Patterns of hearing changes in women and men from denarians to nonagenarians

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\section*{Abstract}

\textbf{Background:} Hearing loss needs to be diagnosed and treated early, especially in older individuals, since presbycusis potentially increases the risk of depression and dementia. However, standard data on hearing thresholds across the life-span in Japanese individuals are lacking.

\textbf{Methods:} In a retrospective consecutive sample of 10681 native-Japanese speakers (37.3\% men; 10–99 years; left-right hearing threshold difference of \textless{} 1.5 dB for all tested pure tones; free of external, middle, or inner ear disease), we determined standard age-decade and sex-specific pure-tone air-conduction (125, 250, 500, 1000, 2000, 4000, and 8000 Hz) hearing threshold norms. The main outcome measures were pure-tone averages for both ears by age-decade and sex.

\textbf{Findings:} For participants in their 20s, hearing thresholds at higher frequencies (\textgreater{}1000 Hz) were significantly worse in men than in women. For participants \textgeq{}70 years, hearing thresholds at low frequencies were higher in women. Hearing thresholds at 1000, 2000, and 4000 Hz tended to deteriorate, starting in the teenage years through the 50s, with some decades showing significantly worse decline. Sex differences were absent in the youngest and oldest groups.

\textbf{Interpretation:} Standard age- and sex-specific audiometric data reported here for Japanese individuals over nine age-decades are based on the largest dataset analyzed to date. While hearing thresholds of men and women in the very young and the very old age groups were indistinguishable in their cohorts, patterns of hearing changes for other age cohorts differed by direction and sex.

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\section*{Research in Context}

\textbf{Evidence before this study}

Many clinicians recognize that normative hearing data are crucial for all age groups and both sexes, and are essential for describing the normal course of clinical conditions in a community and for developing standards of care. Comparing a patient’s standard hearing data (e.g., pure-tone air- and bone-conduction thresholds) to a large sample of his/her healthy age-cohort in their community makes it possible to identify and treat abnormal declines. To the best of our knowledge, such a standard data set is lacking for native-speaking Japanese people in Japan, especially for individuals in their 80s and 90s.

While many hearing-sensitivity studies sampling hundreds to thousands of different-aged subjects have provided much insight into sex- and age-specific hearing loss, these studies used different hearing-test parameters (e.g., range of frequencies) and hearing-loss definitions. Moreover, some studies sampled only older people, which makes it impossible to determine when hearing-thresholds first deteriorate. Finally, some studies had very few subjects 80 years and older and failed to exclude subjects with external, middle, or...
inner ear diseases, which can affect hearing thresholds more than aging.

**Added value of this study**

In this study, we analyzed standard audiogram data retrospectively acquired in a homogeneous population of over 10 000 Japanese men and women between the ages of 10 and 99 years; all were ear-disease free. Three major insights can be drawn from the results: (1) Average hearing thresholds at 1000, 2000, and 4000 Hz tended to increase progressively in the 10–19 years group through the 50–59 years group, but starting in the 20–29 years group, thresholds at higher frequencies were significantly higher in men than in women; (2) women 70 and older had higher thresholds at low frequencies than did men of the same ages; (3) in the oldest of old group (90–99 years) and the youngest group (10–19 years), sex differences were virtually absent across low and high frequencies.

**Implications of all the available evidence**

Our average hearing-threshold data of individuals across the life-span could serve as an objective reference for research and to distinguish age-related hearing loss from other disease-related loss in the clinic. Given that the oldest old is the fastest growing demographic group worldwide, and that individuals with hearing loss in this group are disproportionately at-risk for dementia, use of these standard data to intervene appropriately with hearing-aid devices may represent one way to markedly decrease the global burden of dementia.

**1. Introduction**

Generally, hearing thresholds increase with advancing age [1], and this progression eventually declines into presbycusis [2]. Presbycusis is becoming a public health issue in Japan, given the acceleration of population aging there, which is the highest in the world [3,4]. Similar demographic trends have been emerging in Western countries [5].

Hearing loss not only impairs communication but also increases the risk of depression and dementia [6–10]. Also, age by itself is the greatest risk factor for dementia [3,9]. Livingston reported that hearing loss is the highest modifiable risk factor of dementia among various factors [6]. However, hearing loss is not always identified early on or treated [2,11]. One reason is that clinicians have difficulty judging how poor a patient’s hearing ability is compared to the average hearing ability of their age cohort.

Many clinicians recognize that normative hearing data are crucial for all age groups [13,14] and both sexes [15], and are essential for describing the normal course of clinical conditions in a community and for developing standards of care [16]. Comparing a patient’s standard hearing data (e.g., pure-tone air- and bone-conduction thresholds) to a large sample of his/her healthy age-cohort in their community makes it possible to identify and treat abnormal declines [16]. To the best of our knowledge, such a standard data set is lacking for native-speaking Japanese people in Japan, especially for individuals in their 80s and 90s.

While many hearing-sensitivity studies sampling hundreds to thousands of different-aged subjects have provided much insight into sex- and age-specific hearing loss [14,17–23,31], these studies used different hearing-test parameters (e.g., range of frequencies) and hearing-loss definitions [24]. Moreover, some studies sampled only individuals older than 48 years [17], which makes it impossible to determine when hearing-thresholds first deteriorate. Finally, some studies had very few subjects 80 years and older and failed to exclude subjects with external, middle, or inner ear diseases, which can affect hearing thresholds more than aging.

Our goal was to establish a standard hearing-sensitivity data set of native Japanese-speaking people who were 10–99 years of age and free of ear disease. In this cross-sectional study, we asked the research question: What is the age-decade-specific and sex-specific pattern of changes in pure-tone average hearing thresholds (from 125 to 8000 Hz)? More than 10 000 patients’ air- and bone-conduction audiometric results were available for analysis, including those of 134 nonagenarians. To our knowledge, this is the largest such study to date and is the first to report precise details of hearing sensitivity differences in Japanese people over a large span of ages.

**2. Methods**

**2.1. Study design and study sample**

We conducted a retrospective cross-sectional study of 10 681 patients in Japan from a consecutive sample of 30 147 patients. To be eligible for inclusion, patients had to be native-Japanese speakers between 10 and 99 years old, and visit the department of otolaryngology at National Hospital Organization Tokyo Medical Center from April 2000 to March 2020 for various reasons. We excluded patients who had a left-right ear hearing-threshold difference of ≥15 dB at 250, 500, 1000, 2000, and 4000 Hz; had an air-bone gap of >10 dB; or had verified external, middle, or inner ear disease that affected the patients’ hearing. To exclude bias due to outliers, we also excluded data of patients who had hearing thresholds that deviated from the population means by more than ±0.5 SD. Patient audiometric and demographic data, otoscopic finding, and clinical diagnosis were obtained from electronic medical records. This study was approved by the Tokyo Medical Center’s Institutional Review Board (IRB No. R20-087), and written informed consent was waived because of the study’s retrospective design. Included patients and their data were de-identified [28]. We collected participants’ age at the time of audiometric testing.

**2.2. Hearing exam and pure-tone audiometry**

The hearing examination consisted of an otoscopic evaluation and pure-tone air- and bone-conduction audiometry. Audiometric testing was conducted according to the guidelines of the Japan Otolaryngological Society [29]. Masking was used as necessary. Pure-tone air- and bone-conduction audiometric thresholds were obtained using calibrated clinical audiometers (model #’s AA-H1, AA-M1A, AA-75, and AA-97; RION Co., LTD., Tokyo, Japan) in a soundproof chamber dedicated to conducting hearing tests. Audiometers were calibrated annually to ensure the accuracy and consistency of the data. All patients received audiometric testing after otoscopic evaluation by an otolaryngologist. We did not determine why the pure-tone audiometry was performed, because in many cases there was no reason given in the chart.

Pure-tone audiometry was performed for each ear. Pure-tone air-conduction hearing thresholds (decibels hearing level, [dB HL]) were measured at 125, 250, 500, 1000, 2000, 4000, and 8000 Hz (resolution: 5 dB). Bone-conduction hearing thresholds were measured at 250, 500, 1000, 2000, and 4000 Hz. Pure-tone averages were calculated separately by sex and age-decade or half-decade: 10–19, 20–29, 30–39, 40–49, 50–54, 55–59, 60–64, 65–69, 70–74, 75–79, 80–84, 85–89, and 90s. If a patient underwent pure-tone audiometry multiple times, the mean age at each test and mean hearing threshold for each frequency were used to avoid sampling bias resulting from counting the same patient multiple times. We evaluated gender differences per age group using Welch’s t-tests.

**2.3. Hearing threshold shifts by age and sex**

Visual inspection of the audiograms by age appeared to show that hearing thresholds for men and women changed at a nonlin-
ear rate with advancing age. The rate of hearing loss exacerbation as a function of age was approximated by fitting the air-conduction threshold data to a single exponential curve fitting (Supplementary Appendix 1). This approach allowed us to quantify the steepness of the rate of change over time and by sex.

2.4. Hearing threshold comparisons by study decade

We determined whether hearing changed over the 20 years of the study and whether any changes were restricted to certain frequencies or differed between men and women of all ages by comparing the mean hearing threshold between first decade and second decade of this study (Supplementary Appendix 2). Then, we performed time series analysis using a rolling average over five years which were fitted by linear regression.

2.5. Statistical analysis

Statistical analyses were performed using GraphPad Prism 8 (GraphPad Software, San Diego, CA, USA). Descriptive statistics by sex and age group (means, standard deviations [SD], ranges) were calculated to establish the average data set. \( P < 0.05 \) was considered significant. Data for half-decades were presented in figures and tables to display the finer details of group differences. We used Welch’s t-test [30] to compare sex- and each age-decade audiometric data collected in the first and second decades between 2000 and 2020.

2.6. Role of funding source

The authors had no outside funding for this study.

3. Results

A total of 69222 pure-tone audiometry tests were performed on 30147 patients. Of these, 10681 patients met the inclusion criteria. The distribution of included participants stratified by age-decade and sex is presented in Table 1.

3.1. Hearing thresholds by age and sex

Air-conduction audiograms differed by age-decade and sex, and several trends were apparent (Fig. 1A, 1B; Supplementary Appendix Table S1). The general pattern was that hearing thresholds for men and women were progressively higher in older age groups.
at all frequencies, and were disproportionately higher at frequencies >2000 Hz (Fig. 1). For both men and women younger than 30 years, hearing thresholds at all test frequencies were indistinguishable (Table S1), averaging about 10 dB HL. In older age groups, men's hearing thresholds tended to be higher than women's at 2000 and 4000 Hz, while at 8000 Hz their thresholds were similarly high.

For men in their 20s, the mean threshold at 1000 Hz and higher frequencies showed a clear increasing trend (Fig. 1A; Table S1). For men in their 40s, an increasing trend in mean threshold was apparent at lower frequencies (125, 250, 500 Hz). For men younger than 70, hearing thresholds at lower frequencies overlapped (Fig. 1A). This was consistent with results from exponential approximation analysis of threshold shifts versus age-decade (Fig. 2A), indicating that the rate of hearing threshold shifts in men under 70 was similar. Mean thresholds at higher frequencies (1000, 2000, 4000, 8000 Hz) showed an increasing trend (Fig. 1A), with the rate of threshold shifts showing an increasing trend at higher frequencies (Fig. 2A). Mean thresholds at lower frequencies displayed the same increasing trend in men older than 70 (Fig. 2A).

Women showed a different pattern of changes. For women in their 20s and 30s, the mean thresholds showed an increasing trend only at 8000 Hz (Fig. 1B). For women over 30, mean thresholds in the mid-frequency range (1000–4000 Hz) showed an increasing trend, whereas for women over 40, mean thresholds in the low-frequency range (125–500 Hz) showed an increasing trend (Fig. 1B). For women under 70, mean hearing thresholds at 2000 Hz and 4000 Hz overlapped (Fig. 1B), as did their curves in the exponential approximation analysis (Fig. 2B). At lower frequencies (125–500 Hz), women under 70 displayed almost the same increasing trend in threshold shifts (Fig. 2B).

3.2. Hearing threshold shifts by age and sex

Comparison of threshold shifts per age-decade in men and women revealed differences. In men, regardless of age, rate of
threshold shift showed an increasing trend at frequencies above 1000 Hz (Fig. 2A). By contrast, in women this increasing trend was observed at frequencies below 500 Hz and for only those aged >60 years (Fig. 2B). The exponential approximation analysis showed that for men and women under 70, rate of threshold shifts were observed at frequencies between 2000 and 8000 Hz in men (Fig. 2C). In women, however, rate of threshold shifts at 2000 Hz and 4000 Hz were similar (Fig. 2C).

Direct comparison of mean hearing thresholds at all frequencies for men and women stratified by age-decade failed to identify any significant differences for teenaged subjects (Fig. 3, 10–19 years). However, in men older than 20, mean thresholds over 1000 Hz were significantly higher ($p < 1.0 \times 10^{-5}$) than in women over 20. For men and women in their 30s, we observed the largest significant difference in mean thresholds at 1000 Hz ($p < 1.0 \times 10^{-20}$). However, the largest significant difference in mean thresholds was observed at 4000 Hz for men and women in their 40s ($p < 1.0 \times 10^{-20}$). For men and women in their 60s, mean thresholds at lower frequencies (125–500 Hz) were not significantly different. However, for those above 70, women had significantly higher thresholds than men ($p$ values ranged from <0.05 to < $1.0 \times 10^{-20}$ (Fig. 3).

### 3.3. Hearing threshold changes over 20 years of data collection

We observed frequency-specific differences in hearing thresholds in the two decades of the study (Fig. 4). The mean difference in thresholds showed a trend toward being negative at lower frequency (125 Hz) in women and at higher frequency (8000 Hz) in men and women older than 30 (Fig. 4; Supplemental Tables S2, S3), indicating that hearing at those frequencies may have gotten better in the second decade. By contrast, the mean difference in thresholds at 1000, 2000, and 4000 Hz, tended to be positive, indicating that hearing at those frequencies had gotten worse in the second decade. Some of these differences were significant (Fig. 4; Tables S2, S3).

Time series analysis revealed that the threshold at 8000 Hz showed a significantly negative slope in almost all generations. On the other hand, a significantly positive slope was observed in 2000 and 4000 Hz in men and women younger than 50 (Fig. 5; Tables S4, S5).

A similar trend was observed in both comparisons of mean hearing level and time series analysis.

### 4. Discussion

In this study, we analyzed standard audiogram data retrospectively acquired in a homogeneous population of over 10000 Japanese men and women between the ages of 10 and 99 years; all were ear-disease free. Three major insights can be drawn from the results: (1) Average hearing thresholds at 1000, 2000, and 4000 Hz tended to increase progressively in the 10–19 years group through the 50–59 years group, but starting in the 20–29 years group, thresholds at higher frequencies were significantly higher in men than in women; (2) women 70 and older had higher thresholds at low frequencies than did men of the same ages; (3) in the oldest of old group (90–99 years) and the youngest group (10–19 years), sex differences were virtually absent across low and high frequencies. This reference database could be useful for clinicians to aid diagnosis and treatment when hearing is suspected to be worse than normal range.

Our subjects were patients who had standard clinical audiom-etric testing for their regular health checkup; who presented with vertigo, dizziness, tinnitus, or facial palsy that didn’t affect the patients’ hearing; or who desired hearing aids for their self-diagnosed age-related hearing loss (ARHL). Thus, our sample may have included some cases with hearing loss considered to be more severe than normal. Practically, it is nearly impossible to collect the hearing data of the subjects affected purely by age. In previous studies on ARHL [13,14,19,21,22], since evaluation by an otolaryngologist was absent, their audiometric data likely included pa-ients with external, middle, or inner ear diseases or conditions. The audiometric data in the present study came from only patients judged by an otolaryngologist to have normal tympanic membrane findings and, from their medical history, no middle or inner ear
Fig. 5. Time Series Analysis Using a Rolling Average over Five Years. (A) Men. (B) Women. Regression lines were shown only if they were significant (p < 0.05). X-axis labels indicated the middle of five years which were rolled into average. The threshold at 8000 Hz showed a negative slope in almost all generations. On the other hand, a positive slope was observed in 2000 and 4000 Hz in younger than 50.
disease. And we did exclude patients with mean hearing thresholds that deviated from the sample mean by an ±0.5 SD. Thus, we believe our standard database comprised mean hearing-threshold values by age-decade and sex that was fairly representative of the natural course of ARHL. This should make it possible for physicians and patients to objectively assess hearing levels as they change with age.

How might our database be useful for clinical situations? As deafness reduces effective communication, and increases the risk of dementia and depression [6–10], it is important to proactively encourage patients with hearing loss to use amplification devices such as hearing aids or cochlear implants. This is especially important for older patients, since advancing age is the biggest risk factor for developing dementia [32]. The EuroTrak 2018 survey for the UK, Germany, and France (n = 43499) showed that 10.6% of people self-reported hearing loss, and of those, 41.6% reported using hearing aids [33]. While the JapanTrak 2018 survey (n = 13710), found that 11.3% of Japanese people self-reported hearing loss, only 14.4% of them reported using hearing aids [34]. The results of the present study will arm clinicians with an objective tool to examine if the hearing level of the patient is worse than the mean hearing level of his/her age group and he/she could benefit from hearing aids.

Our study included over 1700 people aged 10 to 29 years, confirming that exacerbation of hearing decline at frequencies between 1000 and 4000 Hz begins earlier in men than in women. Consistent with previous reports, hearing thresholds at middle and high frequencies increased at a faster rate in men than in women [14,17–22]. In men, the exacerbation rate at 4000 Hz was higher than that at 2000 Hz but lower than that at 8000 Hz (Fig. 2A). This was manifested in the gentle-sloping shape of the audiograms at those frequencies (Fig. 1A). By contrast, in women, the exacerbation rate at 4000 Hz was similar to that at 2000 Hz but lower than that at 8000 Hz (Fig. 2B), giving the audiogram at 8000 Hz a steep-slope shape (Fig. 1B).

Regarding hearing levels at low frequencies, women in their 70s and older had higher thresholds than men of that age group, which agrees with previous findings [19–22]. Some suggest that this gender difference might be due to atrophy of the stria vascularis [12,35,36], which may be affected more in older women due to hormonal changes associated with menopause [37]. A postmenopausal decrease in female hormones increases circulating levels of vasopressin [38], inducing endolymph hydrops and higher hearing thresholds at low frequencies [39].

In the present study, we observed that hearing thresholds acquired in the first decade of the study (2000–2010) tended to be better than those acquired during the second decade (2010–2020) for one particular age range and frequency range. Subjects aged 10 to 49 years who were tested in the first decade had thresholds at 1000, 2000, and 4000 Hz that tended to be lower than those tested in the second decade, suggesting that noise-induced hearing loss (NIHL) may account for the change. One estimate suggests that about 17% of teens (ages 12 to 19) may have NIHL [40]. Since this deterioration was limited to our younger subjects, chronic noise exposure from portable audio devices such as smart phones, mp3 players [26,27], and other sources might harm hearing in this frequency range, as the WHO pointed out [25].

Societal changes over the twenty-year study period might explain threshold improvements at higher frequencies. In the present study, hearing thresholds at 8000 Hz tended to be lower in subjects tested in the second decade compared to the first. Hu et al. reported an association between smoking and hearing loss, especially at high frequencies, and this risk declined soon after quitting [41]. In Japan, smoking prevalence has dramatically decreased since 2000. The National Health and Nutrition Survey showed that in 2000, 47.4% of men and 9.0% of women were smokers [42]. By 2018, those percentages decreased to 29.0% and 8.1%, respectively [43]. This hypothesis needs to be tested further.

This study has several limitations. First, it was retrospective. Second, the subjects were patients who visited the otorhinolaryngology department at a major general hospital in Tokyo and who underwent pure-tone audiometry for various reasons. Our sample may be limited to the population of urban area around Tokyo and have included some cases with hearing loss considered to be more severe than normal. Third, we excluded data of patients who had hearing thresholds that deviated from the population means by more than ±0.5 SD. Since our department specializes in the research of hereditary hearing loss, many patients who are suffered from hearing loss of unknown origin, are referred for detailed examination including genetic testing. To avoid to include the patients whom we cannot find any genetic cause of hearing loss, we excluded them with this exclusion criteria. Generally, 10 to 20% of subjects were excluded by this criterion.

In conclusion, these average hearing-threshold data of individuals across the life-span could serve as an objective reference for research and to distinguish age-related hearing loss from other disease-related loss in the clinic. Given that the oldest old is the fastest growing demographic group worldwide [44], and that individuals with hearing loss in this group are disproportionately at-risk for dementia [32], use of these standard data to intervene appropriately with hearing-aid devices may represent one way to markedly decrease the global burden of dementia.

Declaration of Competing Interest

The authors have no financial relationships or conflicts of interest to disclose. The authors had no outside funding for this study.

Author contributions

KW conceived and designed this study. KW acquired, analyzed, and interpreted the data. KW drafted the manuscript, and KK and KO substantively revised it. All authors commented on the manuscript and approved the final version.

Data sharing statements

Will individual participant data be available? Yes

What data in particular will be shared? Individual participant data that underlie the results reported in this article, after de-identification (text, tables, figures, and appendices).

What other documents will be available? Study protocol.

When will data be available (start and end dates)? Beginning 3 months and ending 5 years following article publication.

With whom? Researchers who provide a methodologically sound proposal.

For what types of analyses? To achieve aims in the approved proposal.

By what mechanism will data be made available? Proposals and data should be directed to wasano@A5.keio.jp; to gain access, data requestors will need to sign a data access agreement.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.lanwpc.2021.100131.

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