Estimation of Tinnitus Risk in a Community: The Yakumo Study

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Abstract

Background: Tinnitus is an unpleasant symptom, and its prevalence among the elderly is very high. We conducted annual examinations of people in a community using a health survey with an additional item on tinnitus to investigate the risk factors within this community.

Methods: We conducted a cross-sectional study of 510 Japanese citizens (215 men, 295 women) who attended a health examination. A self-report questionnaire including items on tinnitus and a hearing test were administered. For the examination, body weight, body mass index, body fat percentage, and systolic and diastolic blood pressure were measured. A blood examination included counts of red and white blood cells as well as platelets, and measures of hemoglobin, total protein, total cholesterol, creatinine, blood urea nitrogen, uric acid, and serum calcium.

Results: A logistic regression analysis revealed that subjective hearing loss, vertigo, and a high level of serum calcium were associated with tinnitus after adjustment for age and sex. There was a significant correlation between subjective hearing loss and pure tone audiogram results.

Conclusions: Hearing loss, vertigo, and serum calcium level are independently associated with subjective tinnitus.

Background

Subjective tinnitus is a common symptom among the elderly. Tinnitus is the sensation of sound perceived by a single person, regardless of external sound stimuli[1]. Tinnitus is a symptom, not a disease. It is not considered to be a single-factor condition, but rather a complex one involving various intrinsic and extrinsic factors. Hearing loss, stress, and noise exposure are well-known risk factors for tinnitus. Tinnitus is one of the most common complaints in hospitals and clinics, and its association with hearing loss has been reported in 85–96% of patients[2]. In a study in Baltimore of adults aged 70 years and older, the prevalence of significant age-related hearing loss in the better hearing ear was 63.1%[3]. Because elderly people often lose hearing in the high-frequency range owing to aging, tinnitus is likely to occur.

Although hearing loss is one of the most common factors associated with the onset of tinnitus, many people are unaware of it despite their hearing loss; conversely, some complain of tinnitus without apparent hearing loss. Tinnitus with sensorineural hearing loss exhibits a more complex pathophysiology; it becomes more painful for patients and is more difficult for clinicians to treat. It is known that a decrease in peripheral input because of hearing loss causes an increase in central activity and causes tinnitus in the center. In addition, anxiety, pain, and stress enhance the effect, thereby continuing and exacerbating the tinnitus.

The measurement of tinnitus remains very controversial, and there are no widely used standard audiological measurements. Otologic and psychoacoustic tests may help with clinical diagnosis and

treatment choices but are insufficiently sensitive or specific to measure the quality of life impairments caused by tinnitus. Many studies have described [4–7] the impact of tinnitus on an individual's quality of life, and even without effective treatment, the adverse effects of tinnitus on a patient's quality of life may decrease. Scientific knowledge of tinnitus is essential for evaluating and determining the most appropriate clinical treatment. Moreover, research on the effects of tinnitus may enhance the quality of life of affected individuals. Here, we examined the risk factors for tinnitus based on health examinations of residents of a community.

Methods

The subjects were healthy volunteers who attended an annual health examination in the town of Yakumo in Hokkaido, Japan over 38 years. These examinations are supported by the local government (the Yakumo study)[8]. A cross-sectional study was performed of 510 subjects (215 men and 295 women, average age: 63.8 years, range 40–91 years).

Self-report questionnaire

A detailed questionnaire including questions on health problems and lifestyle was sent to the participants before the health examination. In 2019, the questionnaire included the question, "Do you have tinnitus?" This study includes the 510 questionnaire respondents who agreed to participate, and who responded "no," "sometimes," or "always" to the tinnitus question.

Audiological assessment

An examination of the ears, nose, and throat was performed by an otolaryngologist before the hearing test. Hearing levels were evaluated using an audiometer (Model AA-79S; Rion, Tokyo, Japan) in a quiet room by two speech therapists. The noise level in the examination room was measured every hour using a sound level meter (Rion NL-20; Rion). The equivalent continuous sound level ranged from 41.1 to 53.9 dB with an average of 45.0 dB. Bilateral hearing levels were measured at 1,000 and 4,000 Hz. The average hearing level was expressed as the average score on the worst side at 1,000 and 4,000 Hz.

Measured items

Body weight, body mass index, body fat percentage, and systolic and diastolic blood pressure were measured. The blood test included counts of red and white blood cells and platelets; hemoglobin, total proteins, triglycerides, high density lipoprotein cholesterol, low density lipoprotein cholesterol, creatinine, blood urea nitrogen, uric acid, serum calcium, aspartate transaminase, alanine aminotransfenase, alkaline phosphatase, C-reactive protein, and γ-glutamyl transpeptidase were also evaluated.

For the statistical analysis, a chi-square test, Student's *t* test, Mann–Whitney U test, multivariate logistic regression, and multiple regression analysis were performed, and Pearson correlations calculated using SPSS 26.0 (SPSS Inc., Chicago, IL, USA). Statistical significance was set at $p < 0.05$.

Results

The characteristics of the 510 subjects (295 women, 215 men) are shown in Table 1. The mean age of the participants was 63.8 (range, 40–91) years. A total of 175 subjects (34.3%) reported having “sometimes” or “always” subjective tinnitus. Hearing data were obtained from 396 of the 510 participants.

Almost all examinees reported that noise was not a concern when their hearing was measured, regardless of sex or age. The subjective tinnitus group showed significantly worse hearing levels at 1,000 kHz and 4,000 kHz. Moreover, the subjective tinnitus group presented significant differences among difficulty of conversation, vertigo, and headache in the self-reported questionnaire, and there were also significant differences in total protein and serum calcium level. Difficulty of conversation includes two questions: “Can you hear one-to-one conversations?” and “Can you hear conversations between four or five people?” without a hearing aid. They responded “completely,” “mostly,” “not much,” or “almost nothing” in the questionnaire. “Not much” and “almost nothing” were set as the group with difficulties in conversation.

No significant differences were found in the other questions and measured items, including body weight, body mass index, body fat percentage, systolic and diastolic blood pressure, hemoglobin, albumin, albumin/globulin ratio (A/G ratio), and creatinine. The percentages of replies for the difficulty of conversation in each age group are shown in Figs. 1 and 2. More difficulty was perceived in hearing group conversations than one-to-one conversations, and the older the person, the more difficulty they found in hearing conversations.

The percentages of hearing levels in worst ears for each age group are shown in Figs. 3 and 4. Hearing levels at 4,000 Hz were worse than those at 1,000 Hz for all age groups. As age increased, hearing tended to worsen. There is a significant positive correlation between the difficulty of conversation and worse hearing. The correlation coefficient between hearing one-to-one conversations and hearing level at 1,000 Hz was 0.384 ($p < 0.001$); at 4,000 Hz it was 0.253 ($p < 0.001$). The correlation coefficient between conversations with four or five people and hearing level at 1,000 Hz was 0.282 ($p < 0.001$); at 4,000 Hz it was 0.292 ($p < 0.001$).

Table 2 shows multivariable-adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for subjective tinnitus. Subjects were divided into three groups: group 1 had responded “no” and was compared with those who responded “sometimes” or “always”; group 2 responded “no” or “sometimes” and was compared with those who responded “always”; and group 3 responded “no” and was compared with those who responded “sometimes” and “always.” ORs and 95% CIs for subjective tinnitus in group 1 were significant among worse hearing levels at 1,000 Hz, 4,000 Hz, one-to-one conversations, conversations between four or five people, and vertigo, headaches, total protein, globulin, and calcium levels in an age- and sex-adjusted model, with significantly higher ORs and 95% CIs (difficulty of one-to-one conversation: OR, 8.360; 95% CI: 2.312–30.221). ORs and 95% CIs for subjective tinnitus in group 2 were significant for worst hearing levels at 1,000 Hz, hearing levels at 4,000 Hz, one-to-one conversations, conversations

between four or five people, vertigo, and headaches in an age- and sex-adjusted model, with significantly higher ORs and 95% CIs (difficulty of one-to-one conversation: OR, 12.213; 95% CI: 4.050–36.836).

Table 3 shows the results of a multivariate analysis by stepwise regression for subjective tinnitus. Difficulty of one-to-one conversation, vertigo, headaches, serum globulin and serum calcium levels, age, and sex were selected as independent variables, because they had stronger correlations than the other variables. Difficulty of one-to-one conversation, vertigo, serum globulin level, serum calcium level, and age were identified as independent and significant risk factors for subjective tinnitus.

Discussion

In the present cross-sectional analysis of a general Japanese population, we found a significant positive relationship between subjective tinnitus and hearing, difficulty of conversation, vertigo, serum globulin level, and calcium level. Furthermore, the relationship was independent after adjustment for age and sex. It is well known that hearing loss and vertigo are related to tinnitus; however, serum globulin and calcium as related factors have not been reported. Tinnitus and hearing loss are very closely related, and the results of this study confirm this strong association. For those who complained of tinnitus, the OR was particularly high for the questionnaire item “difficulty of conversation,” and this was found to be more strongly related to tinnitus than the result of the hearing test, which is a more objective index. It is considered that self-reported hearing impairments are affected by speech discrimination or cognitive abilities, which tend to deteriorate in elderly people. Subjective hearing studies can be affected by many factors, including sensory cell function [9], general health [10], symptom severity [11], culture [12], expectations [4], and labor market participation [11] and can be difficult to interpret. A cross-sectional study of young and middle-aged people in Sweden reported that the overall prevalence of PTA hearing loss was lower than that of subjective hearing impairment [13]. In addition, it was noted that self-reported hearing difficulties underestimated the number of people with hearing loss in those 70 years or older, those with a low poverty index ratio, and those with low education levels [14].

Hearing loss is one factor that causes tinnitus, but it is thought that tinnitus may be more easily noticed if the person is aware of hearing loss. It is known that anxiety, pain, and stress cause tinnitus to be felt strongly, and patients with subjective hearing loss may experience these factors. This study included some cases of asymmetric hearing, but the ear with the worst hearing was selected and analyzed. In those patients with asymmetric hearing loss, tinnitus was only reported to be present or was louder in the worst affected side [2].

Dizziness is associated with tinnitus in inner ear diseases such as Meniere’s disease. Tinnitus was reported by 94% of the members of the Finnish Meniere’s Association and was listed as a significant symptom by 37% [6]. A questionnaire survey of cases of Meniere’s disorder-related diseases suggests that mitigation of balance and hearing problems should be included to reduce the severity of tinnitus for those with Meniere’s disease [7].

This study found an association between subjective tinnitus and elevated serum globulin levels. There was no association with serum albumin level and A/G ratio. Globulin includes immunoglobulins and is associated with inflammation. The serum A/G ratio represents a medium- to long-term inflammatory status and was correlated with serum CRP levels [15]. As CRP is known to be an independent explanatory factor for the Japanese version of the Montreal Cognitive Assessment (MoCA-J) scores, similar to the serum A/G ratio, inflammation may be involved in the association between serum A/G ratio and cognitive function. Cognitive functions may also be involved in the formation of complex tinnitus.

This study also found an association between subjective tinnitus and elevated serum calcium levels. There is a calcium ion regulation mechanism in the inner ear, and calcium ions flowing from voltage-dependent calcium channels bind to otoferlin and act on synapses. Calcium channels play an important role in auditory reception. Studies on calcium channel blockers as a therapeutic agent for hearing loss have been conducted. Impaired calcium regulation in the inner ear is widely recognized as the cause of noise impairment. In animal studies, it has been reported that nifedipine [16], T-type calcium blocker [17], and L-type calcium blocker [18] reduce hair cell loss due to acoustic trauma. In addition, it has been reported that T-type calcium blockers are involved in the maintenance of spiral ganglion neurons in animals with age-related hearing loss [19]. Although intracellular calcium and serum calcium behave differently, it is possible that the metabolism of calcium and phosphorus has some influence on subjective tinnitus. Calcium is also known to be associated with cognitive function in addition to hearing loss. High intakes of calcium, potassium, and magnesium were reported to reduce the risk of dementia [20]. In another study, sufficient intakes of carotene, vitamin B2, pantothenate, calcium, and vegetables could help prevent cognitive decline among elderly men with diabetes mellitus [21]. In addition, increased calcium consumption was associated with improved cognition among elderly people, which was evaluated using the mini-mental state examination (MMSE) score during an 8.5-month follow-up [22]. Calcium is closely related to deafness and other nerve and cognitive functions.

We investigated the risk factors for subjective tinnitus in a general population. Although hearing loss, vertigo, serum globulin, and calcium levels were shown to be the main risk factors, these account for only about 10% of the total. It has long been known that hearing loss and vertigo are associated with tinnitus, but there have been no reports of serum globulin and calcium levels as possible related factors. Future work should include prospective cohort studies to examine the range of factors causing tinnitus.

Limitations

All of the participants in this study were middle-aged to elderly people who were likely to be more interested in health issues and available for mass screening, which may have biased the results. However, the study is cross-sectional, making causative relationships impossible to determine. Furthermore, because tinnitus is most often a subjective complaint without a means of objective diagnosis, comparisons between participants and studies are difficult.

Conclusions

We investigated the factors affecting subjective tinnitus using a questionnaire and blood data obtained from general public health examinations in Yakumo, Hokkaido. Deafness, dizziness, and serum calcium levels were significantly associated with subjective tinnitus. Although there have been many reports on hearing loss and dizziness, the relationship between serum calcium levels and tinnitus should be clarified. Calcium is an important ion present in the inner ear and may have some effect on subjective tinnitus.

Abbreviations

A/G ratio: albumin/globulin ratio; ORs: odds ratios; CIs: confidence intervals

Declarations

Acknowledgements

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Authors' contributions

TY coordinated the overall study. TN[2] and MS were involved in the concept and the design of the study. AY contributed to the audiological tests. NK and TN[4] contributed to the acquisition and the interpretation of the data, revised the manuscript and approved the final version of the article.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Nagoya University School of Medicine. (approval number 2014–0207). All participants approved publication of data on condition of anonymity and provided signed consent.

Consent for publication

Not Applicable.

Competing interests

The authors have no conflicts of interest to declare.

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Tables

Table 1: Characteristics of study subjects by subjective tinnitus

	subjective tinnitus		
	yes	no	*p*-value
	(n = 175)	(n = 335)	
Women, n / %	106 / 60.6	189 / 56.4	0.396 [b]
Age, years [a]	63.9 (9.7)	63.8 (10.0)	0.904 [c]
Worse hearing level, dB			
1,000Hz	33.6	31.8	0.007 [d]
4,000Hz	39.9	37.5	0.044 [d]
Difficulty of conversation			
One to one, n / %	12 (6.9)	3 (0.9)	<0.001 [b]
between 4 or 5 people, n / %	24 (13.7)	8 (2.4)	<0.001 [b]
Vertigo, n / %	63 / 36.6	53 / 15.9	<0.001 [b]
Headache, n / %	24 / 55.8	19 / 44.2	0.004 [b]
Hemoglobin, g/dL [a]	13.31 (1.25)	13.49 (1.28)	0.134 [c]
Total protein, g/dL [a]	7.21(0.42)	7.12 (0.38)	0.015 [c]
Albumin, g/dL [a]	4.36 (0.25)	4.36 (0.25)	0.846 [c]
Globulin, g/dL [a]	2.85 (0.39)	2.76 (0.36)	0.015 [c]
Calcium, mg/dL [a]	9.10 (0.34)	9.03(0.33)	0.018 [c]
Creatinine, mg/dL [a]	0.75 (0.17)	0.77 (0.18)	0.399 [c]

[a] Data are expressed as mean value (standard deviation).

[b] Pearson's chi-square test

[c] Student's *t*-test

[d] Mann-Whitney U-test

Table 2

Multivariable-adjusted odds ratios and 95% confidence intervals for subjective tinnitus

		Adjusted ORs (95%CIs)	*p* value
Worse hearing level			
1,000Hz	group 1	1.031 (1.003–1.061)	0.031
	group 2	1.060 (1.028–1.092)	<0.001
4,000Hz	group 1	1.021 (1.002–1.041)	0.03
	group 2	1.051 (1.025–1.079)	<0.001
Difficulty of conversation			
One to one	group 1	8.360 (2.312–30.221)	0.001
	group 2	12.213 (4.050–36.836)	<0.001
between 4 or 5 people	group 1	6.916 (3.005–15.918)	<0.001
	group 2	4.820 (2.059–11.282)	<0.001
Vertigo	group 1	3.045 (1.979–4.685)	<0.001
	group 2	3.421 (1.765–6.632)	<0.001
Headache	group 1	2.717 (1.399–5.278)	0.003
	group 2	3.341 (1.195–9.340)	0.021
Total protein	group 1	1.748 (1.092–2.797)	0.02
	group 2	1.789 (0.844–3.790)	0.129
Globulin	group 1	1.842 (1.127–3.013)	0.015
	group 2	1.823 (0.850–3.911)	0.123
Calcium	group 1	1.886 (1.086–3.274)	0.024
	group 2	2.345 (0.992–5.540)	0.052

Group 1: Subjective tinnitus (no vs sometimes or always), Group 2: Subjective tinnitus (no or sometimes vs always)

*adjusted for sex and age.

Table 3

Multiple linear regression analysis results for subjective tinnitus

Scale	Determinant	*p* value	B±s.e.	R^2
Group 1	vertigo	<0.00	0.23±0.43	0.09
	Difficulty of conversation	<0.01	0.41±0.12	
	globulin	<0.01	0.14±0.05	
Group 2	Difficulty of conversation	<0.00	0.42±0.07	0.10
	vertigo	<0.01	0.09±0.03	
	age	<0.01	0.00±0.00	
Group 3	vertigo	<0.00	0.30±0.06	0.12
	Difficulty of conversation	<0.00	0.86±0.16	
	globulin	<0.05	0.16±0.07	
	calcium	<0.05	0.18±0.08	

Group 1: Subjective tinnitus (no vs sometimes or always), Group 2: Subjective tinnitus (no or sometimes vs always),

Group 3: Subjective tinnitus (no vs sometimes vs always)

Figures

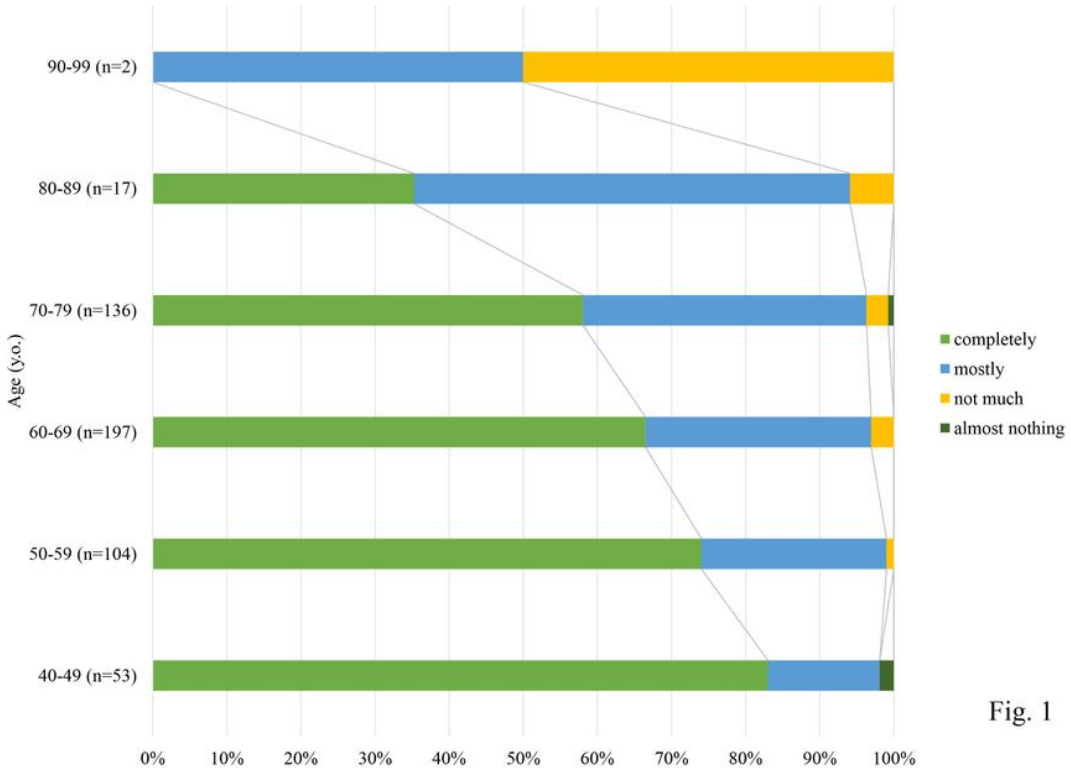

Figure 1

Percentage of respondents who reported difficulties in one-to-one conversation by age

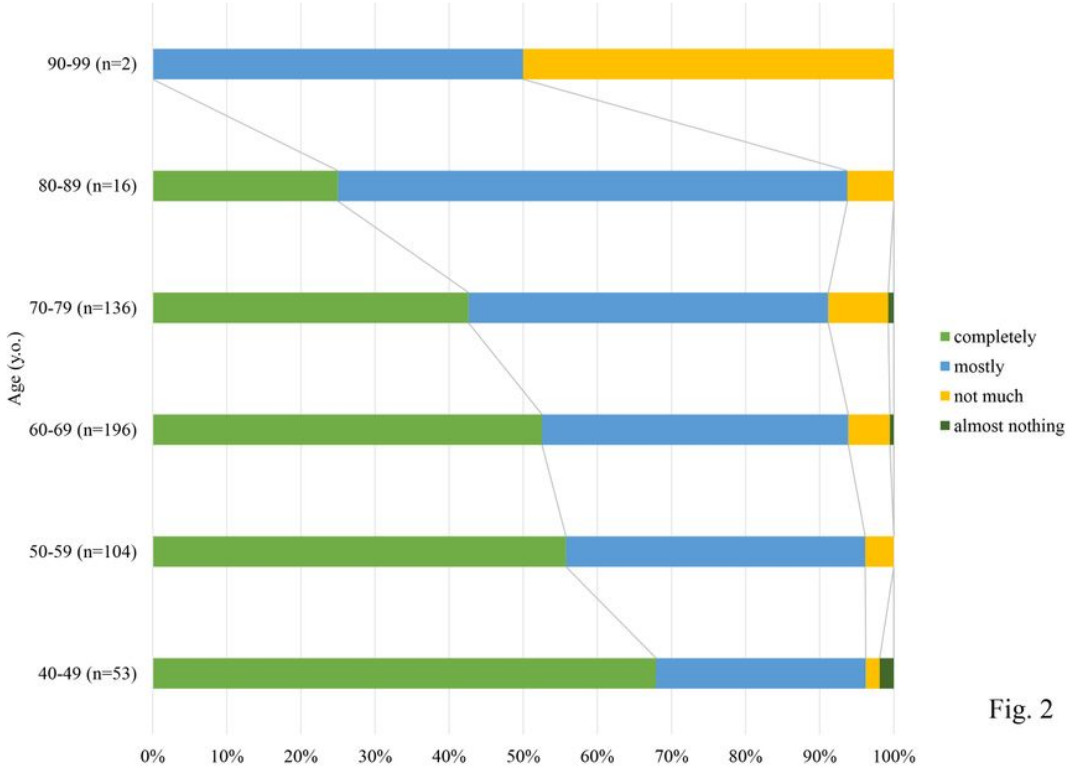

Figure 2

Percentage of respondents who reported difficulties in conversations between four or five people by age

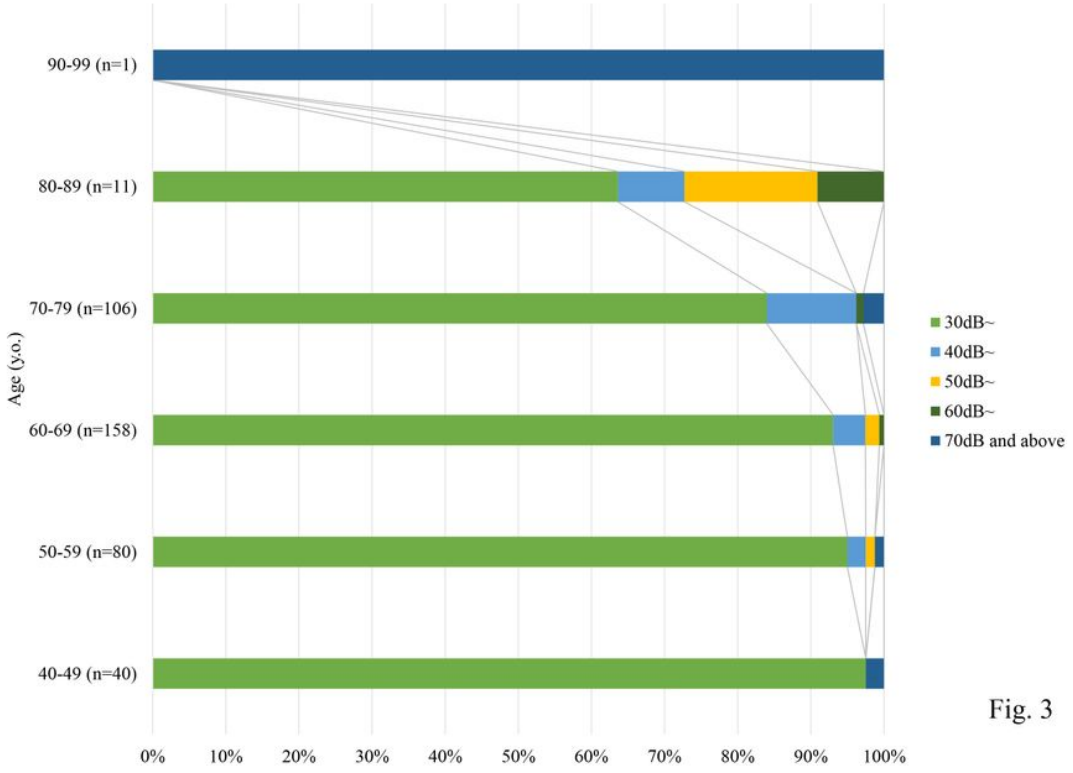

Figure 3

Percentage of hearing levels at 1,000 Hz in the worst hearing ear by age

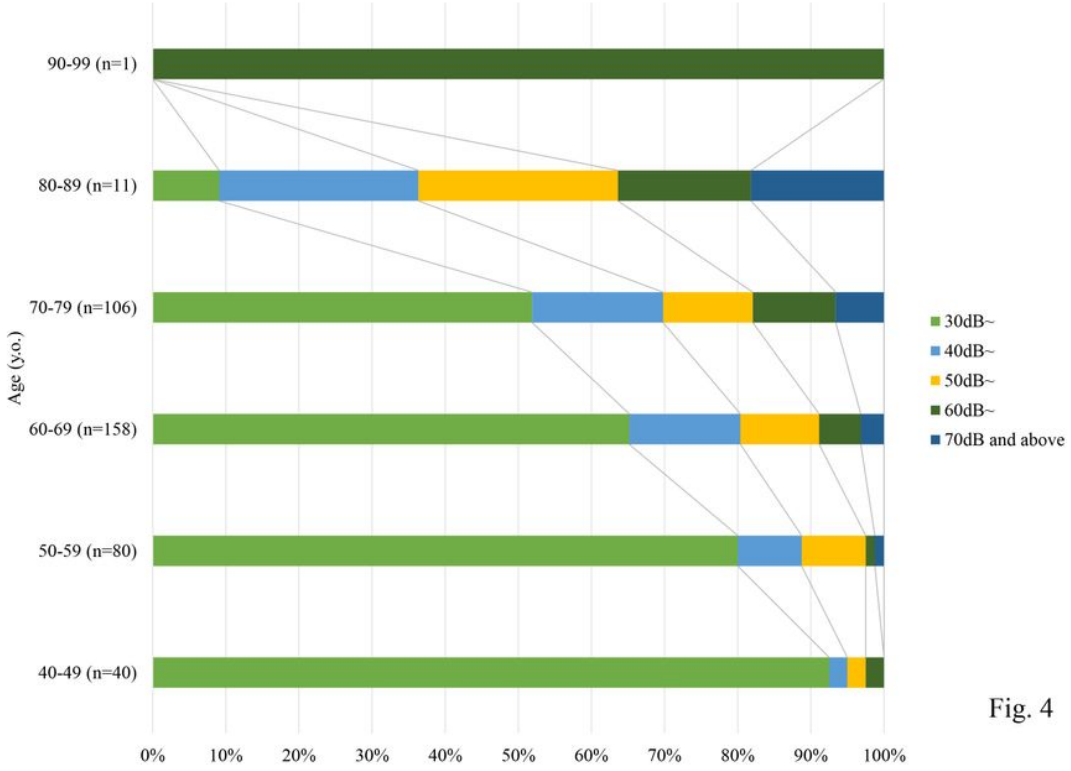

Figure 4

Percentage of hearing levels at 4,000 Hz in the worst hearing ear by age