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Low Bone Mineral Density is Associated with Hearing Impairment in Postmenopausal Women

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Running title: Bone Mineral Density and Hearing Status

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Abstract

Objective : We investigated the association between bone mineral density (BMD) and hearing impairment in a nationally representative sample of Korean female adults.

Study Design : Cross-sectional analysis of a nationwide health survey.

Methods : We studied data from the 2009–2010 Korean National Health and Nutrition Examination Surveys (KNHANES), which included 19,491 participants, 8,773 of whom were enrolled in this study. BMD was measured using dual-energy X-ray absorptiometry. Auditory functioning was evaluated by pure-tone audiometric testing according to established KNHANES protocols. We defined hearing impairment as pure-tone averages (PTA) at frequencies of 0.5, 1.0, 2.0, and 3.0 kHz at a threshold of ≥ 40 decibels hearing level (dBHL) in the ear with better hearing status.

Results*:* Among women aged 19 years and older, the prevalences of bilateral hearing impairment in premenopausal and postmenopausal women were 0.1±0.1% and 11.5±1.1% (mean ± SE), respectively. Hearing impairment was significantly associated with low BMD in postmenopausal women. Logistic regression models indicated that lower BMD of the total femur (OR = 0.779; 95% CI = 0.641–0.946, p = 0.0118) and femur neck (OR = 0.746; 95% CI = 0.576–0.966, p = 0.0265) were significantly associated with hearing impairment among postmenopausal women.

Conclusions: Postmenopausal Korean women with low BMD of the total femur and femoral neck showed an increased risk for developing hearing impairment. Further epidemiological and experimental studies are necessary to clarify this association.

Key words: hearing impairment, bone mineral density, epidemiology

Strengths and limitations of this study

- We used a nationally representative, cross-sectional, civilian non-institutionalized sample of Korean adults.

- We evaluated the relationships between BMD and hearing level including various social, economic, behavioral, and health variables on the population-based database

- We were unable to analyze the temporal association between hearing impairment and BMD, which may make our results biased.

Introduction

Osteoporosis has become a major health problem around the world.[1] Approximately 49 million individuals have osteoporosis in North America, Europe, Japan, and Australia.[2] It has been reported that major demographic changes will occur in Asia.[3] Thus, the prevalence and incidence of osteoporosis are expected to increase in this ageing society.[4] Osteoporosis is characterized by the deterioration of the bone microarchitecture and a reduction in the bone mineral density (BMD).[5] Decreased BMD causes demineralization of the skeletal system. Deterioration of the petrous temporal bone, which encases the cochlear capsule and internal auditory canal, may be associated with impaired hearing function.[5-8] Osteoporosis are classically recognized as a significant health care issue in women, but are now increasingly viewed as an important health care problem in men as well.

Adult-onset hearing impairment is the second most common cause of disability among adults in high-income countries.[9] The overall prevalence of audiometric hearing loss among individuals with bilateral hearing loss aged 12 years and older in the United States was 12.7% (30.0 million) between 2001 and 2008, and this increased to 20.3% (48.1 million) when individuals with unilateral hearing loss were included.[10] Hearing impairment can isolate individuals from their social environment, impair psychosocial functioning, impair cognitive skills, increase individual emotional stress, and have negative health effects at the individual and family levels.[11] Furthermore, it has been recently reported that hearing impairment is associated with a risk of depression among adults, particularly women.[12]

Several studies have evaluated the association between BMD and hearing sensitivity. Among rural Caucasian women, it has been reported that low BMD of the femoral neck was associated with hearing impairment.[5] In contrast, no relationship was observed between BMD and hearing impairment among Caucasian or black women; however, black men showed a correlation between BMD of the lower hip and hearing loss.[13,14] There are discrepancies and limitations in previous studies of associations between BMD and hearing impairment, including differences in race, study design, and measurements of hearing impairment. Thus, we sought to evaluate the relationship between BMD and hearing impairment in a nationally representative sample of Korean adults. We hypothesized that hearing impairment was positively correlated with low BMD in the Korean female or elderly male population.

To our knowledge, no nationwide study on hearing impairment, as diagnosed by otolaryngology doctors, and no study on the association between BMD and hearing impairment in an Asian female population have been published. Thus, we investigated association between BMD and hearing impairment in a large representative population sample from the Korean National Health and Nutrition Examination Surveys (KNHANES).

Methods

Study Population

This study was based on data collected in the 2009–2010 KNHANES study conducted by the Division of Chronic Disease Surveillance, which has been under the supervision of the Korea's Centers for Disease Control and Prevention since 1998. The KNHANES is a nationwide survey designed to accurately assess health and nutritional status at the national level. A field survey team, including an otolaryngologist, an ophthalmologist, and nurses traveled with a mobile examination unit and performed interviews and physical examinations. The survey consisted of a health interview, a nutritional survey, and a health examination survey. The survey collected data via household interviews and by direct standardized physical examinations conducted in specially equipped mobile examination centers. The KNHANES methodology has been described in detail previously and further details are listed in "The 5th KNHANES Sample Design" and reports, made accessible on the KNHANES website https://knhanes.cdc.go.kr/knhanes/index.do. The KNHANES annual reports, user manuals and instructions, and raw data are available on request.[15,16]

During 2009–2010, there were 19,491 KNHANES participants. Of these, 10,718 were excluded from the analysis because of at least one of the following reasons: younger than 19 years; did not undergo the otological, BMD, or 25 hydroxy vitamin D tests; or were missing data from the lifestyle questionnaire. The final sample included 8,773 8,773 adults aged 19 years and over men, premenopausal, and postmenopausal women were 3,885, 2,622, and 2,266, respectively. Written informed consent was obtained from all participants prior to the survey. Approval for this study was obtained from the Institutional Review Board of the Catholic University of Korea, Seoul, Korea. (IRB no. HC14EISE0097; Bucheon, Korea).

Bone Mineral Density and Laboratory Measurements

Subjects wore light clothes without shoes and jewelry, which could interfere with the BMD measurements. BMD was measured by trained technicians at mobile examination centers. The BMD values of the lumbar spine (L1–L4), femoral neck, and total femur were measured using dual-energy X-ray absorptiometry (DXA) using a Discovery fan-beam densitometer (Hologic, Bedford, MA, USA) and the Hologic Discovery software (ver. 3.1). To ensure DXA quality control, daily automatic calibration was performed according to the manufacturer's instructions to maintain a precision standard of 1.5% for total hip measurements.

Standing height was measured with the subject looking forward, barefoot, feet together, arms at the sides, and heels, buttocks, and upper back in contact with the wall. Height was measured in centimeters to one decimal point using a calibrated stadiometer (SECA 225 stadiometer, SECA, Hamburg, Germany). Waist circumference (WC) was measured at the level of the midpoint between the iliac crest and the costal margin at the end of a normal expiration to the nearest 0.1 cm. Weight was measured using a mobile scale

(GL-6000-20; Cas Korea, Seoul, Korea) in kilograms to one decimal point. Body mass index (BMI) was calculated as weight (kg)/height (m^2). Blood samples for biochemical analyses and measurement of serum 25-hydroxyvitamin D (25(OH)D) were obtained from all participants, refrigerated immediately, transported to the Central Testing Institute in Seoul, Korea, and analyzed within 24 h.

Audiometric Measurements

Pure-tone audiometric testing was conducted using a SA 203 audiometer (Entomed; Malmö, Sweden). Pure-tone audiometry is a behavioral test used to measure hearing sensitivity. 'Audiometric' means 'measuring the hearing level'. Testing was conducted in a soundproof booth inside a mobile bus reserved for the KNHANES. Otolaryngologists trained to operate the audiometer provided instructions to participants regarding the automated hearing test and obtained the recordings. All audiometric testing was performed under the supervision of an otolaryngologist. Only air conduction thresholds were measured. Air conduction evaluates the whole ear system -- outer, middle, and inner ear. Threshold is defined as the lowest decibel hearing level at which responses occur in at least one half of a series of ascending trials. The minimum number of responses needed to determine the threshold of hearing is two responses out of three presentations at a single level. Supra-auricular headphones were used in the soundproof booth. Supra-auricular' means 'situated above the ear coverts'. Automated testing was programmed according to a modified Hughson–Westlake procedure and involved the use of a single pure tone of 1–2 s. The lowest level at which the subject responded to 50% of the pure tone was set as the threshold. The test–retest reliability and validity of the automated hearing test involving air-conducted pure-tone stimuli was good and comparable to those obtained in the manual pure-tone audio test.[17,18] Participants responded by pushing a button when they heard a tone, and the results were recorded automatically. The frequency ranges tested were 0.5, 1.0, 2.0, 3.0, 4.0, and 6.0 kHz. We defined hearing impairment as pure-tone averages (PTA) of frequencies at 0.5, 1.0, 2.0, and 3.0 kHz at a threshold of ≥ 40 decibel hearing level (dBHL) in the ear with better hearing.[19]

Participants were asked about their experience of tinnitus: 'Within the past year, have you ever heard a sound (buzzing, hissing, ringing, humming, roaring, machinery noise) originating in your ear?' Examiners were instructed to record 'yes' if a participant reported hearing an odd or unusual sound at any time in the past year. Participants who responded positively to this question were then queried about the resulting annoyance in their lives using the following question: 'How annoying is this sound in daily life?' (not annoying/annoying/severely annoying, and causes sleep problems). The participants were considered to have tinnitus if the severity of tinnitus was annoying or severely annoying.

Lifestyle Habits

Data on medical histories and lifestyle habits were collected using self-report questionnaires. Participants were categorized into three groups according to smoking history: current smoker, ex-smoker, and nonsmoker. Subjects who drank more than 30 g of alcohol/day were designated as drinkers. Regular exercise was defined as strenuous physical activity performed for at least 20 min at a time at least three times per week. Participants reported their level of stress as none, mild, moderate, or severe.

Statistical Analysis

Statistical analyses were performed using the SAS survey procedure (ver. 9.3; SAS Institute, Cary, NC, USA) to reflect the complex sampling design and sampling weights of the KNHANES and to provide nationally representative prevalence estimates. The prevalence and 95% confidence intervals (CIs) for BMD were calculated. In the univariate analysis, the

Rao-Scott χ^2 test (using PROC SURVEYFREQ in SAS) and logistic regression analysis (using PROC SURVEYLOGISTIC in SAS) were used to test the association between hearing impairment and risk factors in a complex sampling design. Participants' characteristics are expressed as means and standard errors for continuous variables and as percentages for categorical variables. To examine the association of hearing level and BMD, the participants were divided into quartiles based on levels of BMD (Q1–Q4). Simple and multiple linear regression analyses were used to examine the association between hearing impairment and BMD.

We first adjusted for age and BMI (model 1) and then adjusted for the variables in model 1 as well as for smoking status, alcohol intake, exercise, education, and income (model 2). Model 3 was adjusted for the variables in model 2 and for vitamin D, stress, and tinnitus. P-values were two-tailed, and P values < 0.05 were considered statistically significant.

Results

Of the 4,888 female participants aged ≥ 19 years, 2,622 and 2,266 were premenopausal and postmenopausal, respectively. Table 1 shows baseline characteristics of men, premenopausal and postmenopausal women. The mean age of men, premenopausal, and postmenopausal women was 43.9±0.3, 35.3±0.2 and 62.7±0.3 years, respectively. The prevalence of bilateral hearing impairment in the postmenopausal women was 11.5±1.1% (mean ± SE). Postmenopausal women were less likely to drink alcohol, more likely to have a low income, compared with men and premenopausal women. The mean values of BMI, WC, and vitamin D were higher among postmenopausal women than among premenopausal women. The BMDs of the lumbar spine, total femur, and femoral neck were lower in postmenopausal women than in men premenopausal women. Table 2 shows subject characteristics according to bilateral hearing impairment.

After categorizing subjects into four groups based on the percentage of BMD (quartile 1, with the highest, to quartile 4, with the lowest), we used analysis of covariance (ANCOVA) to investigate hearing level according to BMD quartile at various skeletal sites after adjusting for confounding variables, such as age, body mass index, smoking status, alcohol intake, regular exercise, educational level, income, 25-hydroxy vitamin D, stress level, and tinnitus. Lumbar spine, total femur, and femoral neck BMD in postmenopausal women showed significantly decreased tendencies in hearing level as BMD decreased in quartiles ($P < 0.0001$; Fig. 1). However, the BMD at the lumbar spine ($P = 0.570$), total femur ($P = 0.358$), and femur neck ($P = 0.268$) of premenopausal women showed no statistically significantly association with hearing level. Also those of men showed no statistically significantly association with hearing level.

Table 3 shows the relationship between hearing impairment and BMD using logistic regression models. In the final regression model for hearing impairment, the BMDs of the total femur (OR = 0.779; 95% CI = 0.641–0.946) and femoral neck (OR = 0.746; 95% CI = 0.576–0.966) were significantly associated with hearing impairment among postmenopausal women after adjusting for age, body mass index, smoking status, alcohol intake, regular exercise, educational level, income, vitamin D, stress level, and tinnitus (Model 3). BMD at the lumbar spine (OR = 0.525; 95% CI = 0.279–0.989) was also significantly associated with hearing impairment in premenopausal women. BMD at the total femur, and femoral neck in men and premenopausal women did not show a significant correlation with hearing impairment. To determine the associations in between hearing impairment and BMD at various skeletal sites, simple linear logistic regression analysis was performed after adjusting for age, BMI, smoking status, alcohol intake, regular exercise, educational level, income, 25-hydroxyvitamin D, stress level, and tinnitus. There was no statistically significant correlations in hearing impairment and BMD at any parts of skeletal sites in men, premenopausal and postmenopausal women (Table 4).

Discussion

The primary objective of this study was to examine the relationship between BMD and hearing impairment using a nationally representative sample of the South Korean population. Our findings indicate that low BMDs of the total femur and femur neck were associated with an increased risk for impairment of hearing function in postmenopausal women.

There have been some previous reports that reduced BMD was closely associated with hearing impairment.[5,13] The bone mass of the femoral neck was associated with hearing loss in a population of rural women aged 60–85 years.[5] Another study enrolled 2052 older adults aged 73–84 years using a randomized method. The population was composed of white men (32.2%), white women (30.8%), black men (15.1%), and black women (22.0%). The results showed that the BMD of the total hip was not associated with hearing loss in white men, white women, and black women, but it was in black men.[13] Unlike our results, that study checked only the BMD of the total hip, and the age range and race of the sample also differed from those of ours. However, the study did show that there were differences in hearing impairment by race and gender.

The mechanism of hearing impairment in postmenopausal women with lower BMD may be that demineralization of cochlear capsule of the temporal bone could lead to loss of the delicate stereocilia of the cochlear.[14] The cochlear capsule is located in the petrous portion of the temporal bone. This portion is composed primarily of cancellous bone components.[20] The demineralization of the cochlear capsule has been associated with hearing loss in subjects with bone diseases, such as Paget's disease, otosclerosis, and osteogenesis imperfecta.[7,14,21] Deteriorated auditory function at a specific frequency has been associated with lower BMD within the cochlear capsule.[22] Demineralization of the petrous temporal bone affects the encasing compartment of the cochlear capsule. Spiral ligament hyalinization may be affected by the toxic effects of enzymes released from otospongiotic foci and can lead to hearing impairment.[21] Lower BMD of the petrous portion of the temporal bone can affect the dissipation of cochlear stereocilia and could be a cause of hearing loss in patients with sensorineural hearing loss.[22] This phenomenon supports the occurrence of age-related sensorineural loss and the fact that the severity of cochlear hearing loss is influenced by the extent of cochlear demineralization.[5,23]

Our study showed that differences related to menopause may contribute to relationships between bone mass and hearing impairment. In this respect, it has been reported that estrogen can exert a positive effect on hearing among older women.[24] Furthermore, estradiol treatment may have a positive effect on the ionic homeostasis of the inner ear and the protection of activated intermediated filaments.[25] Thus, the role of estrogen suggests differences in hearing impairment among women, such as those between women at the premenopausal and postmenopausal stages.[26,27] Estrogen may have an important role in the maintenance or repair of sensory epithelia of the inner ear and may act as an auditory protectant.[28-30]

The screening for hearing impairment is important. Because patients, clinicians, family, and healthcare staff often do not recognize hearing loss, particularly in its early stages, this condition may be undertreated.[31] In addition, hearing impairment may favor the development of dementia and cognitive dysfunction in adults aged 65 years and older.[32] Hearing impairment is positively correlated with depression among US adults of all ages, particularly among women and those younger than 70 years.[12] Therefore, screening tests based on risk factors are essential, and physicians should be aware of the possibility of hearing impairment in postmenopausal women.

Our study has several limitations. First, we did not directly measure the BMD of the cochlear capsule of the temporal bone. There are no data on any association of the BMD between the in the petrous portion of the temporal bone and that of the appendicular skeleton. However, previous research has indicated that osteoporosis can affect the skull bones. Patients with hyperthyroid-related osteoporosis suffered from decreased skull bone density, and demineralization of the petrous portion of the temporal bone has been seen in subjects with severe osteoporosis.[33,34] It has been reported that high-resolution computed tomography was useful for checking the association between the BMD of the petrous portion of the temporal bone and hearing loss.[35] Under ideal conditions, the BMD of the petrous portion of the temporal bone would be measured; however, there is no feasible or accurate method for measuring BMD in large populations. Second, we were unable to analyze the temporal association between hearing impairment and BMD. Adequate assessment of the presence of hearing impairment is limited for prolonged periods. Thus, our study is unable to examine hearing variability in these populations. Despite these limitations, however, no previous study has evaluated the association between hearing impairment and low BMD in a representative general female population in Asia. Additionally, these results may be reliable because the data used were obtained from a government-sponsored survey of the national population of South Korea and were qualified by DXA, validated by audiometry tests, and verified by otolaryngologists.

Conclusion

We found that low BMD in the total femur and femoral neck were associated with impaired hearing status in postmenopausal women. Future longitudinal studies with larger sample sizes and controls for potential confounders are needed to confirm the association between hearing impairment and postmenopause.

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Contributors : SSL wrote the first draft of the manuscript and took part in the data analyses. KDH performed statistical analyses. YHJ designed the study and critically revised the manuscript for important intellectual content.

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Data sharing statement : The KNHANES methodology has been described in detail previously and further details are listed in "The 5th KNHANES Sample Design" and reports, made accessible on the KNHANES website https://knhanes.cdc.go.kr/knhanes/index.do. The KNHANES annual reports, user manuals and instructions, and raw data are available on request.

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TABLE 1. SUBJECT CHARACTERISTICS

	Men (n=3885)	Premenopausal women (n=2622)	Postmenopausal women (n=2266)	p-value
Age (years)	43.9±0.3	35.3±0.2	62.7±0.3	<0.0001*
Average hearing level (dB)	19.1±0.4	12.3±0.4	30.6±0.8	<0.0001*
Smoking - Current smoker (%)	45.4±1.0	7.1±0.7	4.6±0.6	<0.0001*
Drinking - Heavy drinker (%)	18.2±0.8	2.6±0.4	0.9±0.2	<0.0001*
Routine exercise (%)	27.3±0.8	21.3±1.0	22.6±1.3	<0.0001*
Body mass index (kg/m^2)	24.1±0.1	22.6±0.1	24.3±0.1	<0.0001*
Waist circumference (cm)	84.0±0.2	74.8±0.3	82.3±0.3	<0.0001*
Education - ≥High school (%)	77.0±0.9	89.7±0.7	20.7±1.3	<0.0001*
Residential area - Urban (%)	80.1±2.3	85.8±2.0	73.2±2.9	<0.0001*
Income - Lower quartile (%)	14.5±0.8	9.6±0.8	33.0±1.4	<0.0001*
Stress – Moderate to severe (%)	27.4±0.9	35.2±1.1	29.8±1.3	<0.0001*
25-Hydroxyvitamin D (ng/ml)	19.8±0.2	16.4±0.2	19.0±0.3	<0.0001*
BMD of lumbar spine (g/cm^2)	0.971±0.003	0.977±0.003	0.807±0.004	<0.0001*
BMD of total femur (g/cm^2)	0.986±0.003	0.905±0.003	0.782±0.003	<0.0001*
BMD of femoral neck (g/cm^2)	0.829±0.003	0.765±0.003	0.626±0.003	<0.0001*

* P < 0.05 was considered to be statistically significant.

TABLE 2. SUBJECT CHARACTERISTICS ACCORDING TO BILATER HEARING IMPAIRMENT

	Bilateral Hearing Impairment		
	No (n= 8214)	Yes (n= 559)	p-value
Age (years)	43.6 ±0.3	69.9±0.6	<0.0001
Average hearing level (dB)	10.5±0.2	57.1±1.5	<0.0001
Smoking - Current smoker (%)	26.3±1.2	19.5±4.5	0.0086
Drinking - Heavy drinker (%)	10.3±0.9	6.7±2.6	0.0311
Routine exercise (%)	24.9±1.4	18.9±3.8	0.0052
Body mass index (kg/m^2)	23.7±0.0	23.8±0.2	0.3586
Waist circumference (cm)	80.7±0.2	83.7±0.5	<0.0001
Education - ≥High school (%)	73.0±1.8	14.6±3.8	<0.0001
Residential area - Urban (%)	81.1±4.5	67.7±8.6	<0.0001
Income - Lower quartile (%)	14.9±1.5	50.0±4.8	<0.0001
Stress – Moderate to severe (%)	30.4±1.3	25.8±5.1	0.0937
25-Hydroxyvitamin D (ng/ml)	18.5±0.2	20.2±0.6	0.0013
BMD of lumbar spine (g/cm^2)	0.947±0.002	0.841±0.008	<0.0001
BMD of total femur (g/cm^2)	0.929±0.002	0.799±0.008	<0.0001
BMD of femoral neck (g/cm^2)	0.778±0.002	0.629±0.008	<0.0001

Data are presented as mean ± SE (standard error)

TABLE 3. MULTIVARIABLE LOGISTIC REGRESSION ANALYSIS OF ADJUSTED ODD RATIOS (ORs) AND 95% CONFIDENCE INTERVALS (CIs) TO DETERMINE THE EFFECT OF BONE MINERAL DENSITY ON HEARING IMPAIRMENT.

	Men	Premenopausal women	Postmenopausal women
Lumbar spine			
Model 1	0.999(0.892-1.118)	0.486(0.276-0.856)	0.921(0.812-1.044)
Model 2	1.052(0.939-1.178)	0.528(0.273-1.020)	0.966(0.849-1.098)
Model 3	1.058(0.937-1.195)	0.525(0.279-0.989)	0.960(0.835-1.103)
Total femur			
Model 1	0.948(0.821-1.095)	0.683(0.323-1.444)	0.804(0.673-0.959)
Model 2	0.985(0.851-1.140)	0.756(0.348-1.640)	0.820(0.686-0.981)
Model 3	1.009(0.855-1.190)	0.758(0.338-1.703)	0.779(0.641-0.946)
Femoral neck			
Model 1	0.874(0.727-1.050)	0.878(0.412-1.868)	0.760(0.608-0.950)
Model 2	0.914(0.761-1.099)	0.970(0.432-2.180)	0.783(0.623-0.984)
Model 3	0.919(0.747-1.130)	0.953(0.400-2.272)	0.746(0.576-0.966)

Model 1 is adjusted for age and body mass index.

Model 2 is adjusted for age, body mass index, smoking status, alcohol intake, regular exercise, educational level, and income.

Model 3 is adjusted for age, body mass index, smoking status, alcohol intake, regular exercise, educational level, income, 25-hydroxyvitamin D, stress level, and tinnitus.

TABLE 4. MULTIVARIABLE LOGISTIC REGRESSION ANALYSIS IN BONE MINERAL DENSITY

	Men			Premenopausal women			Postmenopausal women		
	Beta	SE	p-value	Beta	SE	p-value	Beta	SE	p-value
Lumbar spine									
Model 1	-0.2899	0.2570	0.2604	-0.1820	0.1338	0.1753	-0.0778	0.1560	0.6186
Model 2	-0.0194	0.2472	0.9375	-0.1244	0.1320	0.3471	0.1261	0.1449	0.3847
Model 3	0.0777	0.2517	0.7578	-0.1400	0.1365	0.3063	0.1055	0.1482	0.4772
Total femur									
Model 1	-1.1271	0.3862	0.0038	0.0260	0.1426	0.8553	-0.2160	0.1653	0.1924
Model 2	-1.0141	0.3913	0.0101	0.0034	0.1454	0.8118	-0.0549	0.1586	0.7296
Model 3	-0.8842	0.3892	0.0240	0.0266	0.1511	0.8609	-0.0038	0.1690	0.8201
Femoral neck									
Model 1	-0.8639	0.4739	0.0695	0.1211	0.1328	0.3625	-0.0713	0.1646	0.6650
Model 2	-0.6742	0.4917	0.1716	0.1004	0.1335	0.4528	0.0031	0.1565	0.8409
Model 3	-0.5278	0.4737	0.2663	0.0847	0.1392	0.5433	-0.0006	0.1648	0.9969

Model 1 is adjusted for age and body mass index.

Model 2 is adjusted for age, body mass index, smoking status, alcohol intake, regular exercise, educational level, and income.

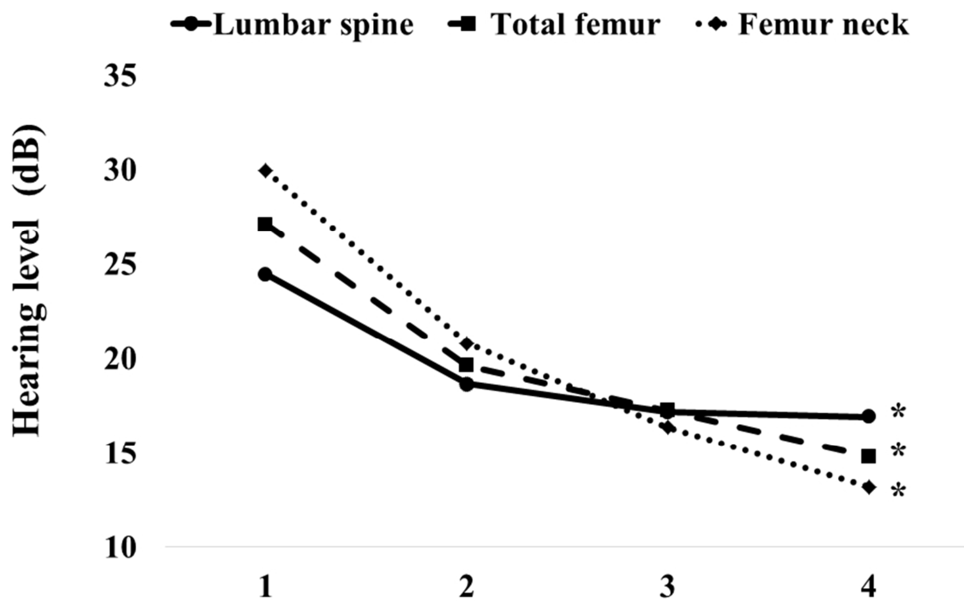
Model 3 is adjusted for age, body mass index, smoking status, alcohol intake, regular exercise, educational level, income, 25-hydroxyvitamin D, stress level, and tinnitus.

Results were represented as a estimated beta with corresponding standard error (SE) and p-value

Figure legend

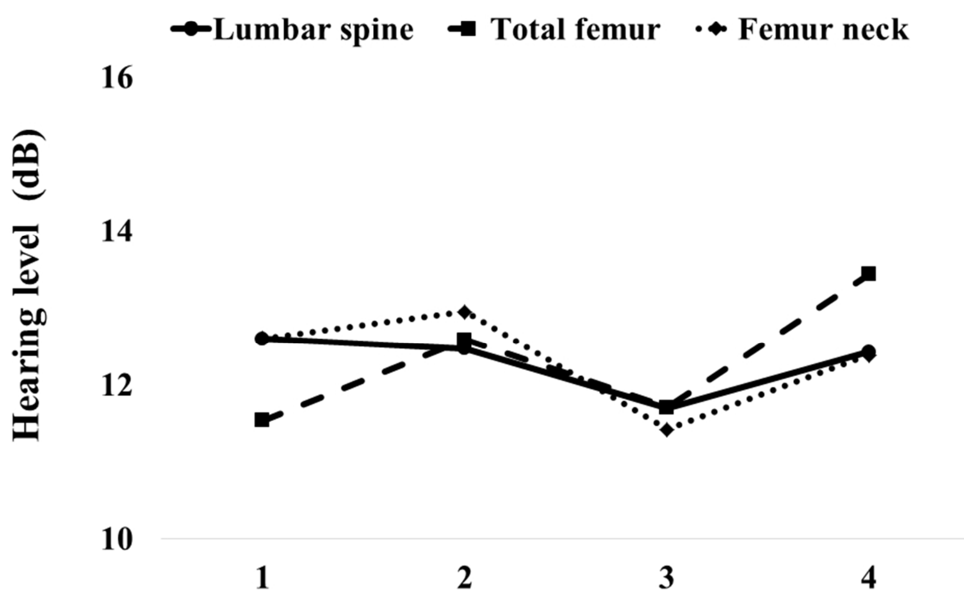
Figure 1. Mean values of hearing level according to bone mineral density for premenopausal (A) postmenopausal (B) women and men(C). After categorizing subjects into four groups based on BMD (quartile 1, with the highest, to quartile 4, with the lowest) in the lumbar spine, total femur, and femur neck, we found a tendency toward significantly decreased hearing as a function of quartile decreases in BMD among postmenopausal women.

* P < 0.05 was considered to be statistically significant.



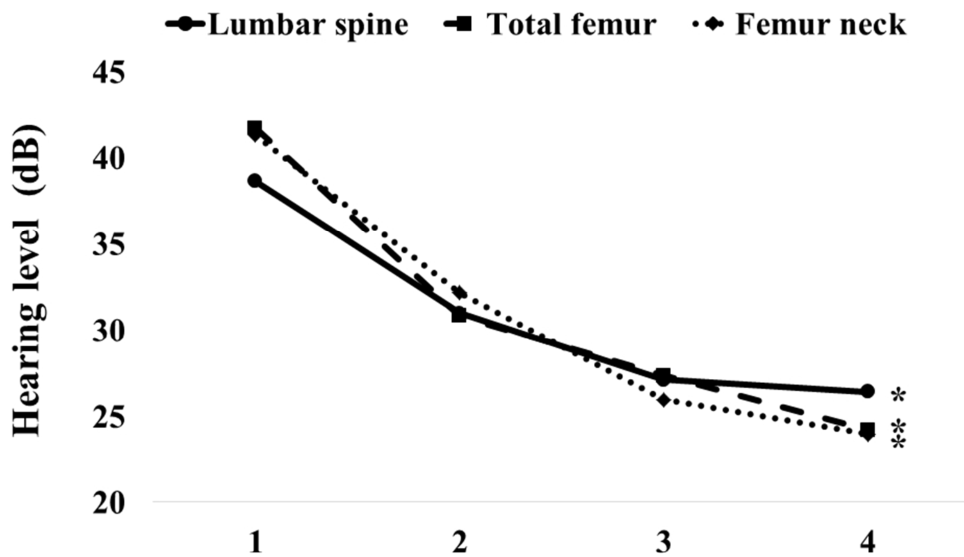
Mean values of hearing level according to bone mineral density for premenopausal women. After categorizing subjects into four groups based on BMD (quartile 1, with the highest, to quartile 4, with the lowest) in the lumbar spine, total femur, and femur neck, we found a tendency toward significantly decreased hearing as a function of quartile decreases in BMD among postmenopausal women.
* $P < 0.05$ was considered to be statistically significant.

254x190mm (96 x 96 DPI)



Mean values of hearing level according to bone mineral density for postmenopausal women. After categorizing subjects into four groups based on BMD (quartile 1, with the highest, to quartile 4, with the lowest) in the lumbar spine, total femur, and femur neck, we found a tendency toward significantly decreased hearing as a function of quartile decreases in BMD among postmenopausal women.
* P < 0.05 was considered to be statistically significant.

254x190mm (96 x 96 DPI)



Mean values of hearing level according to bone mineral density for men. After categorizing subjects into four groups based on BMD (quartile 1, with the highest, to quartile 4, with the lowest) in the lumbar spine, total femur, and femur neck, we found a tendency toward significantly decreased hearing as a function of quartile decreases in BMD among postmenopausal women.
* P < 0.05 was considered to be statistically significant.

254x190mm (96 x 96 DPI)

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Page 1 (title)	The Korea National Health and Nutrition Examination Survey
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Page 2	Abstract
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 3	Several studies have evaluated the association between BMD and hearing sensitivity.
Objectives	3	State specific objectives, including any prespecified hypotheses	Page 4	We sought to evaluate the relationship between BMD and hearing impairment in a nationally representative sample of Korean adults.
Methods				
Study design	4	Present key elements of study design early in the paper	Page 5	KNHANES is a nationwide survey designed to assess national health and nutrition levels accurately
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Page 5	This study was based on data collected during the 2010–2012 KNHANES (Korea Centers for Disease Control and Prevention)
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of	Page 5	The sample included 12,499 participants aged over 19 years.

		participants		
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case		
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Page 5, 6, and 7	tinnitus, Smoking history, alcohol absorption, Regular exercise, Weight and height, Body mass index (BMI), Waist circumference (WC), and Metabolic syndrome
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Page 5	The survey consists of a health interview, a nutritional survey, and a health examination survey. The survey amasses data via household interviews and by direct standardized physical examinations conducted in specially equipped mobile examination centers.
Bias	9	Describe any efforts to address potential sources of bias	Page 8	We first adjusted for age (model 1), adjusted for age, BMI, smoking status, alcohol intake, and regular exercise (model 2), and adjusted for age, BMI, smoking status, alcohol intake, regular exercise, metabolic syndrome, stress, and tinnitus (model 3).
Study size	10	Explain how the study size was arrived at	Page 5	This study was based on data collected during the 2010–2012

	KNHANES (Korea Centers for Disease Control and Prevention).

Continued on next page

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Page 5, 6, and 7	The BMD values of the lumbar spine (L1–L4), femoral neck, and total femur were measured using dual-energy X-ray absorptiometry (DXA) using a Discovery fan-beam densitometer (Hologic, Bedford, MA, USA) and the Hologic Discovery software (ver. 3.1). Smoking history was categorized into the three groups: current smoker, ex-smoker and non-smoker Subjects who drank more than 30 g/day were designated as heavy drinkers. Regular exercise was defined as strenuous physical activity performed for at least 20 min at a time at least three times a week.
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	Page 6 and 7	The prevalence and 95% confidence intervals (CIs) for dizziness were calculated. In the univariate analysis, the Rao-Scott chi-square test (using PROC SURVEYFREQ in SAS) and logistic regression analysis (using PROC SURVEYLOGISTIC in SAS) were used to test the association between gender and risk factors in a complex sampling design. Participants' characteristics were described using means and standard errors for continuous

				variables and numbers and percentages for categorical variables. A final logistic regression model was used to examine the association between sleep duration and dizziness.
		(*b*) Describe any methods used to examine subgroups and interactions	Page 6 and 7	Same as the above.
		(*c*) Explain how missing data were addressed	Page 6 and 7	Statistical analyses were performed using the SAS survey procedure (ver. 9.3; SAS Institute, Cary, NC, USA) to reflect the complex sampling design and sampling weights of KNHANES and to provide nationally representative prevalence estimates. The procedures included unequal probabilities of selection, oversampling, and nonresponse so that inferences could be made about the Korean adolescent participants.
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy		
		(*e*) Describe any sensitivity analyses		
Results				
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Page 9	There were 12,499 respondents in our study, comprising 5406 (43.25%) males and 7093 (56.75%) females, and 2690 had experienced dizziness or imbalance in the prior

				12 months.
		(b) Give reasons for non-participation at each stage	Page 9	Same as the above.
		(c) Consider use of a flow diagram		
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Page 9	The baseline characteristics of the study subjects according to gender are shown in Table 1.
		(b) Indicate number of participants with missing data for each variable of interest	Page 9	There were 12,499 respondents in our study, comprising 5406 (43.25%) males and 7093 (56.75%) females, and 2690 had experienced dizziness or imbalance in the prior 12 months.
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)		
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time		
		Case-control study—Report numbers in each exposure category, or summary measures of exposure		
		Cross-sectional study—Report numbers of outcome events or summary measures	Page 9	There were 12,499 respondents in our study, comprising 5406 (43.25%) males and 7093 (56.75%) females, and 2690 had experienced dizziness or imbalance in the prior 12 months.
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Page 9	The adjusted OR for sleep duration is not significant in dizziness for men. Meanwhile, the risk of dizziness was significantly associated with sleep duration in only women. Compared to participants with optimal sleep duration (six to eight hours), those with severe short sleep duration (≤5 hours) (OR [95% CI]: 1.566 [1.289-

			1.903] in model 1, OR [95% CI]: 1.557 [1.276-1.898] in model 2, and OR [95% CI]: 1.473 [1.194-1.818] in model 3) and severe long sleep duration (≥9 hours) (OR [95% CI]: 1.420 [1.042-1.936] in model 1, OR [95% CI]: 1.418 [1.040-1.934] in model 2, and OR [95% CI]: 1.472 [1.078-2.009] in model 3) had an increased dizziness risk after adjusting for the confounders.
	(*b*) Report category boundaries when continuous variables were categorized	Page 9	Among variables regarding health behavior patterns, current smoker, heavy drinker, routine exercise, job, and waist circumference were significantly associated with men.
	(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period		

Continued on next page

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses		
Discussion				
Key results	18	Summarise key results with reference to study objectives	Page 10	abnormal sleep duration such as short or long duration are associated with dizziness in women
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Page 12	By contrast, this study also had several limitations. First, sleep duration and dizziness were reported only by respondents and were not recorded or observed directly. This may bias our results, as there is only modest correlation between reported and recorded sleep. Although there were some researches with objective sleep data, those measures are not practical for large, nationally representative samples. Furthermore, self-reported sleep duration has been used widely in epidemiological studies examining the relationship between sleep duration and morbidity and mortality. Secondly, our data consider only abnormal duration of sleep. Additional sleep problems, such as snoring, apnea and daytime sleepiness, should be investigated in future studies. Third, the related variables of which the presence or absence may be associated with

				vestibular dysfunction and could affect the results were not able to be evaluated and the participants with other acute disease status, such as BPPV, were not able to be excluded from this study.
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Page 12	Same as the above.
Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 13	KNHANES is a nationwide cross-sectional study to select a representative sample of the Korean population. This survey employed stratified multi-stage design based on age, sex, and residence geographic area.
Other information				
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based		No funding source

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Primary Subject Heading:	Diabetes and endocrinology
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Association between Low Bone Mineral Density and Hearing Impairment in Postmenopausal Women: the Korean National Health and Nutrition Examination Survey

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Running title: Bone Mineral Density and Hearing Status

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Conflict of interest : none

Abstract

Objective : We investigated the relationship between bone mineral density (BMD) and hearing impairment in a nationally demonstrative sample of Korean female adults.

Study Design : Cross-sectional study of a national health survey.

Methods : We studied information from the 2009–2010 Korean National Health and Nutrition Examination Surveys (KNHANES), which involved 19,491 participants, 8,773 of whom were enrolled in this study. BMD was measured using dual-energy X-ray absorptiometry. Auditory functioning was evaluated by pure-tone audiometric testing according to established KNHANES protocols. We deliberated auditory impairment as pure-tone averages (PTA) at frequencies of 0.5, 1.0, 2.0, and 3.0 kHz at a threshold of ≥ 40 decibels hearing level (dBHL) in the auricle with better audible status.

Results: Among women aged 19 years and older, the prevalences of bilateral hearing impairment in premenopausal and postmenopausal women were 0.1±0.1% and 11.5±1.1% (mean ± SE), respectively. Hearing impairment was meaningfully associated with low BMD in postmenopausal women. Logistic regression models indicated that lower BMD of the total femur (OR = 0.779; 95% CI = 0.641–0.946, p = 0.0118) and femur neck (OR = 0.746; 95% CI = 0.576–0.966, p = 0.0265) were significantly associated with hearing impairment among postmenopausal women.

Conclusions: Postmenopausal Korean women with low BMD of the total femur and femoral neck showed an increased risk for developing hearing impairment. Further epidemiological and investigational studies are necessary to elucidate this association.

Key words: hearing impairment, bone mineral density, epidemiology

Strengths and limitations of this study

- We used a nation widely demonstrative, cross-sectional, civilian non-institutionalized sample of Korean adults.

- We evaluated the relationships between BMD and hearing level including various social, economic, behavioral, and health variables on the population-based database

- We were incapable of analyzing the temporal association between hearing impairment and BMD, which may make our results biased.

Introduction

Osteoporosis has become a mainly healthcare problem around the world.[1] Osteoporosis prevalence at the total hip or hip/spine ranged from 9 to 38 % for female and 1 to 8 % for male in nine industrialized nations in North America, Europe, Japan, and Australia.[2] It has been stated that crucial demographic alterations will occur in Asia.[3] Thus, the prevalence and incidence of osteoporosis are expected to increase in this ageing society.[4] Osteoporosis is considered by the worsening of the bone microarchitecture and a reduction in the bone mineral density (BMD).[5] Decreased BMD causes demineralization of the bone system. Deterioration of the petrous temporal bone, which encases the cochlear capsule and internal auditory canal, may be related with impaired audible function.[5-8] Osteoporosis is characteristically accepted as an important health care concern in females, but is now progressively regarded as an significant health care issue in males as well.

Adult-onset hearing impairment is the another most public reason of disability among adults in high-income nations.[9] The total prevalence of audiometric hearing loss among persons with bilateral hearing loss aged 12 years and older in the United States was 12.7% (30.0 million) between 2001 and 2008, and this increased to 20.3% (48.1 million) when individuals with unilateral hearing loss were included.[10] Hearing impairment can isolate individuals from their social environment, impair psychosocial functioning, impair cognitive skills, increase individual emotional stress, and have negative health effects at the individual and family levels.[11] Moreover, it has been recently described that hearing impairment is related with a menace of depression among adults, particularly women.[12]

Several studies have evaluated the suggestion between BMD and audible sensitivity. Clark et al reported that 369 white female aged 60 to 85 years with femoral neck skeletal mass values below the mean value of 0.696 g/cm^2 had a 1.9 greater odds of having a hearing loss.[5] In contrast, Helzner et al. showed no association between hearing and any of the bone measurements in white and black female. [13] There are discrepancies and limitations in previous studies of associations between BMD and audible impairment, including differences in race, study design, and measurements of hearing impairment [14]. Thus, we pursued to assess the relationship between BMD and hearing impairment in a representative example of Korean adult populations. We hypothesized that auditory impairment was positively correlated with low BMD in the Korean female or elderly male population. Understanding and identifying the associations between BMD and hearing impairment in an extensive research would significantly be helpfule for patient management and reduction of social burden for these conditions.

To our knowledge, no nationwide study on hearing impairment, as diagnosed by otolaryngology doctors, and no study on the relationship between BMD and hearing impairment in an Asian female have been published. Thus, we investigated association between BMD and hearing impairment in a large representative population example from the Korean National Health and Nutrition Examination Surveys (KNHANES).

Methods

Study Population

This study was based on data collected in the 2009–2010 KNHANES study conducted by the Division of Chronic Disease Surveillance, which has been under the supervision of the Korea's Centers for Disease Control and Prevention since 1998. The KNHANES is a nationwide survey designed to accurately assess health and nutritional status at the national level. A field survey team, including an otolaryngologist, an ophthalmologist, and nurses traveled with a mobile examination unit and performed interviews and physical examinations. The survey consisted of a health interview, a nutritional survey, and a health examination survey. The survey collected data via household interviews and by direct standardized physical examinations conducted in specially equipped mobile examination centers. The KNHANES methodology has been described in detail previously and further details are listed in “The 5th KNHANES Sample Design” and reports, made accessible on the KNHANES website https://knhanes.cdc.go.kr/knhanes/index.do. The KNHANES annual reports, user manuals and instructions, and raw data are available on request.[15,16]

This study is retrospective cross-sectional analysis of a nationwide health survey. During 2009–2010, there were 19,491 KNHANES participants. Of these, 10,718 were excluded from the analysis because of at least one of the following reasons: younger than 19 years; did not undergo the otological, BMD, or 25 hydroxy vitamin D tests; or were missing data from the lifestyle questionnaire. The final sample included 8,773 adults aged 19 years and men, premenopausal, and postmenopausal women were 3,885, 2,622, and 2,266, respectively. Written informed consent was obtained from all participants prior to the survey. Approval for this study was obtained from the Institutional Review Board of the Catholic University of Korea, Seoul, Korea. (IRB no. HC14EISE0097; Bucheon, Korea).

Bone Mineral Density and Laboratory Measurements

Participants wore light clothes without shoes and jewelry, which could interfere with the BMD measurements. BMD was checked by trained technicians at mobile examination centers. The BMD values of the lumbar spine (L1–L4), femoral neck, and total femur were measured using dual-energy X-ray absorptiometry (DXA) using a Discovery fan-beam densitometer (Hologic, Bedford, MA, USA) and the Hologic Discovery software (ver. 3.1). To guarantee DXA quality control, daily programmed calibration was done according to the manufacturer’s directions to keep a precision standard of 1.5% for total hip measurements.

Standing height was calculated with the subject looking forward, barefoot, feet together, arms at the sides, and heels, buttocks, and upper back in contact with the wall.

Height was measured in centimeters to one decimal point using a calibrated stadiometer (SECA 225 stadiometer, SECA, Hamburg, Germany). Waist circumference (WC) was measured at the level of the midpoint between the iliac crest and the costal margin at the end of a normal expiration to the nearest 0.1 cm. Weight was measured using a mobile scale (GL-6000-20; Cas Korea, Seoul, Korea) in kilograms to one decimal point. Body mass index (BMI) was calculated as weight (kg)/height (m^2). Blood samples for biochemical analyses and measurement of serum 25-hydroxyvitamin D (25(OH)D) were attained from all subjects, refrigerated instantly, carried to the Principal Analysis Foundation in Seoul, Korea, and scrutinized within 24 h.

Audiometric Measurements

Pure-tone audiometric test was done by a SA 203 audiometer (Entomed; Malmö, Sweden). Pure-tone audiometry is a behavioral assessment used to calculate audible sensitivity.

'Audiometric' means 'measuring the hearing level'. Examination was accompanied in a soundproof booth inside a transportable bus set aside for the KNHANES. Otolaryngologists skilled to work the audiometer provided directions to subjects regarding the automated hearing test and attained the records. All audiometric analysis was done under the supervising by an otolaryngologist. Solely thresholds of air conduction were investigated. Air conduction assesses the whole ear system -- outer, middle, and inner ear. Threshold means the lowest decibel hearing level at which responses occur in at least one half of a series of ascending trials. The minimum number of responses needed to determine the threshold of hearing is two responses out of three presentations at a single level. Over-Ear headphones were used in the soundproof booth. Supra-auricular' is defined as 'situated above the ear coverts'. Automated analysis was platformed according to a modified Hughson–Westlake procedure and involved the use of a single pure tone of 1–2 s. The lowest level at which the participant answered to

50% of the pure tone was established as the threshold. The test–retest reliability and validity of the automated audible examination relating air-conducted pure-tone provocations was effective and equivalent of those attained in the manual pure-tone acoustic assessment.[17,18] Subjects answered by touch down a button when they caught a tone, and the outcomes were documented spontaneously. The frequency ranges tested were 0.5, 1.0, 2.0, 3.0, 4.0, and 6.0 kHz. We described hearing impairment as pure-tone averages (PTA) of frequencies at 0.5, 1.0, 2.0, and 3.0 kHz at a threshold of ≥ 40 decibel hearing level (dBHL) in the ear with better hearing.[19]

Participants were requested of their experience of tinnitus: 'Within the past year, have you ever heard a sound (buzzing, hissing, ringing, humming, roaring, machinery noise) come from your ear?' Investigators were instructed to record 'yes' if an applicant stated perceiving an odd or unusual sound at any time in the past year. Subjects who responded certainly to this question were then asked of the causing annoyance in their lives using the following question: 'How annoying is this sound in daily life?' (not annoying/annoying/severely annoying, and causes sleep problems). The participants were deliberated to have tinnitus if the severity of tinnitus was annoying or severely annoying.

Lifestyle Habits

Data on medical histories and lifestyle habits were collected using self-report questionnaires. Participants were categorized into three groups according to smoking history: current smoker, ex-smoker, and nonsmoker. Subjects who drank more than 30 g of ethanol/day were designated as drinkers. Regular exercise was defined as strenuous physical activity performed for at least 20 min at a time at least three times per week. Subjects stated their level of stress as none, mild, moderate, or severe.

Statistical Analysis

Statistical evaluates were done by the SAS survey procedure (ver. 9.3; SAS Institute, Cary, NC, USA) to reveal the complex sampling design and sampling weights of the KNHANES and to provide nationwide demonstrative prevalence assessments. The prevalence and 95% confidence intervals (CIs) for BMD were planned. In the univariate analysis, the Rao-Scott χ^2 test (using PROC SURVEYFREQ in SAS) and logistic regression analysis (using PROC SURVEYLOGISTIC in SAS) were used to exam the relationship between hearing impairment and risk factors in a complex sampling design. Subjects' characteristics are expressed as means and standard errors for continuous variables and as percentages for categorical variables. To examine the association of hearing level and BMD, the participants were divided into quartiles based on levels of BMD (Q1–Q4). Simple and multiple linear regression analyses were done to investigate the relationship between hearing impairment and BMD.

We first adjusted for age and BMI (model 1) and then adjusted for the variables in model 1 as well as for smoking status, ethanol intake, exercise, education, and income (model 2). Model 3 was adjusted for the variables in model 2 and for vitamin D, stress, and tinnitus. P-values were two-tailed, and P values < 0.05 were considered statistically significant.

Results

Of the 4,888 female participants aged ≥ 19 years, 2,622 and 2,266 were premenopausal and postmenopausal, respectively. Table 1 shows baseline features of men, premenopausal and postmenopausal women. The mean age of men, premenopausal, and postmenopausal women was 43.9±0.3, 35.3±0.2 and 62.7±0.3 years, respectively. The prevalence of bilateral hearing impairment in the postmenopausal women was 11.5±1.1% (mean ± SE). Postmenopausal women were less possible to drink ethanol, more possible to have a low income, compared with men and premenopausal women. The mean values of BMI, WC, and the level of vitamin D were lower among premenopausal females than among postmenopausal femlaes. The BMDs of the lumbar spine, total femur, and femoral neck were lower in postmenopausal females than in men premenopausal femlaes. Table 2 shows subject characteristics according to bilateral hearing impairment.

After categorizing subjects into four groups based on the percentage of BMD (quartile 1, with the highest, to quartile 4, with the lowest), we used analysis of covariance (ANCOVA) to investigate hearing level according to BMD quartile at various skeletal sites after adjusting for confounding variables, such as age, BMI, smoking status, ethanol consumption, regular exercise, educational level, income, 25-hydroxy vitamin D, stress level, and tinnitus. Lumbar skeleton, total femur skeleton, and femoral neck BMD in postmenopausal women showed significantly decreased tendencies in hearing level as BMD decreased in quartiles ($P < 0.0001$; Fig. 1). However, the BMD at the lumbar skeleton ($P = 0.570$), total femur skeleton ($P = 0.358$), and femur neck ($P = 0.268$) of premenopausal women showed no statistically significantly association with hearing level. Also those of men showed no statistically significantly association with hearing level.

Table 3 demonstrates the association between hearing impairment and BMD using logistic regression models. In the final regression model for hearing impairment, the BMDs of the total femur (OR = 0.779; 95% CI = 0.641–0.946) and femoral neck (OR = 0.746; 95% CI = 0.576–0.966) were significantly associated with hearing impairment among postmenopausal women after adjusting for age, BMI, smoking status, ethanol intake, regular exercise, educational level, income, vitamin D, stress level, and tinnitus (Model 3). BMD at the lumbar spine (OR = 0.525; 95% CI = 0.279–0.989) was also significantly associated with hearing impairment in premenopausal females. BMD at the total femur, and femoral neck in men and premenopausal women did not show a significant correlation with hearing impairment. To ascertain the relations between hearing impairment and BMD at several skeletal sites, simple linear logistic regression analysis was done after adjusting for age, BMI, smoking status, ethanol intake, regular exercise, educational level, income, 25-hydroxyvitamin D, stress level, and tinnitus. There was no statistically noteworthy association in hearing impairment and BMD at any parts of skeletal sites in male, premenopausal and postmenopausal females (Table 4).

Discussion

The main objective of this research was to examine the association between BMD and hearing impairment using a nationwide representative example of the South Korean population. Our findings indicate that low BMDs of the total femur skeleton and femur neck were related with an increased risk for impairment of hearing function in postmenopausal females.

There have been some previous reports that reduced BMD was closely associated with hearing impairment.[5,13] The bone mass of the femoral neck was related with hearing loss in a population of rural females aged 60–85 years.[5] Another research enrolled 2052 older adults aged 73–84 years using a randomized method. The population was composed of white males (32.2%), white femlaes (30.8%), black males (15.1%), and black females (22.0%). The results showed that the BMD of the total hip was not associated with hearing loss in white males, white females, and black females, but it was in black males.[13] Unlike our results, that study checked only the BMD of the total hip, and the age range and race of the sample also differed from those of ours. However, the study did show that there were differences in hearing impairment by race and sex.

The mechanism of hearing impairment in postmenopausal women with lower BMD may be that demineralization of cochlear capsule of the temporal bone could lead to loss of the delicate stereocilia of the cochlear.[14] The cochlear capsule is situated in the petrous portion of the temporal bone. This portion is composed primarily of cancellous bone components.[20] The demineralization of the cochlear capsule has been related with auditory loss in subjects with skeletal diseases, such as Paget's disease, otosclerosis, and osteogenesis imperfecta.[7,14,21] Deteriorated auditory function at a specific frequency has been associated with lower BMD within the cochlear capsule.[22] Demineralization of the petrous temporal bone affects the encasing compartment of the cochlear capsule. Spiral ligament hyalinization may be affected by the toxic effects of enzymes released from otospongiotic foci and can lead to hearing impairment.[21] Lower BMD of the petrous portion of the temporal bone can affect the dissipation of cochlear stereocilia and could be a cause of hearing loss in subjects with sensorineural hearing loss.[22] This phenomenon supports the occurrence of age-related sensorineural loss and the fact that the severity of cochlear hearing loss is influenced by the extent of cochlear demineralization.[5,23]

Our study showed that differences related to menopause may contribute to relationships between bone mass and hearing impairment. In this respect, it has been reported that estrogen can exert a positive effect on hearing among older women.[24] Furthermore, estradiol treatment may have a positive effect on the ionic homeostasis of the inner ear and the protection of activated intermediated filaments.[25] Thus, the role of estrogen suggests differences in hearing impairment among women, such as those between women at the premenopausal and postmenopausal stages.[26,27] Estrogen may have an important role in the maintenance or repair of sensory epithelia of the inner ear and may act as an auditory protectant.[28-30]

The screening for hearing impairment is important. Because patients, clinicians, family, and healthcare staff often do not identify hearing loss, exactly in its initial periods, this condition may be undertreated.[31] In addition, hearing impairment may favor the development of dementia and intellectual dysfunction in grown-ups aged 65 years and older.[32] Hearing impairment is positively correlated with depression among US grown-ups of all ages, particularly among females and those younger than 70 years.[12] Therefore, screening tests based on risk factors are essential, and physicians should be aware of the likelihood of hearing damage in postmenopausal women.

Our study has several limitations. First, we did not directly quantity the BMD of the cochlear capsule of the temporal bone. There are no data on any association of the BMD between the in the petrous site of the temporal bone and that of the appendicular skeleton. However, previous research has indicated that osteoporosis can affect the skull skeletons. Patients with hyperthyroid-related osteoporosis suffered from decreased skull bone density, and demineralization of the petrous site of the temporal bone has been gotten in patients with severe osteoporosis.[33,34] It has been reported that high-resolution computed tomography was useful for checking the association between the BMD of the petrous portion of the temporal bone and hearing loss.[35] Under ideal conditions, the BMD of the petrous portion of the temporal bone would be measured; however, there is no feasible or accurate method for measuring BMD in large populations. Second, we were incapable of evaluating the temporal relation between hearing impairment and BMD. Acceptable evaluation of the presence of hearing impairment is limited for extended periods. Therefore, our research is incapable of investigating hearing variability in these populations. The final limitation of the our research was the absence of bone-conduction pure tone testing. This audiometric assessment could not entirely exclude conductive hearing losses. Despite these limitations, however, no previous study has evaluated the association between hearing impairment and low BMD in a representative general female population in Asia. Additionally, these results may be reliable because the data used were obtained from a government-sponsored survey of the national population of South Korea and were qualified by DXA, validated by audiometry tests, and verified by otolaryngologists.

Conclusion

We found that low BMD in the total femur and femoral neck were associated with impaired hearing status in postmenopausal women. Future cohort studies with larger sample sizes and controls for possible confounders are required to clarify the association between hearing impairment and postmenopause.

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Contributors : SSL wrote the first draft of the manuscript and took part in the data analyses. KDH performed statistical analyses. YHJ designed the study and critically revised the manuscript for important intellectual content.

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Data sharing statement: The KNHANES methodology has been described in detail previously and further details are listed in "The 5th KNHANES Sample Design" and reports, made accessible on the KNHANES website https://knhanes.cdc.go.kr/knhanes/index.do. The KNHANES annual reports, user manuals and instructions, and raw data are available on request.

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TABLE 1. SUBJECT CHARACTERISTICS

	Bilateral Hearing Impairment		
	No (n= 8214)	Yes (n= 559)	p-value
Age (years)	43.6 ±0.3	69.9±0.6	<0.0001
Average hearing level (dB)	10.5±0.2	57.1±1.5	<0.0001
Smoking - Current smoker (%)	26.3±1.2	19.5±4.5	0.0086
Drinking - Heavy drinker (%)	10.3±0.9	6.7±2.6	0.0311
Routine exercise (%)	24.9±1.4	18.9±3.8	0.0052
Body mass index (kg/m^2)	23.7±0.0	23.8±0.2	0.3586
Waist circumference (cm)	80.7±0.2	83.7±0.5	<0.0001
Education - ≥High school (%)	73.0±1.8	14.6±3.8	<0.0001
Residential area - Urban (%)	81.1±4.5	67.7±8.6	<0.0001
Income - Lower quartile (%)	14.9±1.5	50.0±4.8	<0.0001
Stress – Moderate to severe (%)	30.4±1.3	25.8±5.1	0.0937
25-Hydroxyvitamin D (ng/ml)	18.5±0.2	20.2±0.6	0.0013
BMD of lumbar spine (g/cm^2)	0.947±0.002	0.841±0.008	<0.0001
BMD of total femur (g/cm^2)	0.929±0.002	0.799±0.008	<0.0001
BMD of femoral neck (g/cm^2)	0.778±0.002	0.629±0.008	<0.0001

* $P < 0.05$ was considered to be statistically significant.

	Men (n=3885)	Premenopausal women (n=2622)	Postmenopausal women (n=2266)	p-value
Age (years)	43.9±0.3	35.3±0.2	62.7±0.3	<0.0001*
Average hearing level (dB)	19.1±0.4	12.3±0.4	30.6±0.8	<0.0001*
Smoking - Current smoker (%)	45.4±1.0	7.1±0.7	4.6±0.6	<0.0001*
Drinking - Heavy drinker (%)	18.2±0.8	2.6±0.4	0.9±0.2	<0.0001*
Routine exercise (%)	27.3±0.8	21.3±1.0	22.6±1.3	<0.0001*
Body mass index (kg/m^2)	24.1±0.1	22.6±0.1	24.3±0.1	<0.0001*
Waist circumference (cm)	84.0±0.2	74.8±0.3	82.3±0.3	<0.0001*
Education - ≥High school (%)	77.0±0.9	89.7±0.7	20.7±1.3	<0.0001*
Residential area - Urban (%)	80.1±2.3	85.8±2.0	73.2±2.9	<0.0001*
Income - Lower quartile (%)	14.5±0.8	9.6±0.8	33.0±1.4	<0.0001*
Stress – Moderate to severe (%)	27.4±0.9	35.2±1.1	29.8±1.3	<0.0001*
25-Hydroxyvitamin D (ng/ml)	19.8±0.2	16.4±0.2	19.0±0.3	<0.0001*

TABLE 2. SUBJECT CHARACTERISTICS ACCORDING TO BILATER HEARING IMPAIRMENT

	Men	Premenopausal women	Postmenopausal women	
BMD of lumbar spine (g/cm^2)	0.971±0.003	0.977±0.003	0.807±0.004	<0.0001*
BMD of total femur (g/cm^2)	0.986±0.003	0.905±0.003	0.782±0.003	<0.0001*
BMD of femoral neck (g/cm^2)	0.829±0.003	0.765±0.003	0.626±0.003	<0.0001*
Hearing loss (%)	4.6±0.4	0.2±0.1	11.5±1.1	<0.0001*

Data are presented as mean ± SE (standard error)

TABLE 3. MULTIVARIABLE LOGISTIC REGRESSION ANALYSIS OF ADJUSTED ODD RATIOS (ORs) AND 95% CONFIDENCE INTERVALS (CIs) TO DETERMINE THE EFFECT OF BONE MINERAL DENSITY ON HEARING IMPAIRMENT.

	Men	Premenopausal women	Postmenopausal women
Lumbar spine			
Model 1	0.999(0.892-1.118)	0.486(0.276-0.856)	0.921(0.812-1.044)
Model 2	1.052(0.939-1.178)	0.528(0.273-1.020)	0.966(0.849-1.098)
Model 3	1.058(0.937-1.195)	0.525(0.279-0.98[illegible])	0.960(0.835-1.10[illegible])
Total femur			
Model 1	0.948(0.821-1.095)	0.683(0.323-1.444)	0.804(0.673-0.959)
Model 2	0.985(0.851-1.140)	0.756(0.348-1.640)	0.820(0.686-0.981)
Model 3	1.009(0.855-1.190)	0.758(0.338-1.703)	0.779(0.641-0.946)
Femoral neck			
Model 1	0.874(0.727-1.050)	0.878(0.412-1.868)	0.760(0.608-0.950)
Model 2	0.914(0.761-1.099)	0.970(0.432-2.180)	0.783(0.623-0.984)
Model 3	0.919(0.747-1.130)	0.953(0.400-2.272)	0.746(0.576-0.966)

Model 1 is adjusted for age and body mass index.

Model 2 is adjusted for age, body mass index, smoking status, ethanol intake, regular exercise, educational level, and income.

Model 3 is adjusted for age, body mass index, smoking status, ethanol intake, regular exercise, educational level, income, 25-hydroxyvitamin D, stress level, and tinnitus.

TABLE 4. MULTIVARIABLE LOGISTIC REGRESSION ANALYSIS IN BONE MINERAL DENSITY

	Beta	SE	p-value	Beta	SE	p-value	Beta	SE	p-value
Lumbar spine									
Model 1	-0.2899	0.2570	0.2604	-0.1820	0.1338	0.1753	-0.0778	0.1560	0.6186
Model 2	-0.0194	0.2472	0.9375	-0.1244	0.1320	0.3471	0.1261	0.1449	0.3847
Model 3	0.0777	0.2517	0.7578	-0.1400	0.1365	0.3063	0.1055	0.1482	0.4772
Total femur									
Model 1	-1.1271	0.3862	0.0038	0.0260	0.1426	0.8553	-0.2160	0.1653	0.1924
Model 2	-1.0141	0.3913	0.0101	0.0034	0.1454	0.8118	-0.0549	0.1586	0.7296
Model 3	-0.8842	0.3892	0.0240	0.0266	0.1511	0.8609	-0.0038	0.1690	0.8201
Femoral neck									
Model 1	-0.8639	0.4739	0.0695	0.1211	0.1328	0.3625	-0.0713	0.1646	0.6650
Model 2	-0.6742	0.4917	0.1716	0.1004	0.1335	0.4528	0.0031	0.1565	0.8409
Model 3	-0.5278	0.4737	0.2663	0.0847	0.1392	0.5433	-0.0006	0.1648	0.9969

Model 1 is adjusted for age and body mass index.

Model 2 is adjusted for age, body mass index, smoking status, ethanol intake, regular exercise, educational level, and income.

Model 3 is adjusted for age, body mass index, smoking status, ethanol intake, regular exercise, educational level, income, 25-hydroxyvitamin D, stress level, and tinnitus.

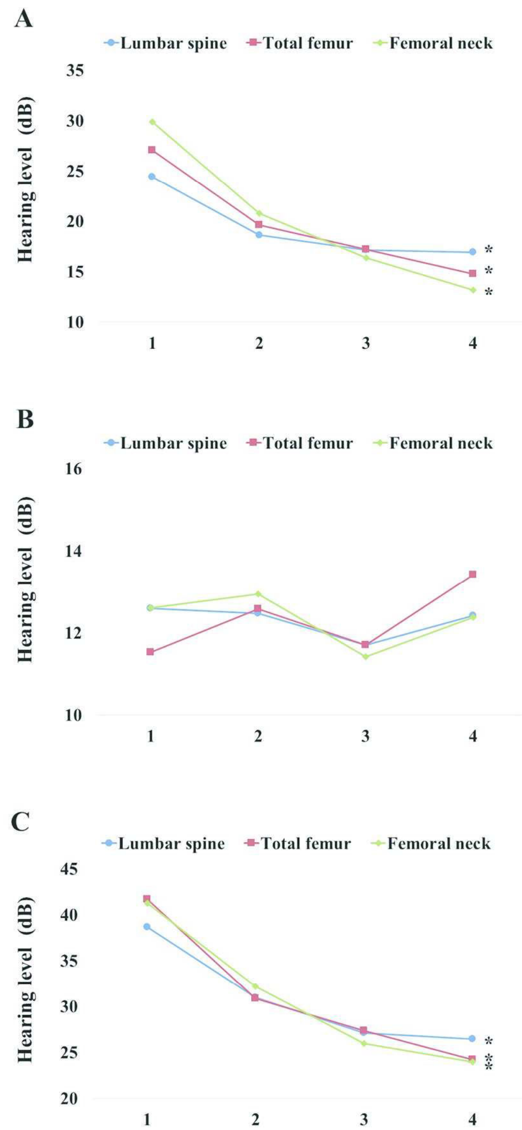
Results were represented as a estimated beta with corresponding standard error (SE) and p-value

Figure legend

Figure 1. Mean values of hearing level according to bone mineral density for premenopausal

(A) postmenopausal (B) women and men(C). After categorizing subjects into four groups based on BMD (quartile 1, with the highest, to quartile 4, with the lowest) in the lumbar spine, total femur, and femur neck, we found a tendency toward significantly decreased hearing as a function of quartile decreases in BMD among postmenopausal women.

* $P < 0.05$ was considered to be statistically significant.



Mean values of hearing level according to bone mineral density for premenopausal (A) postmenopausal (B) women and men(C). After categorizing subjects into four groups based on BMD (quartile 1, with the highest, to quartile 4, with the lowest) in the lumbar spine, total femur, and femur neck, we found a tendency toward significantly decreased hearing as a function of quartile decreases in BMD among postmenopausal women. * $P < 0.05$ was considered to be statistically significant.

112x253mm (600 x 600 DPI)

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Page 1 (title)	The Korea National Health and Nutrition Examination Survey
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Page 2	Abstract
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 3	Several studies have evaluated the association between BMD and hearing sensitivity.
Objectives	3	State specific objectives, including any prespecified hypotheses	Page 4	We sought to evaluate the relationship between BMD and hearing impairment in a nationally representative sample of Korean adults.
Methods				
Study design	4	Present key elements of study design early in the paper	Page 5	KNHANES is a nationwide survey designed to assess national health and nutrition levels accurately
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Page 5	This study was based on data collected during the 2010–2012 KNHANES (Korea Centers for Disease Control and Prevention)
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of	Page 5	The sample included 12,499 participants aged over 19 years.

		participants		
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case		
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Page 5, 6, and 7	tinnitus, Smoking history, alcohol absorption, Regular exercise, Weight and height, Body mass index (BMI), Waist circumference (WC), and Metabolic syndrome
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Page 5	The survey consists of a health interview, a nutritional survey, and a health examination survey. The survey amasses data via household interviews and by direct standardized physical examinations conducted in specially equipped mobile examination centers.
Bias	9	Describe any efforts to address potential sources of bias	Page 8	We first adjusted for age (model 1), adjusted for age, BMI, smoking status, alcohol intake, and regular exercise (model 2), and adjusted for age, BMI, smoking status, alcohol intake, regular exercise, metabolic syndrome, stress, and tinnitus (model 3).
Study size	10	Explain how the study size was arrived at	Page 5	This study was based on data collected during the 2010–2012

	KNHANES (Korea Centers for Disease Control and Prevention).

Continued on next page

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Page 5, 6, and 7	The BMD values of the lumbar spine (L1–L4), femoral neck, and total femur were measured using dual-energy X-ray absorptiometry (DXA) using a Discovery fan-beam densitometer (Hologic, Bedford, MA, USA) and the Hologic Discovery software (ver. 3.1). Smoking history was categorized into the three groups: current smoker, ex-smoker and non-smoker Subjects who drank more than 30 g/day were designated as heavy drinkers. Regular exercise was defined as strenuous physical activity performed for at least 20 min at a time at least three times a week.
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	Page 6 and 7	The prevalence and 95% confidence intervals (CIs) for dizziness were calculated. In the univariate analysis, the Rao-Scott chi-square test (using PROC SURVEYFREQ in SAS) and logistic regression analysis (using PROC SURVEYLOGISTIC in SAS) were used to test the association between gender and risk factors in a complex sampling design. Participants' characteristics were described using means and standard errors for continuous

				variables and numbers and percentages for categorical variables. A final logistic regression model was used to examine the association between sleep duration and dizziness.
		(*b*) Describe any methods used to examine subgroups and interactions	Page 6 and 7	Same as the above.
		(*c*) Explain how missing data were addressed	Page 6 and 7	Statistical analyses were performed using the SAS survey procedure (ver. 9.3; SAS Institute, Cary, NC, USA) to reflect the complex sampling design and sampling weights of KNHANES and to provide nationally representative prevalence estimates. The procedures included unequal probabilities of selection, oversampling, and nonresponse so that inferences could be made about the Korean adolescent participants.
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy		
		(*e*) Describe any sensitivity analyses		
Results				
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Page 9	There were 12,499 respondents in our study, comprising 5406 (43.25%) males and 7093 (56.75%) females, and 2690 had experienced dizziness or imbalance in the prior

				12 months.
		(b) Give reasons for non-participation at each stage	Page 9	Same as the above.
		(c) Consider use of a flow diagram		
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Page 9	The baseline characteristics of the study subjects according to gender are shown in Table 1.
		(b) Indicate number of participants with missing data for each variable of interest	Page 9	There were 12,499 respondents in our study, comprising 5406 (43.25%) males and 7093 (56.75%) females, and 2690 had experienced dizziness or imbalance in the prior 12 months.
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)		
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time		
		Case-control study—Report numbers in each exposure category, or summary measures of exposure		
		Cross-sectional study—Report numbers of outcome events or summary measures	Page 9	There were 12,499 respondents in our study, comprising 5406 (43.25%) males and 7093 (56.75%) females, and 2690 had experienced dizziness or imbalance in the prior 12 months.
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Page 9	The adjusted OR for sleep duration is not significant in dizziness for men. Meanwhile, the risk of dizziness was significantly associated with sleep duration in only women. Compared to participants with optimal sleep duration (six to eight hours), those with severe short sleep duration (≤5 hours) (OR [95% CI]: 1.566 [1.289-

			1.903] in model 1, OR [95% CI]: 1.557 [1.276-1.898] in model 2, and OR [95% CI]: 1.473 [1.194-1.818] in model 3) and severe long sleep duration (≥9 hours) (OR [95% CI]: 1.420 [1.042-1.936] in model 1, OR [95% CI]: 1.418 [1.040-1.934] in model 2, and OR [95% CI]: 1.472 [1.078-2.009] in model 3) had an increased dizziness risk after adjusting for the confounders.
	(*b*) Report category boundaries when continuous variables were categorized	Page 9	Among variables regarding health behavior patterns, current smoker, heavy drinker, routine exercise, job, and waist circumference were significantly associated with men.
	(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period		

Continued on next page

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses		
Discussion				
Key results	18	Summarise key results with reference to study objectives	Page 10	abnormal sleep duration such as short or long duration are associated with dizziness in women
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Page 12	By contrast, this study also had several limitations. First, sleep duration and dizziness were reported only by respondents and were not recorded or observed directly. This may bias our results, as there is only modest correlation between reported and recorded sleep. Although there were some researches with objective sleep data, those measures are not practical for large, nationally representative samples. Furthermore, self-reported sleep duration has been used widely in epidemiological studies examining the relationship between sleep duration and morbidity and mortality. Secondly, our data consider only abnormal duration of sleep. Additional sleep problems, such as snoring, apnea and daytime sleepiness, should be investigated in future studies. Third, the related variables of which the presence or absence may be associated with

				vestibular dysfunction and could affect the results were not able to be evaluated and the participants with other acute disease status, such as BPPV, were not able to be excluded from this study.
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Page 12	Same as the above.
Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 13	KNHANES is a nationwide cross-sectional study to select a representative sample of the Korean population. This survey employed stratified multi-stage design based on age, sex, and residence geographic area.
Other information				
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based		No funding source

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Association between Low Bone Mineral Density and Hearing Impairment in Postmenopausal Women: the Korean National Health and Nutrition Examination Survey

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Abstract

Objective: To investigate the relationship between bone mineral density (BMD) and hearing impairment using a nationally demonstrative sample of Korean female adults.

Study Design: Cross-sectional study of a national health survey.

Methods: Data from the 2009–2010 Korean National Health and Nutrition Examination Surveys (KNHANES) with 19,491 participants were analyzed and 8,773 of these participants were enrolled in this study. BMD was measured using dual-energy X-ray absorptiometry. Auditory functioning was evaluated by pure-tone audiometric testing according to established KNHANES protocols. We deliberated auditory impairment as pure-tone averages (PTA) at frequencies of 0.5, 1.0, 2.0, and 3.0 kHz at a threshold of ≥ 40 decibels hearing level (dBHL) in the auricle with better audible status.

Results: Among women aged 19 years and older, prevalences of bilateral hearing impairment in premenopausal and postmenopausal women were 0.1 ± 0.1% and 11.5 ± 1.1% (mean ± SE), respectively. Hearing impairment was meaningfully associated with low BMD in postmenopausal women. Logistic regression models indicated that lower BMD of the total femur (OR = 0.779; 95% CI = 0.641–0.946, p = 0.0118) and femur neck (OR = 0.746; 95% CI = 0.576–0.966, p = 0.0265) were significantly associated with hearing impairment among postmenopausal women.

Conclusions: Postmenopausal Korean women with low BMD of the total femur and femoral neck showed an increased risk for developing hearing impairment. Further epidemiological and investigational studies are needed to elucidate this association.

Keywords: hearing impairment, bone mineral density, epidemiology

Strengths and limitations of this study

- We used a nation widely demonstrative, cross-sectional, civilian non-institutionalized sample of Korean adults.

- We evaluated the relationship between BMD and hearing level including various social, economic, behavioral, and health variables using a population-based database.

- We were unable to analyze temporal association between hearing impairment and BMD, which may make our results biased.

Introduction

Osteoporosis has become a mainly healthcare problem around the world.[1] Osteoporosis prevalence at the total hip or hip/spine ranges from 9% to 38% in females and 1% to 8% in males after analyse data from nine industrialized nations in North America, Europe, Japan, and Australia.[2] It has been stated that crucial demographic alterations might occur in Asia.[3] The prevalence and incidence of osteoporosis are expected to increase in an ageing society.[4] Osteoporosis is considered when there is worsening of bone microarchitecture and reduction in bone mineral density (BMD).[5] Decreased BMD causes demineralization of the bone system. Deterioration of the petrous temporal bone which encases the cochlear capsule and internal auditory canal might be associated with impaired audible function.[5-8] Osteoporosis is characteristically accepted as an important health care concern in females. However, it is now progressively regarded as a significant health care issue in males as well.

Adult-onset hearing impairment is another important public concern of disability among adults in high-income nations.[9] The total prevalence of audiometric hearing loss among persons with bilateral hearing loss aged 12 years and older in the United States was 12.7% (30.0 million) between 2001 and 2008. This was increased to 20.3% (48.1 million) when individuals with unilateral hearing loss were included.[10] Hearing impairment can isolate individuals from their social environment, impair psychosocial functioning, impair cognitive skills, increase individual emotional stress, and have negative health effects at individual and family levels.[11] Moreover, it has been recently described that hearing impairment is associated with a menace of depression among adults, particularly women.[12]

Several studies have evaluated the relationship between BMD and audible sensitivity. Clark et al. have reported that 369 white female aged 60 to 85 years with femoral neck skeletal mass values below the mean value of 0.696 g/cm^2 have a 1.9-fold greater odds of having a hearing loss.[5] In contrast, Helzner et al. have shown no association between hearing and any of bone measurements in white or black females.[13] There are discrepancies and limitations in previous studies on associations between BMD and audible impairment, including differences in race, study design, and measurements of hearing impairment [14]. Thus, the objective of this study was to assess the relationship between BMD and hearing impairment in a representative example of Korean adult populations. Understanding and identifying the association between BMD and hearing impairment in an extensive research could provide important information for patient management and reduction of social burden for these conditions.

To the best of our knowledge, that has been no report of a nationwide study on hearing impairment diagnosed by otolaryngology doctors or the relationship between BMD and hearing impairment in Asian females. Thus, we investigated the association between BMD and hearing impairment in a large representative population example from the Korean National Health and Nutrition Examination Surveys (KNHANES).

Methods

Study Population

This study was based on data collected from the 2009–2010 KNHANES study conducted by the Division of Chronic Disease Surveillance under the supervision of the Korea's Centers for Disease Control and Prevention since 1998. The KNHANES is a nationwide survey designed to accurately assess health and nutritional status at national level. A field survey team including an otolaryngologist, an ophthalmologist, and nurses traveled with a mobile examination unit. They performed interviews and physical examinations. The survey consisted of a health interview, a nutritional survey, and a health examination survey. The survey collected data via household interviews and by direct standardized physical examinations conducted in specially equipped mobile examination centers. The KNHANES methodology has been described in detail previously. [15,16] Further details are listed in "The 5th KNHANES Sample Design" and reports, made accessible on the KNHANES website https://knhanes.cdc.go.kr/knhanes/index.do. The KNHANES annual reports, user manuals and instructions, and raw data are available upon request.

This study was a retrospective cross-sectional analysis of a nationwide health survey. We hypothesized that auditory impairment was positively correlated with low BMD in Korean population before looking at the data. During 2009–2010, there were 19,491 KNHANES participants. Of these, 10,718 were excluded from the analysis because of at least one of the following reasons: younger than 19 years; did not undergo ontological, BMD, or 25 hydroxy vitamin D test; or with missing data for the lifestyle questionnaire. The final sample included 8,773 adults aged 19 years, including 3,885 males, 2,622 premenopausal women, and 2,266 postmenopausal women. Written informed consent was obtained from all participants prior to the survey. Approval for this study was obtained from the Institutional Review Board of the Catholic University of Korea, Seoul, Korea (IRB no. HC14EISE0097; Bucheon, Korea).

Bone Mineral Density and Laboratory Measurements

Participants wore light clothes without shoes or jewelry that could interfere with BMD measurements. BMD was checked by trained technicians at mobile examination centers. BMD values of the lumbar spine (L1–L4), femoral neck, and total femur were measured using dual-energy X-ray absorptiometry (DXA) and a Discovery fan-beam densitometer (Hologic, Bedford, MA, USA) with Hologic Discovery software (ver. 3.1).

To guarantee DXA quality control, daily programmed calibration was done according to the manufacturer's directions to keep a precision standard of 1.5% for total hip measurements.

Standing height was calculated with the subject looking forward, barefoot, feet together, arms at sides with heels, buttocks, and upper back in contact with the wall. Height was measured in centimeters to one decimal point using a calibrated stadiometer (SECA 225 stadiometer, SECA, Hamburg, Germany). Waist circumference (WC) was measured at the level of the midpoint between the iliac crest and the costal margin at the end of a normal expiration to the nearest 0.1 cm. Weight was measured using a mobile scale (GL-6000-20; Cas Korea, Seoul, Korea) in kilograms to one decimal point. Body mass index (BMI) was calculated as weight (kg)/height (m^2). Blood samples for biochemical analyses and measurement of serum 25-hydroxyvitamin D (25(OH)D) were collected from all subjects, refrigerated instantly, carried to Principal Analysis Foundation (Seoul, Korea), and scrutinized within 24 h.

Audiometric Measurements

Pure-tone audiometric test was done with a SA 203 audiometer (Entomed; Malmö, Sweden). Pure-tone audiometry is a behavioral assessment used to calculate audible sensitivity. 'Audiometric' means 'measuring the hearing level'. Examination was accompanied in a soundproof booth inside a transportable bus set aside for the KNHANES. Otolaryngologists skilled to work on the audiometer provided directions to subjects regarding the automated hearing test. Records were attained. All audiometric analyses were performed under the supervision of an otolaryngologist. Solely thresholds of air conduction were investigated. Air conduction assessed the whole ear system -- outer, middle, and inner ear. Threshold meant the lowest decibel hearing level at which responses occurred in at least one half of a series of ascending trials. The minimum number of responses needed to determine the threshold of hearing was two responses out of three presentations at a single level. Over-Ear headphones were used in the soundproof booth. Supra-auricular' was defined as 'situated above the ear coverts'. Automated analysis was platformed according to a modified Hughson–Westlake procedure using a single pure tone of 1–2 s. The lowest level at which the participant answered to 50% of the pure tone was established as the threshold. Test–retest reliability and validity of the automated audible examination relating to air-conducted pure-tone provocations were effective and equivalent to those attained in the manual pure-tone acoustic assessment.[17,18] Subjects answered by pressing a button when they caught a tone. Outcomes were documented spontaneously. Frequency ranges tested were 0.5, 1.0, 2.0, 3.0, 4.0, and 6.0 kHz. We described hearing impairment as pure-tone averages (PTA) of frequencies at 0.5, 1.0, 2.0, and 3.0 kHz at a threshold of ≥ 40 decibel hearing level (dBHL) in the ear with better hearing.[19]

Participants were requested about their experience of tinnitus: 'Within the past year, have you ever heard a sound (buzzing, hissing, ringing, humming, roaring, machinery noise) come from your ear?' Investigators were instructed to record 'yes' if an applicant stated perceiving an odd or unusual sound at any time in the past year. Subjects who responded certainly to this question were then asked about the annoyance in their lives using the following question: 'How annoying is this sound in daily life?' (not annoying/annoying/severely annoying, and causes sleep problems). Participants were deliberated to have tinnitus if the severity of tinnitus was annoying or severely annoying.

Lifestyle Habits

Data on medical histories and lifestyle habits were collected using self-report questionnaires. Participants were categorized into three groups according to smoking history: current smoker, ex-smoker, and nonsmoker. Subjects who drank more than 30 g of ethanol/day were designated as drinkers. Regular exercise was defined as strenuous physical activity performed for at least 20 min at a time at least three times per week. Subjects stated their levels of stress as none, mild, moderate, or severe.

Statistical Analysis

All statistical analyses were performed using SAS version 9.3 (SAS Institute, Cary, NC, USA) to reveal the complex sampling design and sampling weights of the KNHANES and to provide nationwide demonstrative prevalence assessments. The prevalence and 95% confidence intervals (CIs) for BMD were calculated. In univariate analysis, Rao-Scott χ^2 test (using PROC SURVEYFREQ in SAS) and logistic regression analysis (using PROC SURVEYLOGISTIC in SAS) were used to examine the relationship between hearing impairment and risk factors in a complex sampling design. Subjects' characteristics were expressed as means and standard errors for continuous variables or as percentages for categorical variables. To examine the association between hearing level and BMD, participants were divided into quartiles based on levels of BMD (Q1–Q4). Simple and multiple linear regression analyses were performed to investigate the relationship between hearing impairment and BMD.

We first adjusted for age and BMI (model 1). We then adjusted for variables in model 1 as well as smoking status, ethanol intake, exercise, education, and income (model 2). Model 3 was adjusted for variables in model 2 as well as vitamin D, stress, and tinnitus. P-values were two-tailed. Statistical significance was considered at $P < 0.05$.

Results

Of 4,888 female participants aged ≥ 19 years, 2,622 and 2,266 were premenopausal and postmenopausal, respectively. Table 1 shows baseline features of men, premenopausal women, and postmenopausal women. Mean ages of men, premenopausal women, and postmenopausal women were 43.9 ± 0.3, 35.3 ± 0.2, and 62.7 ± 0.3 years, respectively. The prevalence of bilateral hearing impairment in postmenopausal women was 11.5 ± 1.1% (mean ± SE). Postmenopausal women had lower percentages of ethanol drinkers but higher percentages of those with low income compared with men and premenopausal women. Mean values of BMI, WC, and vitamin D level were lower in premenopausal females than those in postmenopausal females. BMDs of the lumbar spine, total femur, and femoral neck were lower in postmenopausal females than those in men or premenopausal females. Subject characteristics according to bilateral hearing impairment are shown in Table 2.

After categorizing subjects into four groups based on the percentage of BMD (quartile 1, with the highest, to quartile 4, with the lowest), we performed analysis of covariance (ANCOVA) to investigate hearing level according to BMD quartile at various skeletal sites after adjusting for confounding variables such as age, BMI, smoking status, ethanol consumption, regular exercise, educational level, income, 25-hydroxy vitamin D, stress level, and tinnitus. Lumbar skeleton, total femur skeleton, and femoral neck BMD in postmenopausal women showed significantly decreased tendencies in hearing level as BMD decreased in quartiles (P < 0.0001; Fig. 1). However, BMDs at the lumbar skeleton (P = 0.570), total femur skeleton (P = 0.358), or femur neck (P = 0.268) of premenopausal women showed no statistically significantly association with hearing level. Those of men showed no statistically significantly association with hearing level either.

Table 3 demonstrates the association between hearing impairment and BMD using logistic regression models. In the final regression model for hearing impairment, BMDs of the total femur (OR = 0.779; 95% CI = 0.641–0.946) and femoral neck (OR = 0.746; 95% CI = 0.576–0.966) were significantly associated with hearing impairment in postmenopausal women after adjusting for age, BMI, smoking status, ethanol intake, regular exercise, educational level, income, vitamin D, stress level, and tinnitus (Model 3). BMD at the lumbar spine (OR = 0.525; 95% CI = 0.279–0.989) was also significantly associated with hearing impairment in premenopausal females. However, BMD at the total femur or femoral neck in men or premenopausal women did not show any significant correlation with hearing impairment. To ascertain the relations between hearing impairment and BMD at several skeletal sites, simple linear logistic regression analysis was performed after adjusting for age, BMI, smoking status, ethanol intake, regular exercise, educational level, income, 25-hydroxyvitamin D, stress level, and tinnitus. There was no statistically significant association between hearing impairment and BMD at any parts of skeletal sites in male, premenopausal, or postmenopausal females (Table 4).

Discussion

The main objective of this research was to examine the association between BMD and hearing impairment using a nationwide representative example of South Korean population. Our findings indicated that low BMDs of the total femur skeleton and femur neck were associated with an increased risk for impairment of hearing function in postmenopausal females.

Some previous studies have reported that reduced BMD is closely associated with hearing impairment.[5,13] The bone mass of the femoral neck is associated with hearing loss in a population of rural females aged 60–85 years.[5] Another research has enrolled 2052 older adults aged 73–84 years using a randomized method.[13] The population was composed of white males (32.2%), white females (30.8%), black males (15.1%), and black females (22.0%). Their results showed that the BMD of the total hip was not associated with hearing loss in white males, white females, or black females. However, it was associated with hearing loss in black males.[13] Unlike our results, that study only checked BMD of the total hip. Age range and race of the sample also differed from those of ours. However, their study did show that there were differences in hearing impairment by race and sex.

The mechanism of hearing impairment in postmenopausal women with lower BMD might involve demineralization of cochlear capsule of the temporal bone which could lead to loss of the delicate stereocilia of the cochlear.[14] The cochlear capsule is situated in the petrous portion of the temporal bone. This portion is primarily composed of cancellous bone components.[20] The demineralization of the cochlear capsule has been related to auditory loss in subjects with skeletal diseases, such as Paget's disease, otosclerosis, and osteogenesis imperfecta.[7,14,21] Deteriorated auditory function at a specific frequency has been associated with lower BMD within the cochlear capsule.[22] Demineralization of the petrous temporal bone affects the encasing compartment of the cochlear capsule. Spiral ligament hyalinization might be affected by toxic effects of enzymes released from otospongiotic foci, thus leading to hearing impairment.[21] Lower BMD of the petrous portion of the temporal bone can affect the dissipation of cochlear stereocilia. It could be a cause of hearing loss in subjects with sensorineural hearing loss.[22] This phenomenon supports the occurrence of age-related sensorineural loss and the fact that the severity of cochlear hearing loss is influenced by the extent of cochlear demineralization.[5,23]

Our study showed that differences related to menopause might contribute to the relationship between bone mass and hearing impairment. It has been reported that estrogen can exert a positive effect on hearing among older women.[24] Furthermore, estradiol treatment might have a positive effect on ionic homeostasis of the inner ear and offer protection of activated intermediated filaments.[25] Thus, estrogen might contribute to differences in hearing impairment among women such as those between premenopausal and postmenopausal women.[26,27] Estrogen may play an important role in the maintenance or repair of sensory epithelia of the inner ear. It may act as an auditory protectant.[28-30]

Screening for hearing impairment is important. Patients, clinicians, family, and healthcare staff often do not identify hearing loss exactly in its initial period. This condition might have been undertreated.[31] In addition, hearing impairment may favor the development of dementia and intellectual dysfunction in grown-ups aged 65 years and older.[32] Hearing impairment is positively correlated with depression among US grown-ups of all ages, particularly among females and those younger than 70 years.[12] Therefore, screening tests of hearing based on risk factors are essential. Physicians should be aware of the likelihood of hearing damage in postmenopausal women.

Our study has several limitations. First, we did not directly quantity BMD of the cochlear capsule of the temporal bone. There were no data on any association between BMD in the petrous site of the temporal bone and that of the appendicular skeleton. However, previous research has indicated that osteoporosis can affect skull skeletons. Patients with hyperthyroid-related osteoporosis suffered from decreased skull bone density. Demineralization of the petrous site of the temporal bone has been observed in patients with severe osteoporosis.[33,34] It has been reported that high-resolution computed tomography is useful for checking the association between BMD of the petrous portion of the temporal bone and hearing loss.[35] Under ideal conditions, BMD of the petrous portion of the temporal bone should be measured. However, there is no feasible or accurate method for measuring BMD in large populations. Second, we were unable to evaluate the temporal relation between hearing impairment and BMD. Acceptable evaluation of the presence of hearing impairment is limited for extended periods. Therefore, we were unable to investigate hearing variabilities in these populations. The final limitation of this study was the absence of bone-conduction pure tone testing. The audiometric assessment could not entirely exclude conductive hearing losses. Despite these limitations, no previous study has evaluated the association between hearing impairment and low BMD in a representative general female population in Asia. Additionally, these results might be reliable because data used in this study were obtained from a government-sponsored survey of the national population of South Korea, qualified by DXA, validated by audiometry tests, and verified by otolaryngologists.

Conclusion

Low BMDs in the total femur and femoral neck were associated with impaired hearing status in postmenopausal women. Future cohort studies with larger sample sizes and controls for possible confounders are needed to clarify the association between hearing impairment and BMD in postmenopausal women.

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Contributions: SSL wrote the first draft of the manuscript and took part in data analyses. KDH performed statistical analyses. YHJ designed the study and critically revised the manuscript for important intellectual content.

Competing interests: None declared.

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Data sharing statement: The KNHANES methodology has been described in detail previously. Further details are listed in "The 5th KNHANES Sample Design" and reports accessible at the KNHANES website (https://knhanes.cdc.go.kr/knhanes/index.do). KNHANES annual reports, user manuals and instructions, and raw data are available upon request.

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TABLE 1. SUBJECT CHARACTERISTICS

	Bilateral Hearing Impairment		
	No (n= 8214)	Yes (n= 559)	p-value
Age (years)	43.6 ±0.3	69.9±0.6	<0.0001
Average hearing level (dB)	10.5±0.2	57.1±1.5	<0.0001
Smoking - Current smoker (%)	26.3±1.2	19.5±4.5	0.0086
Drinking - Heavy drinker (%)	10.3±0.9	6.7±2.6	0.0311
Routine exercise (%)	24.9±1.4	18.9±3.8	0.0052
Body mass index (kg/m^2)	23.7±0.0	23.8±0.2	0.3586
Waist circumference (cm)	80.7±0.2	83.7±0.5	<0.0001
Education - ≥High school (%)	73.0±1.8	14.6±3.8	<0.0001
Residential area - Urban (%)	81.1±4.5	67.7±8.6	<0.0001
Income - Lower quartile (%)	14.9±1.5	50.0±4.8	<0.0001
Stress – Moderate to severe (%)	30.4±1.3	25.8±5.1	0.0937
25-Hydroxyvitamin D (ng/ml)	18.5±0.2	20.2±0.6	0.0013
BMD of lumbar spine (g/cm^2)	0.947±0.002	0.841±0.008	<0.0001
BMD of total femur (g/cm^2)	0.929±0.002	0.799±0.008	<0.0001
BMD of femoral neck (g/cm^2)	0.778±0.002	0.629±0.008	<0.0001

* P < 0.05 was considered statistically significant.

TABLE 2. SUBJECT CHARACTERISTICS ACCORDING TO BILATER HEARING IMPAIRMENT

	Men (n=3885)	Premenopausal women (n=2622)	Postmenopausal women (n=2266)	p-value
Age (years)	43.9±0.3	35.3±0.2	62.7±0.3	<0.0001*
Average hearing level (dB)	19.1±0.4	12.3±0.4	30.6±0.8	<0.0001*
Smoking - Current smoker (%)	45.4±1.0	7.1±0.7	4.6±0.6	<0.0001*
Drinking - Heavy drinker (%)	18.2±0.8	2.6±0.4	0.9±0.2	<0.0001*
Routine exercise (%)	27.3±0.8	21.3±1.0	22.6±1.3	<0.0001*
Body mass index (kg/m^2)	24.1±0.1	22.6±0.1	24.3±0.1	<0.0001*
Waist circumference (cm)	84.0±0.2	74.8±0.3	82.3±0.3	<0.0001*
Education - ≥High school (%)	77.0±0.9	89.7±0.7	20.7±1.3	<0.0001*
Residential area - Urban (%)	80.1±2.3	85.8±2.0	73.2±2.9	<0.0001*
Income - Lower quartile (%)	14.5±0.8	9.6±0.8	33.0±1.4	<0.0001*
Stress – Moderate to severe (%)	27.4±0.9	35.2±1.1	29.8±1.3	<0.0001*
25-Hydroxyvitamin D (ng/ml)	19.8±0.2	16.4±0.2	19.0±0.3	<0.0001*
BMD of lumbar spine (g/cm^2)	0.971±0.003	0.977±0.003	0.807±0.004	<0.0001*
BMD of total femur (g/cm^2)	0.986±0.003	0.905±0.003	0.782±0.003	<0.0001*
BMD of femoral neck (g/cm^2)	0.829±0.003	0.765±0.003	0.626±0.003	<0.0001*
Hearing loss (%)	4.6±0.4	0.2±0.1	11.5±1.1	<0.0001*

Data are presented as mean ± SE (standard error)

TABLE 3. MULTIVARIABLE LOGISTIC REGRESSION ANALYSIS OF ADJUSTED ODD RATIOS (ORs) AND 95% CONFIDENCE INTERVALS (CIs) TO DETERMINE THE EFFECT OF BONE MINERAL DENSITY ON HEARING IMPAIRMENT

	Men	Premenopausal women	Postmenopausal women
Lumbar spine			
Model 1	0.999(0.892-1.118)	0.486(0.276-0.856)	0.921(0.812-1.044)
Model 2	1.052(0.939-1.178)	0.528(0.273-1.020)	0.966(0.849-1.098)
Model 3	1.058(0.937-1.195)	0.525(0.279-0.989)	0.960(0.835-1.103)
Total femur			
Model 1	0.948(0.821-1.095)	0.683(0.323-1.444)	0.804(0.673-0.959)
Model 2	0.985(0.851-1.140)	0.756(0.348-1.640)	0.820(0.686-0.981)
Model 3	1.009(0.855-1.190)	0.758(0.338-1.703)	0.779(0.641-0.946)
Femoral neck			
Model 1	0.874(0.727-1.050)	0.878(0.412-1.868)	0.760(0.608-0.950)
Model 2	0.914(0.761-1.099)	0.970(0.432-2.180)	0.783(0.623-0.984)
Model 3	0.919(0.747-1.130)	0.953(0.400-2.272)	0.746(0.576-0.966)

Model 1 is adjusted for age and body mass index.

Model 2 is adjusted for age, body mass index, smoking status, ethanol intake, regular exercise, educational level, and income.

Model 3 is adjusted for age, body mass index, smoking status, ethanol intake, regular exercise, educational level, income, 25-hydroxyvitamin D, stress level, and tinnitus.

TABLE 4. MULTIVARIABLE LOGISTIC REGRESSION ANALYSIS IN BONE MINERAL DENSITY

	Men			Premenopausal women			Postmenopausal women		
	Beta	SE	p-value	Beta	SE	p-value	Beta	SE	p-value
Lumbar spine									
Model 1	-0.2899	0.2570	0.2604	-0.1820	0.1338	0.1753	-0.0778	0.1560	0.6186
Model 2	-0.0194	0.2472	0.9375	-0.1244	0.1320	0.3471	0.1261	0.1449	0.3847
Model 3	0.0777	0.2517	0.7578	-0.1400	0.1365	0.3063	0.1055	0.1482	0.4772
Total femur									
Model 1	-1.1271	0.3862	0.0038	0.0260	0.1426	0.8553	-0.2160	0.1653	0.1924
Model 2	-1.0141	0.3913	0.0101	0.0034	0.1454	0.8118	-0.0549	0.1586	0.7296
Model 3	-0.8842	0.3892	0.0240	0.0266	0.1511	0.8609	-0.0038	0.1690	0.8201
Femoral neck									
Model 1	-0.8639	0.4739	0.0695	0.1211	0.1328	0.3625	-0.0713	0.1646	0.6650
Model 2	-0.6742	0.4917	0.1716	0.1004	0.1335	0.4528	0.0031	0.1565	0.8409
Model 3	-0.5278	0.4737	0.2663	0.0847	0.1392	0.5433	-0.0006	0.1648	0.9969

Model 1 is adjusted for age and body mass index.

Model 2 is adjusted for age, body mass index, smoking status, ethanol intake, regular exercise, educational level, and income.

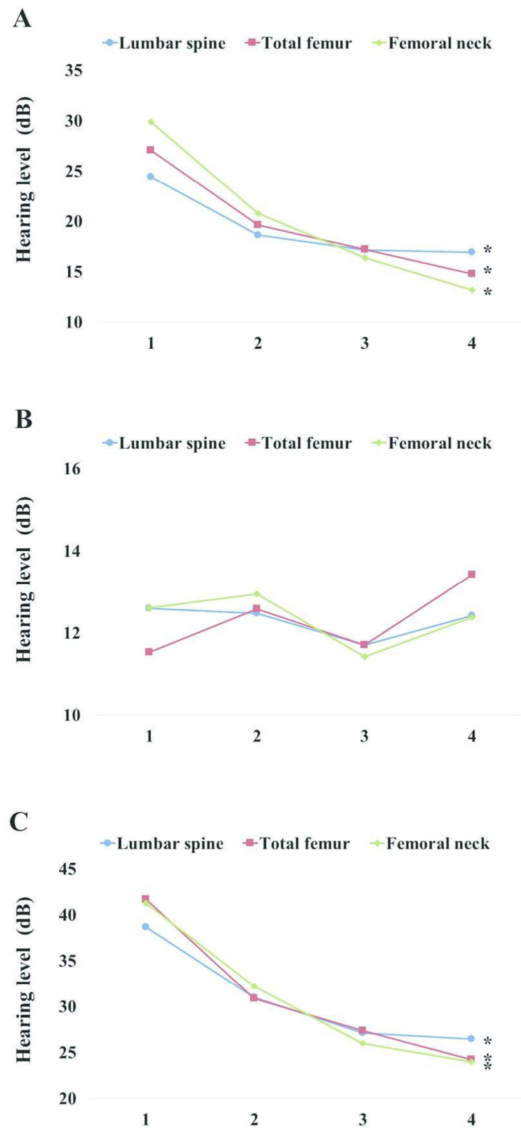
Model 3 is adjusted for age, body mass index, smoking status, ethanol intake, regular exercise, educational level, income, 25-hydroxyvitamin D, stress level, and tinnitus.

Results are presented as an estimated beta with corresponding standard error (SE) and p-value.

Figure legend

Figure 1. Mean values of hearing level according to bone mineral density for premenopausal women (A), postmenopausal women (B), and men (C). After categorizing subjects into four groups based on BMD (quartile 1, with the highest, to quartile 4, with the lowest) in the lumbar spine, total femur, and femur neck, we found a tendency toward significantly decreased hearing as a function of quartile decreases in BMD among postmenopausal women.

* $P < 0.05$ was considered statistically significant.



Mean values of hearing level according to bone mineral density for premenopausal (A) postmenopausal (B) women and men(C). After categorizing subjects into four groups based on BMD (quartile 1, with the highest, to quartile 4, with the lowest) in the lumbar spine, total femur, and femur neck, we found a tendency toward significantly decreased hearing as a function of quartile decreases in BMD among postmenopausal women.
* $P < 0.05$ was considered to be statistically significant.

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STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Page 1 (title)	The Korea National Health and Nutrition Examination Survey
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Page 2	Abstract
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 3	Several studies have evaluated the association between BMD and hearing sensitivity.
Objectives	3	State specific objectives, including any prespecified hypotheses	Page 4	We sought to evaluate the relationship between BMD and hearing impairment in a nationally representative sample of Korean adults.
Methods				
Study design	4	Present key elements of study design early in the paper	Page 5	KNHANES is a nationwide survey designed to assess national health and nutrition levels accurately
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Page 5	This study was based on data collected during the 2010–2012 KNHANES (Korea Centers for Disease Control and Prevention)
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of	Page 5	The sample included 12,499 participants aged over 19 years.

		participants		
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case		
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Page 5, 6, and 7	tinnitus, Smoking history, alcohol absorption, Regular exercise, Weight and height, Body mass index (BMI), Waist circumference (WC), and Metabolic syndrome
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Page 5	The survey consists of a health interview, a nutritional survey, and a health examination survey. The survey amasses data via household interviews and by direct standardized physical examinations conducted in specially equipped mobile examination centers.
Bias	9	Describe any efforts to address potential sources of bias	Page 8	We first adjusted for age (model 1), adjusted for age, BMI, smoking status, alcohol intake, and regular exercise (model 2), and adjusted for age, BMI, smoking status, alcohol intake, regular exercise, metabolic syndrome, stress, and tinnitus (model 3).
Study size	10	Explain how the study size was arrived at	Page 5	This study was based on data collected during the 2010–2012

	KNHANES (Korea Centers for Disease Control and Prevention).

Continued on next page

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Page 5, 6, and 7	The BMD values of the lumbar spine (L1–L4), femoral neck, and total femur were measured using dual-energy X-ray absorptiometry (DXA) using a Discovery fan-beam densitometer (Hologic, Bedford, MA, USA) and the Hologic Discovery software (ver. 3.1). Smoking history was categorized into the three groups: current smoker, ex-smoker and non-smoker Subjects who drank more than 30 g/day were designated as heavy drinkers. Regular exercise was defined as strenuous physical activity performed for at least 20 min at a time at least three times a week.
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	Page 6 and 7	The prevalence and 95% confidence intervals (CIs) for dizziness were calculated. In the univariate analysis, the Rao-Scott chi-square test (using PROC SURVEYFREQ in SAS) and logistic regression analysis (using PROC SURVEYLOGISTIC in SAS) were used to test the association between gender and risk factors in a complex sampling design. Participants' characteristics were described using means and standard errors for continuous

				variables and numbers and percentages for categorical variables. A final logistic regression model was used to examine the association between sleep duration and dizziness.
		(*b*) Describe any methods used to examine subgroups and interactions	Page 6 and 7	Same as the above.
		(*c*) Explain how missing data were addressed	Page 6 and 7	Statistical analyses were performed using the SAS survey procedure (ver. 9.3; SAS Institute, Cary, NC, USA) to reflect the complex sampling design and sampling weights of KNHANES and to provide nationally representative prevalence estimates. The procedures included unequal probabilities of selection, oversampling, and nonresponse so that inferences could be made about the Korean adolescent participants.
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy		
		(*e*) Describe any sensitivity analyses		
Results				
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Page 9	There were 12,499 respondents in our study, comprising 5406 (43.25%) males and 7093 (56.75%) females, and 2690 had experienced dizziness or imbalance in the prior

				12 months.
		(b) Give reasons for non-participation at each stage	Page 9	Same as the above.
		(c) Consider use of a flow diagram		
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Page 9	The baseline characteristics of the study subjects according to gender are shown in Table 1.
		(b) Indicate number of participants with missing data for each variable of interest	Page 9	There were 12,499 respondents in our study, comprising 5406 (43.25%) males and 7093 (56.75%) females, and 2690 had experienced dizziness or imbalance in the prior 12 months.
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)		
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time		
		Case-control study—Report numbers in each exposure category, or summary measures of exposure		
		Cross-sectional study—Report numbers of outcome events or summary measures	Page 9	There were 12,499 respondents in our study, comprising 5406 (43.25%) males and 7093 (56.75%) females, and 2690 had experienced dizziness or imbalance in the prior 12 months.
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Page 9	The adjusted OR for sleep duration is not significant in dizziness for men. Meanwhile, the risk of dizziness was significantly associated with sleep duration in only women. Compared to participants with optimal sleep duration (six to eight hours), those with severe short sleep duration (≤5 hours) (OR [95% CI]: 1.566 [1.289-

			1.903] in model 1, OR [95% CI]: 1.557 [1.276-1.898] in model 2, and OR [95% CI]: 1.473 [1.194-1.818] in model 3) and severe long sleep duration (≥9 hours) (OR [95% CI]: 1.420 [1.042-1.936] in model 1, OR [95% CI]: 1.418 [1.040-1.934] in model 2, and OR [95% CI]: 1.472 [1.078-2.009] in model 3) had an increased dizziness risk after adjusting for the confounders.
	(*b*) Report category boundaries when continuous variables were categorized	Page 9	Among variables regarding health behavior patterns, current smoker, heavy drinker, routine exercise, job, and waist circumference were significantly associated with men.
	(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period		

Continued on next page

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses		
Discussion				
Key results	18	Summarise key results with reference to study objectives	Page 10	abnormal sleep duration such as short or long duration are associated with dizziness in women
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Page 12	By contrast, this study also had several limitations. First, sleep duration and dizziness were reported only by respondents and were not recorded or observed directly. This may bias our results, as there is only modest correlation between reported and recorded sleep. Although there were some researches with objective sleep data, those measures are not practical for large, nationally representative samples. Furthermore, self-reported sleep duration has been used widely in epidemiological studies examining the relationship between sleep duration and morbidity and mortality. Secondly, our data consider only abnormal duration of sleep. Additional sleep problems, such as snoring, apnea and daytime sleepiness, should be investigated in future studies. Third, the related variables of which the presence or absence may be associated with

				vestibular dysfunction and could affect the results were not able to be evaluated and the participants with other acute disease status, such as BPPV, were not able to be excluded from this study.
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Page 12	Same as the above.
Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 13	KNHANES is a nationwide cross-sectional study to select a representative sample of the Korean population. This survey employed stratified multi-stage design based on age, sex, and residence geographic area.
Other information				
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based		No funding source

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.