, and reactive oxygen species in the cochlea.[6,7] Furthermore, mice with age-related HL fed with a diet containing statins for 2 months showed significantly improved response thresholds in distortion-product otoacoustic emission compared to non-treated mice, indicating the preserved function of the outer hair cells.[25] In humans, a recent study demonstrated that statins can reduce cisplatin ototoxicity, resulting in improved hearing thresholds after cisplatin treatment.[7] In addition, in a cohort study of a population aged ≥40 years (514,866 individuals), patients with a history of statin treatment showed a significant decrease in the prevalence of hearing impairment among the elderly compared to the non-statin treatment group.[26] However, the therapeutic effects of statins on ISSNHL in humans have not been investigated. To our knowledge, this is the first study to investigate the effects of statins on hearing prognosis in patients with ISSNHL. Our results showed that a high TC level was a poor prognostic factor for ISSNHL; however, hearing outcomes were not significantly different between the statin-and non-statin-treated groups (Table 5). Patients in the statin-treated group were significantly older and experienced more diabetic complications than those in the non-statin-treated group. As diabetes worsens the prognosis of ISSNHL,[27] it may have influenced hearing outcomes in the patients in the statin-treated group.

The results of this study provide important information on the prognosis, treatment, and prevention of ISSNHL in patients with dyslipidemia. However, this study had some limitations. It was difficult to investigate the severity of dyslipidemia, circumstances that led to the use of statins, and duration of the disease based on clinical records; therefore, it was impossible to consider the effects of the above factors. Furthermore, the effects of statins on participants with normal lipid levels remain unclear. It is also unclear whether oral statins can prevent the onset of ISSNHL. Further detailed large-scale studies on the effects of statins in patients with ISSNHL are needed.

5 | CONCLUSION

In this study, a high TC level was a poor prognostic factor for ISSNHL, suggesting that the prevention and treatment of dyslipidemia may contribute to improved prognosis. In addition, TC levels were significantly lower in patients with dyslipidemia treated with statins than in those not treated with statins; however, significant improvement in hearing outcome was observed between the two groups. Participants in the statin-treated group were significantly older and experienced more diabetic complications, which may have affected hearing prognosis and should be further investigated.

ACKNOWLEDGMENTS

We would like to thank Editage (www.editage.com) for English language editing.

FUNDING INFORMATION

The authors received no financial support.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest associated with this manuscript.

ORCID

Yoshihiro Nitta https://orcid.org/0000-0003-4260-4673
Takaomi Kurioka https://orcid.org/0000-0001-6273-8527

REFERENCES

1. Byl FM Jr. Sudden hearing loss: eight years' experience and suggested prognostic table. *Laryngoscope*. 1984;94(5 Pt 1):647-661.
2. Rauch SD. Clinical practice. Idiopathic sudden sensorineural hearing loss. *N Engl J Med*. 2008;359(8):833-840.
3. Chandrasekhar SS, Tsai Do BS, Schwartz SR, et al. Clinical practice guideline: sudden hearing loss (update). *Otolaryngol Head Neck Surg*. 2019;161(1 suppl):S1-S45.
4. Liao JK, Laufs U. Pleiotropic effects of statins. *Annu Rev Pharmacol Toxicol*. 2005;45:89-118.
5. Vaughan CJ, Delanty N. Neuroprotective properties of statins in cerebral ischemia and stroke. *Stroke*. 1999;30(9):1969-1973.
6. Lee CH, Jeon J, Lee SM, Kim SY. Pravastatin administration alleviates kanamycin-induced cochlear injury and hearing loss. *Int J Mol Sci*. 2022;23(9):4524.
7. Park JS, Kim SW, Park K, Choung YH, Jou I, Park SM. Pravastatin attenuates noise-induced cochlear injury in mice. *Neuroscience*. 2012; 208:123-132.
8. Kurioka T, Sano H, Furuki S, Yamashita T. Iron deficiency is associated with poor prognosis in idiopathic sudden sensorineural hearing loss. *J Laryngol Otol*. 2021;135(6):508-512.
9. Furuhashi A, Matsuda K, Asahi K, Nakashima T. Sudden deafness: long-term follow-up and recurrence. *Clin Otolaryngol Allied Sci*. 2002; 27(6):458-463.
10. Kanzaki J, Taiji H, Ogawa K. Evaluation of hearing recovery and efficacy of steroid treatment in sudden deafness. *Acta Otolaryngol Suppl*. 1988;456:31-36.
11. Quaranta N, De Ceglie V, D'Elia A. Endothelial dysfunction in idiopathic sudden sensorineural hearing loss: a review. *Audiol Res*. 2016;6(1):151.
12. Nagaoka J, Anjos MF, Takata TT, Chaim RM, Barros F, Penido NO. Idiopathic sudden sensorineural hearing loss: evolution in the presence of hypertension, diabetes mellitus and dyslipidemias. *Braz J Otorhinolaryngol*. 2010;76(3):363-369.
13. Yoon SH, Kim ME, Kim HY, Lee JS, Jang CH. Inflammatory cytokines and mononuclear cells in sudden sensorineural hearing loss. *J Laryngol Otol*. 2019;133(2):95-101.
14. Ahmadzai N, Kilty S, Cheng W, et al. A systematic review and network meta-analysis of existing pharmacologic therapies in patients with idiopathic sudden sensorineural hearing loss. *PLoS One*. 2019; 14(9):e0221713.
15. Lee JB, Choi SJ, Park K, Park HY, Choo OS, Choung YH. The efficiency of intratympanic dexamethasone injection as a sequential treatment after initial systemic steroid therapy for sudden sensorineural hearing loss. *Eur Arch Otorhinolaryngol*. 2011; 268(6):833-839.
16. Li P, Zeng XL, Ye J, Yang QT, Zhang GH, Li Y. Intratympanic methylprednisolone improves hearing function in refractory sudden sensorineural hearing loss: a control study. *Audiol Neurootol*. 2011;16(3): 198-202.
17. Kim JY, Han JJ, Sunwoo WS, et al. Sudden sensorineural hearing loss in children and adolescents: clinical characteristics and age-related prognosis. *Auris Nasus Larynx*. 2018;45(3):447-455.
18. Huafeng Y, Hongqin W, Wenna Z, Yuan L, Peng X. Clinical characteristics and prognosis of elderly patients with idiopathic sudden sensorineural hearing loss. *Acta Otolaryngol*. 2019;139(10): 866-869.
19. Lionakis N, Mendrinos D, Sanidas E, Favatas G, Georgopoulou M. Hypertension in the elderly. *World J Cardiol*. 2012;4(5):135-147.
20. Kirkman MS, Briscoe VJ, Clark N, et al. Diabetes in older adults. *Diabetes Care*. 2012;35(12):2650-2664.
21. Oreskovic Z, Shejbal D, Bicanic G, Kekic B. Influence of lipoproteins and fibrinogen on pathogenesis of sudden sensorineural hearing loss. *J Laryngol Otol*. 2011;125(3):258-261.
22. Rinaldi M, Cavallaro G, Cariello M, Scialpi N, Quaranta N. Metabolic syndrome and idiopathic sudden sensori-neural hearing loss. *PLoS One*. 2020;15(8):e0238351.
23. Suckfull M, Hearing Loss Study G. Fibrinogen and LDL apheresis in treatment of sudden hearing loss: a randomised multicentre trial. *Lancet*. 2002;360(9348):1811-1817.
24. Brand Y, Setz C, Levano S, et al. Simvastatin protects auditory hair cells from gentamicin-induced toxicity and activates Akt signaling in vitro. *BMC Neurosci*. 2011;12:114.
25. Syka J, Ouda L, Nachtigal P, et al. Atorvastatin slows down the deterioration of inner ear function with age in mice. *Neurosci Lett*. 2007; 411(2):112-116.
26. Kim SY, Lee CH, Min C, Yoo DM, Choi HG. Association between statin medication and hearing impairment in a national health screening cohort. *Sci Rep*. 2021;11(1):14388.
27. Weng SF, Chen YS, Hsu CJ, Tseng FY. Clinical features of sudden sensorineural hearing loss in diabetic patients. *Laryngoscope*. 2005; 115(9):1676-1680.

SUPPORTING INFORMATION

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

How to cite this article: Nitta Y, Kurioka T, Furuki S, Sano H, Yamashita T. Effect of statins on hearing outcome in patients with idiopathic sudden sensorineural hearing loss. *Laryngoscope Investigative Otolaryngology*. 2023;8(6): 1631-1636. doi:10.1002/lio2.1170