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## Relationships among drinking and smoking habits, history of diseases, body mass index and idiopathic sudden sensorineural hearing loss in Japanese patients

Mitsumasa Umesawa<sup>a</sup>, Gen Kobashi<sup>a</sup>, Ryoshuke Kitoh<sup>b</sup>, Shin-ya Nishio<sup>b</sup>, Kaoru Ogawa<sup>c</sup>, Naohito Hato<sup>d</sup>, Michihiko Sone<sup>e</sup>, Satoshi Fukuda<sup>f</sup>, Akira Hara<sup>g</sup>, Tetsuo Ikezono<sup>h</sup>, Kotaro Ishikawa<sup>i</sup>, Satoshi Iwasaki<sup>j</sup>, Kimitaka Kaga<sup>k</sup>, Seiji Kakehata<sup>l</sup>, Atsushi Matsubara<sup>m</sup>, Tatsuo Matsunaga<sup>k</sup>, Takaaki Murata<sup>n</sup>, Yasushi Naito<sup>o</sup>, Takashi Nakagawa<sup>p</sup>, Kazunori Nishizaki<sup>q</sup>, Yoshihiro Noguchi<sup>b</sup>, Hajime Sano<sup>r</sup>, Hiroaki Sato<sup>s</sup>, Mikio Suzuki<sup>t</sup>, Hideo Shojaku<sup>u</sup>, Haruo Takahashi<sup>v</sup>, Hidehiko Takeda<sup>w</sup>, Tetsuya Tono<sup>x</sup>, Hiroshi Yamashita<sup>y</sup>, Tatsuya Yamasoba<sup>z</sup> and Shin-ichi Usami<sup>b</sup>

<sup>a</sup>Department of Public Health, Dokkyo Medical University, School of Medicine, Mibu, Japan; <sup>b</sup>Department of Otorhinolaryngology, Shinshu University School of Medicine, Matsumoto, Japan; <sup>c</sup>Department of Otorhinolaryngology Head and Neck Surgery, Keio University School of Medicine, Tokyo, Japan; <sup>d</sup>Department of Otolaryngology, Ehime University School of Medicine, Toon, Japan; <sup>e</sup>Department of Otorhinolaryngology, Nagoya University, Graduate School of Medicine, Nagoya, Japan; <sup>f</sup>Department of Otolaryngology-Head and Neck Surgery, Hokkaido University Graduate School of Medicine, Sapporo, Japan; <sup>g</sup>Department of Otolaryngology, Faculty of Medicine, University of Tsukuba, Tsukuba, Japan; <sup>h</sup>Department of Otorhinolaryngology, Saitama School of Medicine, Moroyama, Japan; <sup>i</sup>Department of Otolaryngology, Hospital, National Rehabilitation Center for Persons with Disabilities, Tokorozawa, Japan; <sup>j</sup>Department of Otolaryngology, International University of Health and Welfare, Mita Hospital, Tokyo, Japan; <sup>k</sup>Division of Hearing and Balance Research, National Institute of Sensory Organs, National Hospital Organization Tokyo Medical Center, Tokyo, Japan; <sup>l</sup>Department of Otorhinolaryngology, Yamagata University School of Medicine, Yamagata, Japan; <sup>m</sup>Department of Otorhinolaryngology, Hirosaki University Graduate School of Medicine, Hirosaki, Japan; <sup>n</sup>Department of Otolaryngology, Gunma University Graduate School of Medicine, Maebashi, Japan; <sup>o</sup>Department of Otolaryngology, Kobe City Medical Center General Hospital, Kobe, Japan; <sup>p</sup>Department of Otorhinolaryngology, Kyushu University Graduate School of Medical Sciences, Fukuoka, Japan; <sup>q</sup>Department of Otolaryngology-Head and Neck Surgery, Okayama University Graduate School of Medicine, Dentistry and Pharmacy, Okayama, Japan; <sup>r</sup>Department of Otolaryngology, Kitasato University School of Medicine, Sagami-hara, Japan; <sup>s</sup>Department of Otorhinolaryngology, Iwate Medical University, Morioka, Japan; <sup>t</sup>Department of Otorhinolaryngology, Head and Neck Surgery, Graduate School of Medicine, University of the Ryukyus, Nishihara, Japan; <sup>u</sup>Department of Otorhinolaryngology, Head and Neck Surgery, University of Toyama, Toyama, Japan; <sup>v</sup>Department of Otolaryngology, Nagasaki University Faculty of Medicine, Nagasaki, Japan; <sup>w</sup>Department of Otolaryngology, Okinaka Memorial Institute for Medical Research, Toranomon Hospital, Tokyo, Japan; <sup>x</sup>Department of Otolaryngology, Faculty of Medicine, University of Miyazaki, Miyazaki, Japan; <sup>y</sup>Department of Otolaryngology, Yamaguchi University Graduate School of Medicine, Ube, Japan; <sup>z</sup>Department of Otolaryngology, Faculty of Medicine, University of Tokyo, Tokyo, Japan

### ABSTRACT

**Objectives:** To present the cardiovascular risk factors in idiopathic sudden sensorineural hearing loss (SSNHL) patients enrolled in a nationwide epidemiological survey of hearing disorders in Japan.

**Materials and methods:** We compiled the cardiovascular risk factors in 3073 idiopathic SSNHL subjects (1621 men and 1452 women) and compared their proportions with controls as part of the National Health and Nutrition Survey in Japan, 2014. The cardiovascular risk factors consisted of drinking and smoking habits, a history of five conditions related to cardiovascular disease and body mass index.

**Results:** The proportion of current smokers was significantly higher among men aged 50–59, 60–69 and 70+ and among women aged 30–39, 40–49 and 60–69. The proportion of patients with a history of diabetes mellitus was significantly higher among men aged 50–59, 60–69 and 70+, but not in women. In addition, male and female SSNHL subjects aged 60–69 showed lower proportions of current drinking; and female SSNHL subjects aged 60–69 showed higher proportions of overweight (BMI  $\geq 25$  kg/m<sup>2</sup>).



**Conclusions:** The present cross-sectional study revealed showed significantly higher proportions of current smokers among both men and women as well as those with a history of diabetes mellitus among men across many age groups in patients with idiopathic SSNHL compared with the controls.

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### KEYWORDS

Idiopathic sudden sensorineural hearing loss; epidemiology; multicenter study; cross-sectional study; smoking; drinking

**CONTACT** Gen Kobashi  genkoba@dokkyomed.ac.jp  usami@shinshu-u.ac.jp 

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## Introduction

Idiopathic sudden sensorineural hearing loss (SSNHL) is a major cause of acquired hearing impairment. Idiopathic SSNHL is reported to occur in 5–20 per 100,000 persons per year [1]. However, in Japan, the prevalence of idiopathic SSNHL was reported to be 60.9 per 100,000 persons, which is higher than the incidence reported in the previous study [1,2]. This difference may be caused by the method of data collection. In the previous study, private otolaryngology clinics were included in survey, and authors found that 65% of SSNHL patients only visited private clinics [2]. Epidemiological study of idiopathic SSNHL is therefore warranted in order to clarify risk factors.

Previous epidemiological studies suggested various risk factors for idiopathic SSNHL [3–5], such as genetic variants including single nucleotide polymorphism (SNP)s, viral infection, nervous system abnormalities and so on. Among them, cardiovascular risk factors appeared to have an important role in the development of idiopathic SSNHL. However, the evidence for a relationship between cardiovascular risk factors and idiopathic SSNHL is limited. A meta-analysis mainly consisting of case-control studies showed that smoking and heavy alcohol intake, but not hypertension or diabetes, were positively associated with a risk of SSNHL [4]. However, in a recent case-control study of Taiwanese, hypertension, diabetes mellitus and hyperlipidemia were positively associated with risk of SSNHL [5].

The aims of the present study were to present the distribution of cardiovascular risk factors in patients with idiopathic SSNHL and to examine the association between lifestyle-related cardiovascular risk factors and idiopathic SSNHL severity based on data from a nationwide epidemiological survey of hearing disorders.

## Methods

### Subjects and surveys

The subjects consisted of idiopathic SSNHL patients, aged 20–89 years, in the 30 university hospitals and medical centers involved in this epidemiological survey. The registration of patients was undertaken between April 2014 and March 2016. The criteria for a diagnosis of idiopathic SSNHL and protocol for this survey have been described in detail elsewhere [6]. In short, we defined idiopathic SSNHL as having main symptoms; sudden onset, sensorineural hearing loss and unknown etiology, and categorized the severity of SSNHL into Grades 1–4 according to the pure tone average (PTA) of the five frequencies; 250, 500, 1000, 2000 and 4000 Hz. We defined PTA <40 dB as Grade 1,  $40 \leq \text{PTA} < 60$  dB as Grade 2,  $60 \leq \text{PTA} < 90$  dB as Grade 3 and  $90 \leq \text{PTA}$  as Grade 4. The total number of subjects was 3101. We excluded 28 subjects because of lack of information regarding gender. Therefore, data from 3073 subjects (1621 men and 1452 women) were used for the analysis.

A survey of cardiovascular risk factors was carried out as part of the registration of cases. The risk factors consisted of

drinking and smoking habits, and a history of five conditions diseases related to cardiovascular disease (CVD); diabetes mellitus, hyperlipidemia, renal disease, ischemic stroke and heart disease. Three answers were allowed; ‘yes’, ‘no’ and ‘unknown’. The answer was based on the patient medical records. We excluded patients from each analysis when the data were ‘unknown’. We also calculated body mass index (BMI) as a cardiovascular risk factor for patients for whom the information on height and weight was valid. BMI was calculated by dividing weight (in kg) by height (in m<sup>2</sup>).

The present study was approved by the ethics committees of Shinshu University, Dokkyo Medical University and the other participating institutions.

### Statistical analysis

Patient characteristics, including the severity of idiopathic SSNHL, were compiled by sex and age group (20–29, 30–39, 40–49, 50–59, 60–69 and 70+). Age-adjusted mean values and proportions for each characteristic were calculated using analysis of covariance to compare differences between men and women. We compared the proportions of subjects with overweight (BMI  $\geq 25$  kg/m<sup>2</sup>), drinking habit, smoking habit and history of diabetes mellitus with controls from the National Health and Nutrition Survey in Japan, 2014 ( $N = 6016$  for health status survey,  $N = 3504$  for blood testing, and  $N = 7641$  for life-style habitat survey) [7]. As for the controls, we regarded a drinking habit as consuming an alcoholic beverage once per week or more; a smoking habit as consuming cigarettes daily and a history of diabetes mellitus as an indication of diabetes mellitus by a doctor or health check-up or the prescription of medication for diabetes mellitus. We used a chi-squared test for comparisons between the groups.

We also examined the associations between the severity of idiopathic SSNHL at first visit and BMI, presence of overweight, drinking habit and smoking habit using a chi-squared test. The comparison of median PTA at first visit according to the presence of overweight, drinking habit and smoking habit was conducted using Wilcoxon’s rank test. Age-adjusted mean values for BMI and the proportions of subjects with smoking and drinking habits were also calculated and examined by analysis of covariance.

We used SAS version 9.4 software (SAS Institute, Cary, NC) for the data compilation, Wilcoxon’s rank test and analysis of covariance. We used age at first visit for the adjustment. We also used Microsoft Excel 2013 (15.0.4875.1000) for the chi-squared test. Values of  $p < .05$  (two-tailed) were considered to be statistically significant.

## Results

Table 1 summarizes the characteristics of the subjects stratified by sex. The age-adjusted proportions of current drinkers, current smokers, and those having a history of diabetes mellitus, heart disease and renal disease were significantly higher among men than among women ( $p < .001$ ,  $p < .001$ ,  $p < .001$  and  $p = .030$ , respectively).

Tables 2 and 3 show the characteristics of the subjects stratified by sex and age group in 10-year increments. Mean value of BMI was high in the 40–49 and 50–59 year-old groups among men, and in the 60–69 year-old group among women. For current drinking, the proportion of current drinkers was high in the 50–59 year-old group among men, whereas it was high in the 40–49 year-old group among women. With regard to current smoking, the proportion of current smokers was high in the 50–59 year-old group among men, whereas it was high in the 30–39 and 40–49 year-old groups among women. With regard to history of diseases, the proportions of patients with disease histories gradually increased with age group among both men and women.

**Table 1.** Characteristics of the subjects at first visit according to sex.

	Men (N = 1621)	Women (N = 1452)
Age (mean, years) <sup>a</sup>	55.9 (15.1)	55.7 (15.3)
Body mass index (kg/m <sup>2</sup> ) <sup>b,c</sup>	23.9	23.0
Current drinker (%) <sup>b,d</sup>	52.1	19.7
Current smoker (%) <sup>b,e</sup>	38.0	12.2
History of diabetes mellitus (%) <sup>b,f</sup>	21.9	13.0
History of hyperlipidemia (%) <sup>b,g</sup>	11.6	11.0
History of heart disease (%) <sup>b,h</sup>	15.1	8.8
History of ischemic stroke (%) <sup>b,i</sup>	3.6	2.9
History of renal disease (%) <sup>b,j</sup>	5.8	4.0
Grade of SSNHL (%) <sup>k</sup>		
Grade 1	13.5	17.3
Grade 2	22.7	22.5
Grade 3	39.2	34.8
Grade 4	24.6	25.5

<sup>a</sup>Mean ± SD.

<sup>b</sup>Age-adjusted.

<sup>c</sup>N = 756 for men and 705 for women.

<sup>d</sup>N = 1003 for men and 895 for women.

<sup>e</sup>N = 1129 for men and 1015 for women.

<sup>f</sup>N = 1531 for men and 1369 for women.

<sup>g</sup>N = 1450 for men and 1299 for women.

<sup>h</sup>N = 1463 for men and 1305 for women.

<sup>i</sup>N = 1459 for men and 1306 for women.

<sup>j</sup>N = 1454 for men and 1306 for women.

<sup>k</sup>N = 1615 for men and 1449 for women.

Figures 1–4 show the proportions of idiopathic SSNHL subjects with overweight (Figure 1), drinking habit (Figure 2), smoking habit (Figure 3) and history of diabetes mellitus (Figure 4), compared with controls from the National Health and Nutrition Survey in Japan, 2014 (N = 6061 for health status survey, N = 3504 for blood testing, and N = 7641 for life-style habitat survey). For overweight, the proportion of idiopathic SSNHL subjects who were overweight was significantly higher in the 60–69 year-old group among women ( $p = .034$ ). For current drinking, the proportions of current drinkers among the SSNHL subjects were significantly lower in the 60–69 year-old group among both men and women ( $p = .001$  and  $p = .021$ , respectively). For current smoking, the proportions of current smokers among the idiopathic SSNHL subjects were significantly higher in the 50–59, 60–69 and 70+ year-old groups among men and in the 30–39, 40–49 and 60–69 year-old groups among women ( $p = .023$ ,  $p = .004$ ,  $p < .001$ ,  $p = .030$ ,  $p = .011$  and  $p = .009$ , respectively). With regard to the proportions of patients with a history of diabetes mellitus, the proportions were significantly higher in the 50–59, 60–69 and 70+ year-old groups among men ( $p = .009$ ,  $p = .007$  and  $p = .017$ , respectively), but not among women.

Table 4 shows the number of subjects and median PTA at first visit according to the presence of overweight, drinking status and smoking status. The presence of each factor was not associated with the severity of SSNHL or PTA at first visit.

Table 5 shows the age-adjusted means and proportions of lifestyle-related risk factors and severity of idiopathic SSNHL. In men, compared with the Grade 1 group, the Grade 2–4 groups showed significantly higher proportions of current smokers ( $p = .021$ ,  $p = .008$  and  $p = .033$ , respectively). In women, the Grades 2 and 4 groups showed significantly higher proportions of current drinkers ( $p = .039$  and  $p = .049$ , respectively) in comparison with the Grade 1 group.

**Table 2.** Characteristics of the male subjects at first visit according to age group in 10-year increments.

	Men (N = 1621)					
	20–29 (N = 97)	30–39 (N = 177)	40–49 (N = 254)	50–59 (N = 317)	60–69 (N = 454)	70+ (N = 322)
Body mass index (kg/m <sup>2</sup> ) <sup>a</sup>	22.5	23.6	24.5	24.5	23.7	23.9
Current drinker (%) <sup>b</sup>	37.7	52.7	53.1	56.9	54.2	46.7
Current smoker (%) <sup>c</sup>	36.6	39.7	41.1	43.6	39.3	27.1
History of diabetes mellitus (%) <sup>d</sup>	1.1	8.3	8.0	23.6	31.3	31.8
History of hyperlipidemia (%) <sup>e</sup>	2.3	2.5	5.5	14.6	12.6	19.6
History of heart disease (%) <sup>f</sup>	3.3	0.6	6.3	11.5	18.1	33.0
History of ischemic stroke (%) <sup>g</sup>	0.0	0.0	1.4	3.1	4.9	6.8
History of renal disease (%) <sup>h</sup>	1.1	1.9	4.1	5.9	7.2	8.6
Grade of SSNHL (%) <sup>i</sup>						
Grade 1	25.8	24.4	19.0	12.7	9.5	5.9
Grade 2	18.6	25.6	21.0	24.1	23.9	20.9
Grade 3	38.1	34.1	36.4	40.5	40.7	41.1
Grade 4	17.5	15.9	23.7	22.8	25.9	32.1

<sup>a</sup>N = 42 for 20s, 78 for 30s, 119 for 40s, 163 for 50s, 201 for 60s and 153 for 70s and over.

<sup>b</sup>N = 61 for 20s, 110 for 30s, 160 for 40s, 195 for 50s, 295 for 60s and 182 for 70s and over.

<sup>c</sup>N = 71 for 20s, 126 for 30s, 168 for 40s, 218 for 50s, 328 for 60s and 218 for 70s and over.

<sup>d</sup>N = 92 for 20s, 169 for 30s, 237 for 40s, 297 for 50s, 425 for 60s and 311 for 70s and over.

<sup>e</sup>N = 89 for 20s, 161 for 30s, 218 for 40s, 287 for 50s, 404 for 60s and 291 for 70s and over.

<sup>f</sup>N = 90 for 20s, 161 for 30s, 224 for 40s, 287 for 50s, 404 for 60s and 297 for 70s and over.

<sup>g</sup>N = 90 for 20s, 161 for 30s, 222 for 40s, 288 for 50s, 405 for 60s and 293 for 70s and over.

<sup>h</sup>N = 90 for 20s, 161 for 30s, 219 for 40s, 287 for 50s, 405 for 60s and 292 for 70s and over.

<sup>i</sup>N = 97 for 20s, 176 for 30s, 253 for 40s, 316 for 50s, 452 for 60s and 321 for 70s and over.

**Table 3.** Characteristics of the female subjects at first visit according to age group in 10-year increments.

	Women (N = 1452)					
	20–29 (N = 96)	30–39 (N = 183)	40–49 (N = 189)	50–59 (N = 300)	60–69 (N = 400)	70+ (N = 284)
Body mass index (kg/m <sup>2</sup> ) <sup>a</sup>	21.0	22.7	21.9	23.1	23.8	23.1
Current drinker (%) <sup>b</sup>	22.7	24.1	31.6	23.2	16.4	8.4
Current smoker (%) <sup>c</sup>	12.3	20.6	20.6	12.7	10.5	3.1
History of diabetes mellitus (%) <sup>d</sup>	0.0	2.9	5.8	12.9	18.9	20.3
History of hyperlipidemia (%) <sup>e</sup>	0.0	1.2	0.0	11.7	16.7	19.2
History of heart disease (%) <sup>f</sup>	1.1	0.6	1.2	4.5	10.9	22.4
History of ischemic stroke (%) <sup>g</sup>	0.0	0.0	1.2	1.9	2.2	8.8
History of renal disease (%) <sup>h</sup>	1.1	1.2	3.0	4.1	5.6	5.0
Grade of SSNHL (%) <sup>i</sup>						
Grade 1	32.3	27.9	30.2	15.7	12.3	5.3
Grade 2	14.6	18.0	19.6	27.1	24.5	22.3
Grade 3	27.1	30.6	28.0	31.1	40.3	40.8
Grade 4	26.0	23.5	22.2	26.1	23.0	31.6

<sup>a</sup>N = 41 for 20s, 91 for 30s, 88 for 40s, 140 for 50s, 201 for 60s and 144 for 70s and over.

<sup>b</sup>N = 66 for 20s, 116 for 30s, 117 for 40s, 185 for 50s, 244 for 60s and 167 for 70s and over.

<sup>c</sup>N = 73 for 20s, 131 for 30s, 136 for 40s, 205 for 50s, 277 for 60s and 193 for 70s and over.

<sup>d</sup>N = 90 for 20s, 173 for 30s, 174 for 40s, 280 for 50s, 381 for 60s and 271 for 70s and over.

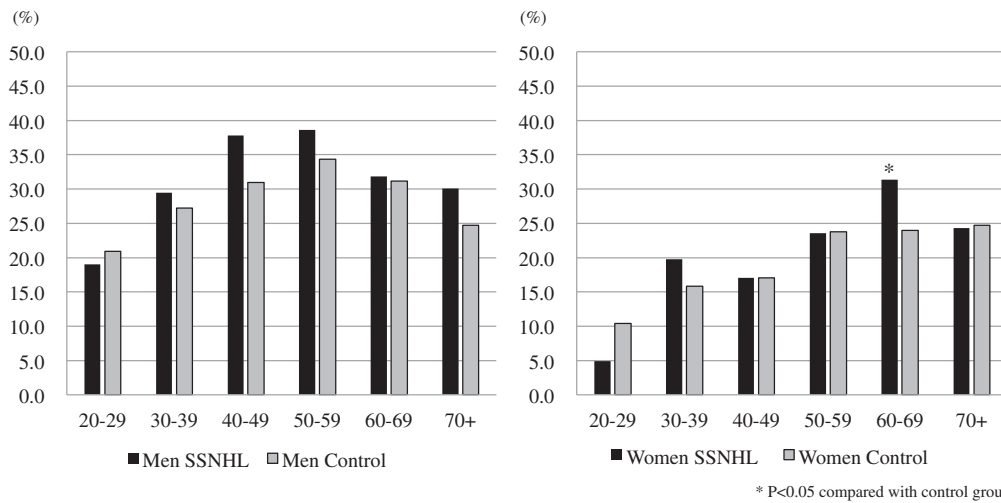
<sup>e</sup>N = 88 for 20s, 163 for 30s, 167 for 40s, 266 for 50s, 360 for 60s and 255 for 70s and over.

<sup>f</sup>N = 88 for 20s, 163 for 30s, 167 for 40s, 267 for 50s, 357 for 60s and 263 for 70s and over.

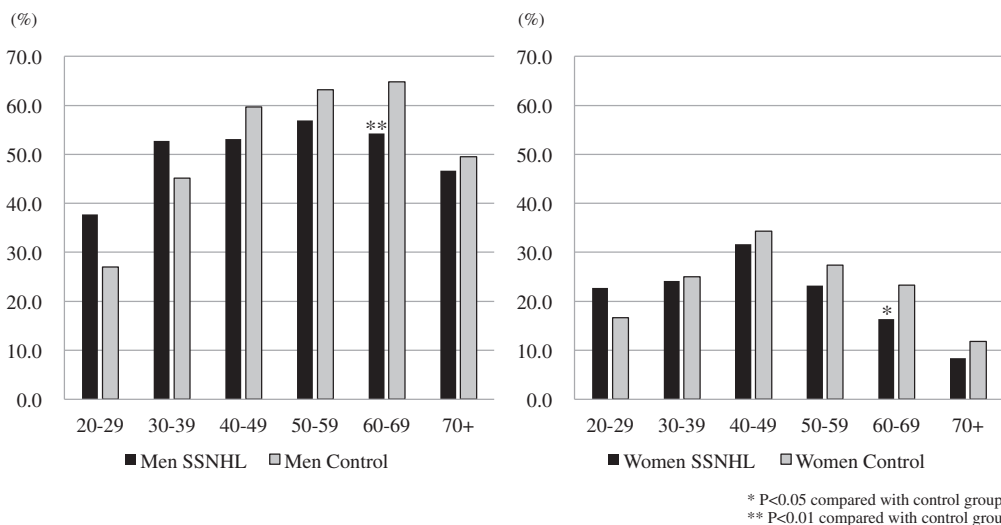
<sup>g</sup>N = 88 for 20s, 163 for 30s, 167 for 40s, 267 for 50s, 360 for 60s and 261 for 70s and over.

<sup>h</sup>N = 88 for 20s, 162 for 30s, 166 for 40s, 269 for 50s, 360 for 60s and 261 for 70s and over.

<sup>i</sup>N = 96 for 20s, 183 for 30s, 189 for 40s, 299 for 50s, 400 for 60s and 282 for 70s and over.

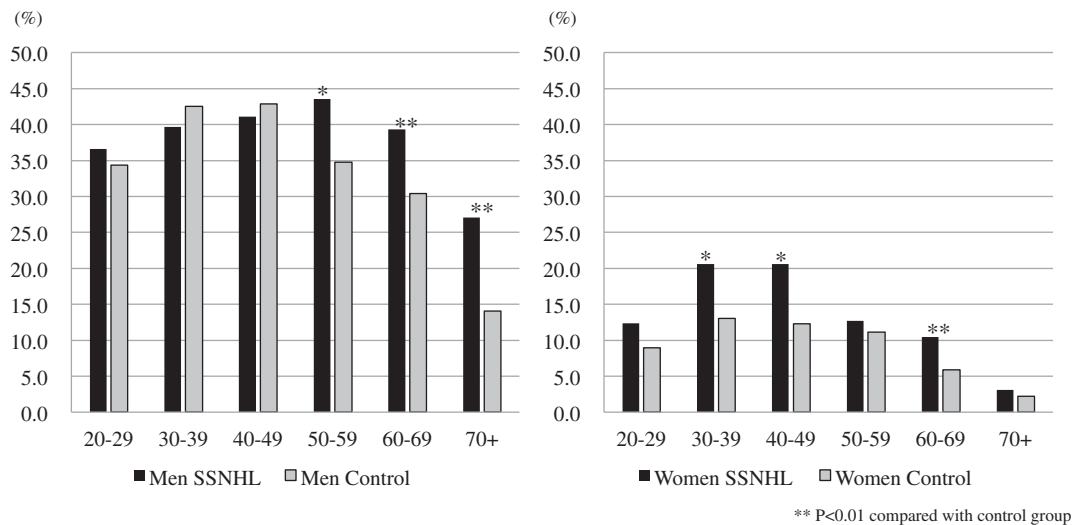


**Figure 1.** Proportions of overweight subjects (BMI  $\geq 25$  kg/m<sup>2</sup>). Left panel indicates the proportion of male overweight idiopathic SSNHL patients (black) and control population (gray). Right panel indicates the proportion of female overweight idiopathic SSNHL patients (black) and control population (gray). The proportion of overweight subjects in the control population was calculated from data obtained in the National Health and Nutrition Survey in Japan, 2014.

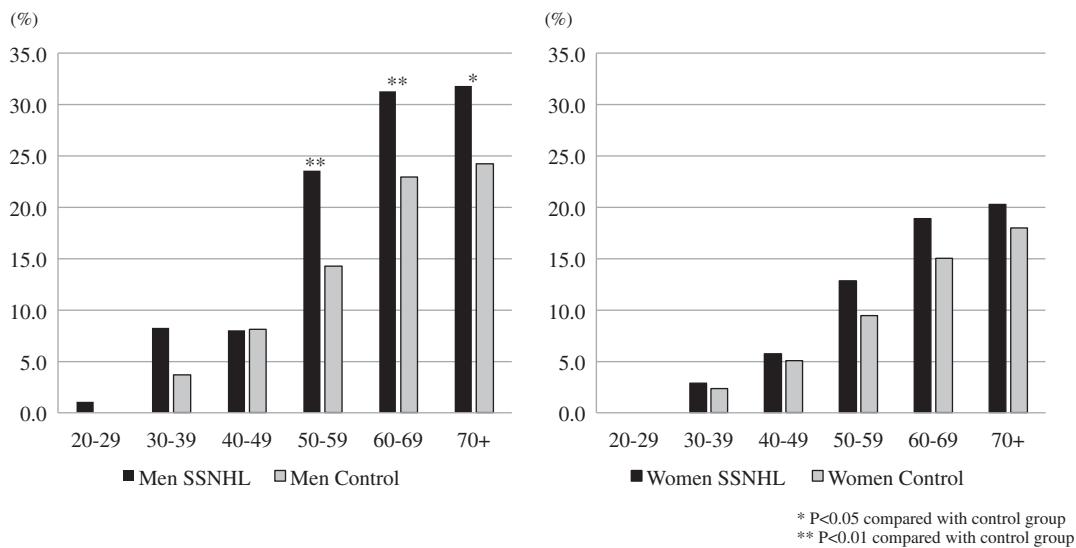


**Figure 2.** Proportions of current drinkers. Left panel indicates the proportion of male current drinkers among idiopathic SSNHL patients (black) and control population (gray). Right panel indicates the proportion of female current drinkers among idiopathic SSNHL patients (black) and control population (gray). The proportion of overweight subjects in control population was calculated from data obtained in the National Health and Nutrition Survey in Japan, 2014.





**Figure 3.** Proportions of current smokers. Left panel indicates the proportion of male current smokers among idiopathic SSNHL patients (black) and control population (gray). Right panel indicates the proportion of female current smokers among idiopathic SSNHL patients (black) and control population (gray). The proportion of overweight subjects in control population was calculated from data obtained in the National Health and Nutrition Survey in Japan, 2014.



**Figure 4.** Proportions of subjects having a history of diabetes mellitus. Left panel indicates the proportion of males having a history of diabetes among idiopathic SSNHL patients (black) and control population (gray). Right panel indicates the proportion of females having a history of diabetes among idiopathic SSNHL patients (black) and control population (gray). The proportion of overweight subjects in control population was calculated from data obtained in the National Health and Nutrition Survey in Japan, 2014.

## Discussion

The present study showed the distribution of cardiovascular risk factors in patients with idiopathic SSNHL and the relationship between cardiovascular risk factors and idiopathic SSNHL severity. Compared with the subjects from the National Health and Nutrition Survey in Japan, 2014, subjects in the present study of idiopathic SSNHL patients showed higher proportions of current smokers in the higher age groups among men and in the middle age groups among women. With regard to a history of diabetes mellitus, the proportion of those with a history of diabetes mellitus was higher among men in the present study compared with the control. Current smoking was found to be positively associated with the severity of idiopathic SSNHL among men.

From the results of previous epidemiological studies, diabetes mellitus appeared to be a risk factor for idiopathic

SSNHL [4,5]. A meta-analysis consisting of four case-control studies of 65 cases and 42 controls reported that a medical history of diabetes mellitus was associated with a risk of idiopathic SSNHL with borderline significance: odds ratio (OR) = 1.53, 95% confidence intervals (95%CI) = 0.96–2.42 [4]. In Taiwan, subjects who had a history of diabetes mellitus were at a 1.47 times higher risk of developing idiopathic SSNHL [5]. In the present study, we could not examine the association between diabetes mellitus and the risk of idiopathic SSNHL because all participants in the present study were idiopathic SSNHL patients. Thus, we compared the proportion of patients with a history of diabetes mellitus in the present study to subjects from the latest National Health and Nutrition Survey in Japan, 2014 and identified that the proportion of those with a history of diabetes mellitus in the idiopathic SSNHL patients was significantly higher than that

**Table 4.** Number of subjects and median PTA at first visit according to presence of cardiovascular risk factors.

	Severity of SSNHL at first visit				<i>P</i> for Chi-squared test	Median PTA At first visit	<i>P</i> for Wilcoxon's rank test
	Grade 1	Grade 2	Grade 3	Grade 4			
<b>Men</b>							
Overweights	21	56	110	61	0.747	71 dB	0.534
Non-overweights	51	106	212	136	–	73 dB	–
Drinkers	73	121	210	117	0.511	71 dB	0.350
Non-drinkers	58	104	193	125	–	72 dB	–
Smokers	49	103	175	100	0.175	73 dB	0.084
Non-smokers	113	158	265	164	–	70 dB	–
<b>Women</b>							
Overweights	18	40	69	39	0.167	72 dB	0.214
Non-overweights	67	107	194	169	–	75 dB	–
Drinkers	25	45	59	48	0.663	70 dB	0.479
Non-drinkers	127	164	240	184	–	69 dB	–
Smokers	22	28	40	35	0.863	71 dB	0.549
Non-smokers	165	211	294	217	–	67 dB	–

**Table 5.** Age-adjusted means and proportions of cardiovascular risk factors according to severity of SSNHL at first visit.

	Severity of SSNHL at first visit			
	Grade 1	Grade 2	Grade 3	Grade 4
<b>Men</b>				
<i>N</i>	72	162	332	197
Age-adjusted means of BMI (kg/m <sup>2</sup> )	23.4	23.8	24.2	23.8
<i>P</i> for difference	(reference)	0.338	0.070	0.318
<i>N</i>	130	222	397	240
Age-adjusted proportions of current drinker (%)	56.1	53.8	52.1	48.2
<i>P</i> for difference	(reference)	0.682	0.435	0.157
<i>N</i>	162	261	440	264
Age-adjusted proportions of current smoker (%)	28.1	39.5	40.1	38.7
<i>P</i> for difference	(reference)	0.021	0.008	0.033
<b>Women</b>				
<i>N</i>	85	147	263	208
Age-adjusted means of BMI (kg/m <sup>2</sup> )	22.3	23.7	23.1	22.7
<i>P</i> for difference	(reference)	0.014	0.125	0.492
<i>N</i>	152	209	299	232
Age-adjusted proportions of current drinker (%)	13.1	22.0	20.5	21.4
<i>P</i> for difference	(reference)	0.039	0.068	0.049
<i>N</i>	187	239	334	252
Age-adjusted proportions of current smoker (%)	8.9	12.2	12.8	14.4
<i>P</i> for difference	(reference)	0.308	0.201	0.086

in the normal population, especially among men. In the present multicenter study, we found a positive association between a history of diabetes mellitus and idiopathic SSNHL severity (Kitoh et al. [6], in this special issue) that is strongly indicative of a correlation between diabetes and idiopathic SSNHL. Thus, this association is not only related to the development of the disease but also to the severity of idiopathic SSNHL.

In addition to diabetes mellitus, the proportion of current smokers in the idiopathic SSNHL patients was relatively higher in men over 50 years and women aged 30–49 and 60–69 years (Figure 3). Current smoking also tends to be associated with the severity of idiopathic SSNHL, but this tendency was not significant in women (Table 5). As for smoking, a smoking habit was shown to be significantly associated with the risk of idiopathic SSNHL in a meta-analysis; OR = 1.34, 95%CI = 1.12–1.61 [4], and our results were consistent with this previous finding.

The strength of the present study was that we used data from a nationwide epidemiological survey of hearing disorders. In the present study, we dealt with a large number of cases of idiopathic SSNHL, which allowed us to compile

detailed data stratified by sex and age group, and evaluate the association between cardiovascular risk factors and the severity of idiopathic SSNHL.

Some limitations to the present study warrant discussion. First, we used data collected in large hospitals and medical centers. Therefore, our results may lack generalizability. Second, we have no precise data concerning each disease, such as hemoglobin A1c (HbA1c) or blood sugar for diabetes mellitus. In addition, we also have no information regarding treatment. Therefore, we could not examine the association between the severity of or treatment for each disease and idiopathic SSNHL. Finally, the present study is cross-sectional in design, and therefore does not prove causal relationships.

In conclusion, the present study showed the distribution of cardiovascular risk factors in patients with idiopathic SSNHL and found significantly higher proportions of current smokers among both idiopathic SSNHL men and women and proportions of those with a history of diabetes mellitus among idiopathic SSNHL men compared with controls from the National Health and Nutrition Survey in Japan. The present study also showed a positive association



between a smoking habit in men and idiopathic SSNHL severity.

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### Disclosure statement

The authors declare that they have no competing interests.

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