Am J Otolaryngol 40 (2019) 573–576

Contents lists available at ScienceDirect

Am J Otolaryngol

journal homepage: www.elsevier.com/locate/amjoto

Impact of metabolic syndrome on recovery of idiopathic sudden sensorineural hearing loss

Yilong Zhou, Shuyao Qiu, Dabo Liu*

Department of Pediatric Otolaryngology, Shenzhen Hospital of Southern Medical University, Shenzhen, Guangdong 518100, PR China

ARTICLE INFO

Keywords:
Idiopathic sudden sensorineural hearing loss
Metabolic syndrome
Prognostic factors

ABSTRACT

Purpose: Metabolic syndrome (MetS) was reported to a risk factor of developing idiopathic sudden sensorineural hearing loss (ISSNHL), but limited data exist on its effect on the recovery.

The purpose of this study was to evaluate the impact of (MetS) and its components on recovery of patients with ISSNHL.

Material and methods: 228 ISSNHL patients were divided into MetS group and Non-MetS group according to the diagnostic criteria of MetS, and demographic and clinical characteristics and hearing recovery were reviewed between two groups.

Results: In total, 86 (37.7%) patients in MetS group, and 142 (62.3%) patients in Non-MetS group. The rate of hypertension, diabetes mellitus, low HDL-C, high TG and obesity were significantly higher in the MetS group than those in the Non-MetS group ($P < 0.05$). The complete recovery rate and partial recovery rate were significantly lower in the MetS group than those in the Non-MetS group. According to the multivariate analysis, MetS was significantly associated with a poor prognosis; high initial hearing threshold and presence of diabetes mellitus were correlated with a poor prognosis ($P < 0.05$).

Conclusions: These results suggest that MetS has a negative impact on the hearing recovery of ISSNHL. High initial hearing threshold and diabetes mellitus were indictors of a poor prognosis of ISSNHL.

1. Introduction

Idiopathic sudden sensorineural hearing loss (ISSNHL) is generally defined as a loss > 30 dB of hearing sensitivity across three contiguous frequencies occurring within 72 h [1]. The exact pathophysiology of ISSNHL remains unidentifiable and several etiological factors have been proposed including viral infection, trauma and vascular disorders [2], among these etiologies, vascular risk factors appeared to have an important role in the development of ISSNHL including hypertension, diabetes mellitus, obesity, hypercholesterolemia and smoking [3–6], however, the evidence for a relationship between vascular risk factors and ISSNHL is limited.

Metabolic syndrome (MetS) is a cluster of metabolic dysfunctions including hypertension, central obesity, diabetes and dyslipidemia, its prevalence is increasing at a dramatic rate as a result of the obesity epidemic and aging population [7]. Numerous published studies reported that MetS was associated with an increased risk of various clinical diseases including stroke, myocardial infarction, cardiovascular disease mortality and cancer [8,9], but the relationship between MetS and ISSNHL is less investigated. To identify the impact of MetS and its components on recovery among patients with ISSNHL, a retrospective cohort study was conducted.

2. Materials and methods

2.1. Patients and setting

We reviewed the medical records of 228 patients with ISSNHL in our department between January 2014 and August 2018 in our retrospective data analysis. ISSNHL was diagnosed by pure tone audiometry according to diagnostic criteria, and all patients underwent general otolaryngological examination, and blood tests for the components of MetS. We excluded following patients: sudden hearing loss caused by a identified etiology, such as acoustic trauma history, Meniere's disease, exposure to ototoxic medications; previous surgery in the affected ear; age < 18 years; treatment delay time > 14 days; bilateral hearing loss. All patients got a series of standard ISSNHL treatments in our department including oral prednisolone (1 mg/kg for 3 days, tapered down over the following 7 days), blood flowing promoting agents (20 μg alprostadil +100 mL normal saline, intravenous for 10 days) and

* Corresponding author.
E-mail address: daboliuent@126.com (D. Liu).

https://doi.org/10.1016/j.amjoto.2019.05.011
Received 26 February 2019

hyperbaric oxygen therapy (60 min a day for 10 days).

2.2. Audiologic evaluation and hearing improvement assessment

The audiograms were categorized into four patterns as previous study: ascending, descending, flat and profound [2]. Pure tone average was performed when ISSNHL was diagnosed to determine the initial hearing threshold and performed again 1 month after treatment to assess the hearing improvement. We followed the Siegel's criteria [10]: Complete recovery was considered as “final hearing level is better than 25dB”. Patients who showed > 15 dB hearing gain and whose final hearing level is between 25 and 45 dB was defined as “partial recovery”. “Slight recovery” meant a final hearing level over 45 dB with hearing gain > 15 dB. Patients who showed < 15 dB gain was “no improvement”. In this study, we defined complete recovery and partial recovery as “recovered”, and the last two were considered as “no recovered”.

2.3. Definition of MetS

MetS was defined according to National Cholesterol Education Programme Adult Treatment Panel III (NCEP ATP III) [11] including hyperglycemia, hypertriglyceridemia, low HDL-C level and hypertension, and 1 criterion for obesity, determined by BMI according to the American Association of Clinical Endocrinologists (AACE) guidelines [12]. Subjects with MetS must fulfill more than three of following criteria: 1) blood pressure > 130/85 mmHg, 2) TG level > 150 mg/dL, 3) HDL-C level < 40 mg/dL in males and < 50 mg/dL in females, (4) fasting plasma glucose level > 110 mg/dL and (5) BMI > 25 kg/m^2. 228 patients were divided into the MetS group and Non-MetS group according to the above diagnostic criteria.

2.4. Statistical analysis

All statistical analysis was performed using SPSS version 19.0. Continuous variables were statistically analyzed with Student *t*-tests, and Chi-square tests or Fisher's exact tests were performed in categorical variables. Variables that were statistically significant in the univariate analysis were included in the multivariate analysis. $P < 0.05$ was considered statistically significant.

3. Results

Of the 228 patients with ISSNHL, 86 were in the MetS group and 142 in the Non-MetS. The rate of hypertension, diabetes mellitus, low HDL-C, high TG and obesity were significantly higher in the MetS group than those in the Non-MetS group ($P < 0.05$), but there was no significant difference in sex ratio, age, location, treatment delay time, initial hearing threshold, rate of tinnitus, vertigo and smoking and audiogram patterns ($P > 0.05$) (Table 1).

The hearing recovery after treatment in each group was shown in Table 2. The complete recovery and partial recovery rate of the MetS group were significantly lower than those in the Non-MetS group ($P < 0.05$), and the no recovery rate was significantly higher than that in the Non-MetS group ($P < 0.05$). Based on treatment outcomes, all patients were divided into two groups: recovered group and no recovered group. Variables with a P value < 0.05 in the Table 3 were included in the multivariate analysis. According to the multivariate analysis, MetS was significantly correlated with a poor prognosis (OR = 2.672, $P = 0.009$), high initial hearing threshold and presence of diabetes mellitus were associated with a poor prognosis ($P < 0.05$) (Table 4).

4. Discussion

Accordingly, MetS is becoming a worldwide medical and public health challenge with its prevalence increasing over the years [13]. MetS is a cluster of cardiovascular risk factors shown to increase the risk of developing various clinical diseases, as well as ISSNHL [4]. Most publications just reported the association between individual components of MetS and ISSNHL, only Chien et al. [4] reported that patients with MetS had a 3.54-fold increased risk for suffering ISSNHL compared with those without MetS, [3,5,6]. In our study, we try to exam the effects of MetS and its individual components on the hearing recovery of ISSNHL after treatment.

Searching the literature, there is a lack of sufficient studies reporting the negative effect of MetS on the prognosis of ISSNHL. A prior publication reported that MetS was a risk factor for developing ISSNHL, but it failed to observe its effect on the recovery prognosis [4]. In the present research, we found that recovered rate was significantly lower in the MetS group than that in the Non-MetS group, additionally, the multivariate analysis results showed that MetS was significantly correlated with a poor prognosis. The mechanism by which MetS causes ISSNHL and affects its prognosis remains unclear. MetS is a condition involving several metabolic dysfunctions including hypertension, dyslipidemia, obesity and hyperglycemia, the insulin resistance is thought to be the primary cause of MetS and it can induce lipid accumulation, when adipocytes become larger, they will release fatty acids and adipokines which can lead to the lipotoxicity of blood vessels, following

Table 1
Demographic characteristics of patients with ISSNHL included in the study.

	Overall (n = 228)	MetS (n = 86)	Non-MetS (n = 142)	*P*
Male: female (n)	120:108	46:40	74:68	0.840
Age, yr	43.9 ± 13.3	42.3 ± 13.3	44.4 ± 12.9	0.201
Right: left	114:114	42:44	72:70	0.785
Treatment delay time, d	7.5 ± 4.6	8.2 ± 4.3	7.1 ± 4.8	0.079
Initial hearing threshold, dB	67.1 ± 13.6	69.6 ± 14.2	63.5 ± 13.2	0.157
Tinnitus (%)	171 (75.0)	70 (81.4)	101 (71.1)	0.083
Vertigo (%)	61 (26.8)	27 (31.4)	34 (23.9)	0.218
Smoking (%)	55 (24.1)	20 (23.3)	35 (24.6)	0.812
Hypertension (%)	66 (28.9)	44 (51.2)	22 (15.5)	0.000*
Diabetes mellitus (%)	42 (18.4)	26 (30.2)	16 (11.3)	0.000*
Low HDL-C (%)	73 (32.0)	46 (53.5)	27 (19.0)	0.000*
High TG (%)	56 (24.6)	38 (44.2)	18 (12.7)	0.000*
Obesity (%)	75 (32.9)	49 (57.0)	26 (18.3)	0.000*
Audiogram patterns				0.084
Ascending (%)	46 (20.2)	17 (19.8)	29 (20.4)	
Descending (%)	29 (12.7)	5 (5.8)	24 (16.9)	
Flat (%)	58 (25.4)	26 (30.2)	32 (22.5)	
Profound (%)	95 (41.7)	38 (44.2)	57 (40.1)	

MetS = metabolic syndrome; ISSNHL = idiopathic sudden sensorineural hearing loss.
HDL-C = high-density lipoprotein cholesterol; TG = triglyceride.
* $P < 0.05$.

Table 2
Recovery of ISSNHL according Siegel's criteria.

	Overall (n = 228)	MetS (n = 86)	Non-Mets (n = 142)	*P*
Complete recovery (%)	46 (20.2)	11 (12.8)	35 (27.8)	0.031*
Partial recovery (%)	39 (17.1)	9 (10.5)	32 (24.7)	0.021*
Slight recovery (%)	70 (30.7)	30 (34.9)	40 (25.3)	0.287
No recovery (%)	73 (32.0)	36 (44.2)	35 (22.2)	0.007*

ISSNHL = idiopathic sudden sensorineural hearing loss; MetS = metabolic syndrome.
HDL-C = high-density lipoprotein cholesterol; TG = triglyceride.
* $P < 0.05$.

Table 3
Factors influencing the recovery after the treatment of ISSNHL.

	Recovered (n = 85)	No recovered (n = 143)	*P*
Male: female (n)	45:40	75:68	0.942
Age, yr	42.1 ± 12.9	45.0 ± 13.4	0.103
Right: left	40:45	74:69	0.493
Treatment delay time, d	7.1 ± 4.7	7.7 ± 4.5	0.385
Initial hearing threshold, dB	57.2 ± 11.2	70.5 ± 12.9	0.007*
Tinnitus (%)	58 (68.2)	113 (79.0)	0.069
Vertigo (%)	17 (20.0)	44 (30.8)	0.076
Smoking (%)	18 (21.2)	37 (23.8)	0.423
Hypertension (%)	24 (28.2)	42 (29.4)	0.855
Diabetes mellitus (%)	7 (8.2)	35 (24.5)	0.002*
Low HDL-C (%)	16 (18.8)	57 (39.9)	0.001*
High TG (%)	20 (23.5)	36 (25.2)	0.780
Obesity (%)	29 (34.1)	46 (36.2)	0.762
MetS (%)	24 (28.2)	62 (43.4)	0.023*
Audiogram patterns			0.789
Ascending (%)	20 (23.5)	26 (18.2)	
Descending (%)	11 (12.9)	18 (12.6)	
Flat (%)	21 (24.7)	37 (25.9)	
Profound (%)	33 (38.8)	62 (43.4)	

MetS = metabolic syndrome; ISSNHL = idiopathic sudden sensorineural hearing loss.
HDL-C = high-density lipoprotein cholesterol; TG = triglyceride.
* $P < 0.05$.

Table 4
Multivariate analysis of the recovery after the treatment of ISSNHL.

	OR	95% CI	*P*
Initial hearing threshold	1.679	1.242–2.112	0.005*
Diabetes mellitus	2.072	1.598–2.451	0.032*
Low HDL-C	1.982	1.366–2.347	0.106
MetS	2.672	2.104–3.467	0.009*

ISSNHL = idiopathic sudden sensorineural hearing loss; MetS = metabolic syndrome.
HDL-C: high-density lipoprotein cholesterol.
* $P < 0.05$; OR = odds ratios; CI = confidence interval.

the atherosclerostc changes and endothelia injury, finally induced cochlear microangiopathy, resulting in a decreased blood supply [6,14]. The inner ear is a high metabolic organ without collateral blood supply, and the impaired cochlear blood perfusion because of microangiopathy will prevent the therapeutic agents reaching the impaired tissue through the blood circulation, and the inner hair cells will not get an effective repair. Several studies have reported that an underlying microangiopathy (not caused by MetS) may influence the potential for developing ISSNHL, and evidence from human temporal bone anatomy has proven the occurrence of cochlear microangiopathy [14–16]. Hence, microangiopathy itself may be one of the mechanisms underlying ISSNHL, and a confounding factor when we analyzing the prognosis of ISSNHL. However it is beyond the scope of this study, we don't go into the details.

Previous publications have investigated the effect of the comorbid diabetes mellitus on the prognosis of ISSNHL, but the conclusion is still controversial. Some argued that diabetes mellitus significantly affected hearing recovery negatively in ISSNHL patients [3,14,15], but Ciorba et al. [17] disagreed, they reported no significant effect in patients with ISSNHL. In the present study, the multivariate analysis results support the idea that diabetes mellitus has a negative effect on the hearing improvement of ISSNHL. The underlying mechanism has not been confirmed, but the hyperglycemia-mediated endothelial injury has been reported to be associated with a poor prognosis in many diseases [3]. According to a prior study, cochlear microangiopathy and atrophy of the spiral ganglion were observed during human temporal bone study in patients with diabetes mellitus [14], these findings may help us understand the mechanisms underlying the relationship between diabetes mellitus and ISSNHL. Hence, it is reasonable to expect a negative influence on hearing prognosis in ISSNHL patients with diabetes mellitus.

The initial hearing threshold is a widely reported prognostic factor for hearing improvement in ISSNHL patients [18,19], most authors hold that the initial hearing threshold was a negative prognostic indicator for hearing recovery [2,18], however, Hosokawa et al. [20] found no association between the initial hearing level and hearing outcome in ISSNHL patients. According to our multivariate analysis, we found that the initial hearing threshold was a significant prognostic indicator for poor hearing recovery, which was in line with most previous studies. It was believed that in ISSNHL patients with severe hearing loss, the injure of inner hair cell was more extensive, hence, it was more difficult to get a satisfied hearing prognosis, although therapeutic agents were applied [2,18,19].

This study has some limitations. First of all, it is a retrospective analysis which entails the risk of selection bias; Secondly, the diagnostic criteria of MetS are different worldwide because of different countries, regions, ethnic groups and research institutions; Finally, because waist circumference was not routinely recorded in our department, we did not include it in our definition, which may cause the underestimation of the incidence of MetS.

5. Conclusion

These results suggest that MetS has a negative impact on the hearing recovery of ISSNHL. High initial hearing threshold and diabetes mellitus were indictors of a poor prognosis of ISSNHL. Further studies are needed to confirm the findings of this study.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not for-profit sectors.

Declaration of Competing Interest

None.

References

[1] Schreiber BE, Agrup C, Haskard DO, Luxon LM. Sudden sensorineural hearing loss. Lancet 2010;375:1203–11. https://doi.org/10.1016/S0140-6736(09)62071-7.
[2] Chung JH, Cho SH, Jeong JH, Park CW, Lee SH. Multivariate analysis of prognostic factors for idiopathic sudden sensorineural hearing loss in children. Laryngoscope 2015;125:2209–15. https://doi.org/10.1002/lary.25196.
[3] Lin CF, Lee KJ, Yu SS, Lin YS. Effect of comorbid diabetes and hypercholesterolemia on the prognosis of idiopathic sudden sensorineural hearing loss. Laryngoscope 2016;126:142–9. https://doi.org/10.1002/lary.25333.
[4] Chien CY, Tai SY, Wang LF, Hsi E, Chang NC, Wu MT, et al. Metabolic syndrome increases the risk of sudden sensorineural hearing loss in Taiwan: a case-control study. Otolaryngol Head Neck Surg 2015;153:105–11. https://doi.org/10.1177/0194599815575713.
[5] Mosnier I, Stepanian A, Baron G, Bodenez C, Robier A, Meyer B, et al. Cardiovascular and thromboembolic risk factors in idiopathic sudden sensorineural hearing loss: a case-control study. Audiol Neurootol 2011;16:55–66. https://doi.org/10.1159/000312640.
[6] Aimoni C, Bianchini C, Borin M, Ciorba A, Fellin R, Martini A, et al. Diabetes, cardiovascular risk factors and idiopathic sudden sensorineural hearing loss: a case-control study. Audiol Neurootol 2010;15:111–5. https://doi.org/10.1159/000231636.
[7] Jung SY, Jung J, Byun JY, Park MS, Kim SH, Yeo SG. The effect of metabolic syndrome on Bell's palsy recovery rate. Acta Otolaryngol 2018;138:670–4. https://doi.org/10.1080/00016489.2018.1425902.
[8] Mottillo S, Filion KB, Genest J, Joseph L, Pilote L, Poirier P, et al. The metabolic syndrome and cardiovascular risk. a systematic review and meta-analysis J Am Coll Cardiol 2010;56:1113–32. https://doi.org/10.1016/j.jacc.2010.05.034.
[9] Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. Lancet 2005;365(9468):1415–28. https://doi.org/10.1016/S0140-6736(05)66378-7.
[10] Siegel LG. The treatment of idiopathic sudden sensorineural hearing loss.

Otolaryngol Clin North Am 1975;8:467–73.
[11] Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive summary of the third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III). JAMA 2001;285:2486–97.
[12] Garvey WT, Mechanick JI, Brett EM, Garber AJ, Hurley DL, Jastreboff AM, et al. American Association of Clinical Endoclinoloists and Aerican College of Endocrinology comprehensive clinical practice guidelines for medical care of patients with obesity. Endocr Pract 2016;22:1–203. https://doi.org/10.4158/EP161365.GL.
[13] Erdur SK, Aydin R, Ozsutcu M, Olmuscelik O, Eliacik M, Demirci G, et al. The relationship between metabolic syndrome, its components, and dry eye: a cross-sectional study. Curr Eye Res 2017;42:1115–7. https://doi.org/10.1080/02713683.2017.1280511.
[14] Kakarlapudi V, Sawyer R, Staecker H. The effect of diabetes on sensorineural hearing loss. Otol Neurotol 2003;24:382–6.
[15] Nagaoka J, Anjos MF, Takata TT, Chaim RM, Barros F, Penido Nde O. Idiopathic sudden sensorineural hearing loss: evolution in the presence of hypertension, diabetes mellitus and dyslipidemias. Braz J Otorhinolaryngol 2010;76:363–9.
[16] Lin SW, Lin YS, Weng SF, Chou CW. Risk of developing sudden sensorineural hearing loss in diabetic patients: a population-based cohort study. Otol Neurotol 2012;33:1482–8. https://doi.org/10.1097/MAO.0b013e318271397a.
[17] Ciorba A, Hatzopoulos S, Bianchini C, Iannini V, Rosignoli M, Skarzynski H, et al. Idiopathic sudden sensorineural hearing loss: cardiovascular risk factors do not influence hearing threshold recovery. Acta Otorhinolaryngol Ital 2015;35:103–9.
[18] Thomas JP, Drewermann S, Voelter C, Dazert S. Prognostic factors regarding the hearing outcome in severe to profound sudden sensorineural hearing loss treated by tympanotomy and sealing of labyrinthine windows after ineffective systemic corticosteroid application. Eur Arch Otorhinolaryngol 2018;275:1749–58. https://doi.org/10.1007/s00405-018-5023-3.
[19] Xie S, Qiang Q, Mei L, He C, Feng Y, Sun H, et al. Multivariate analysis of prognostic factors for idiopathic sudden sensorineural hearing loss treated with adjuvant hyperbaric oxygen therapy. Eur Arch Otorhinolaryngol 2018;275:47–51. https://doi.org/10.1007/s00405-017-4784-4.
[20] Hosokawa S, Sugiyama K, Takahashi G, Takebayashi S, Mineta H. Prognostic factors for idiopathic sudden sensorineural hearing loss treated with hyperbaric oxygen therapy and intravenous steroids. J Laryngol Otol 2017;131:77–82. https://doi.org/10.1017/S0022215116009725.