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Prevalence of osteoporosis among North Korean women refugees living in South Korea: a case-control study

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Abstract

Objective To investigate the prevalence of osteoporosis among North Korean women refugees when compared with South Korean women, who have identical genetic backgrounds but experience different environments.

Design Case-control study.

Setting: North Korean Refugee Health in South Korea (NORNS) study in South Korea.

Participants We evaluated 122 North Korean women who participated in NORNS study and 366 age-/menopausal status-matched South Korean women from the Korea University Medical Center (KUMC) health examination cohort. The median age of the NORNS participants was 46 years (interquartile range [IQR], 40–60 years) with 52 women (42.6%) being postmenopausal.

Results: Among the postmenopausal women, NORNS participants had a higher body mass index and number of pregnancies and lower physical activity than the KUMC participants. The overall prevalence of osteoporosis was 48% (25/52) and 17% (27/156) in NORNS and KUMC participants, respectively. The bone mineral density (BMD) values at the lumbar spine, femur neck, and total hip were significantly lower in postmenopausal NORNS women than in the postmenopausal KUMC women. Old age, low body weight, low vitamin D level, and late age of menarche were associated with low BMD among the postmenopausal North Korean refugees. In premenopausal participants, the NORNS women had lower body weight and physical activity than the KUMC women at baseline. All the NORNS women had normal Z-scores, although the BMD at the lumbar spine was significantly lower in NORNS women than in the KUMC women (0.952 vs. 1.002 g/cm^2, $P < 0.001$).

Conclusions: Osteoporosis is a prevalent health problem in postmenopausal North Korean women refugees living in South Korea. It is conceivable to prepare vigilant countermeasures for bone health deterioration in this growing population, especially for postmenopausal women. Further research is warranted to determine the cause of the differences between participants of the same ethnic group.

Keywords: Bone density, Osteoporosis, Democratic People's Republic of Korea, Republic of Korea, Case-control study

Strengths and limitations of this study

- We compared the prevalence of osteoporosis between North Korean women refugees and age-/menopausal status-matched South Korean women of same ethnicity but with different environmental factors.
- Fastidious screening and management of osteoporosis in this unique postmenopausal North Korean refugee is reasonable.
- Our analysis, restricted to relatively small portion of North Korean women refugees, minimize the representativeness of the entire North Korean women population.

INTRODUCTION

Osteoporosis is one of the most common health problems in an aged society, particularly among older women, leading to fractures that are closely associated with morbidity and mortality.[1-3] Early detection and risk management can reduce the osteoporosis incidence and prevent fractures. Older age, female sex, current smoking, physical inactivity, and medications such as corticosteroids are well-known risk factors for osteoporosis.[4, 5] Moreover, recent epidemiologic studies have demonstrated that immigration may be a risk factor for osteoporosis, suggesting that Asian women immigrants have a high prevalence of osteoporosis and low bone mineral density (BMD). In a study of 73 premenopausal Chinese immigrant women living in Denmark, their BMD was significantly lower than that of the general population of premenopausal Danish women.[6] Similarly, Marquez et al. reported that immigrants from Southeast Asia had a lower BMD than that of white residents living in Minnesota, USA.[7] However, most previous studies had a small sample size consisting of heterogeneous ethnic groups and compared the prevalence of osteoporosis between immigrants and their host nation's general population with a different ethnicity from that of the immigrants. In this regard, how environmental factors influence the bone health in groups with the same ethnicity has not been clearly elucidated.

The Korean peninsula has been the only divided country in the world since 1945. In the subsequent decades, South and North Korea have experienced stark differences in politics, economics, and culture. North Korea has experienced severe poverty due to its economic deterioration and global sanctions;[8] therefore, most North Korean refugees who left North Korea and resettled in South Korea have experienced penury and malnutrition.[9, 10] Moreover, we previously reported a high prevalence of vitamin D deficiency in North Korean refugees

that has been well documented for its role in the maintenance of bone health.[11, 12]

In the present study, we evaluated the prevalence of osteoporosis in North Korean women refugees compared with that in South Korean women, who are of the same ethnicity but who have encountered completely different socioeconomic environments. Furthermore, we analyzed the associated risk factors for osteoporosis in North Korean women refugees.

METHODS

Participants and study design

The North Korea Refugee Health in South Korea (NORNS) study, which started in October 2008 and is still ongoing, aimed to evaluate the medical health and disease status of North Korean refugees in South Korea. The NORNS study is a longitudinal study comprising two surveys, with the second survey conducted 3.5 years after the first survey. The NORNS study consisted of interviews, structural surveys, physical examinations, and blood sampling in both the first and second surveys and dual-energy x-ray absorptiometry (DXA) only in the second survey. The entire study process was conducted in Anam Hospital at the Korea University Medical Center in Seoul. More specific details on the NORNS study design and general features have been published elsewhere.[11, 13]

Figure 1 illustrates the study design. Age- and menopausal status-matched control subjects were selected at a 1:3 ratio of cases to controls from the Korea University Medical Center (KUMC) Anam Hospital Health Examination cohort to compare the prevalence of osteoporosis between North Korean women refugees (NORNS group) and South Korean women (KUMC group). Written informed consent was obtained from all participants, and this study was approved by the Institutional Review Board (IRB) of Korea University's Anam Hospital under

IRB process No. ED08023. We used the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) case-control reporting guidelines.[14]

Questionnaire and anthropometric measurements

General demographic data including age, sex, year of emigration from North Korea, year of entry into South Korea, menarche age, and menopausal status as well as health-related lifestyle behaviors including smoking, alcohol consumption, and physical activity were included in the questionnaire. Anthropometric measurements including height and body weight were conducted after an overnight fast. Blood samples for vitamin D (25-hydroxyvitamin D [25(OH)D]) were collected after overnight fasting and measured using a gamma counter (1470 WIZARD; Perkin-Elmer, Turku, Finland). For handling the missing data of questionnaire and anthropometric measurements, available-case analyses (also known as pairwise deletion) were used without additional data handing.

BMD measurements

BMD at the lumbar spine, left femur neck, and total hip was measured in the NORNS and KUMC cohorts by DXA using the Hologic Discovery system (HOLOGIC Inc., Waltham, MA, USA). BMD was expressed as the total bone mineral content (g) divided by the area (cm^2). The lumbar spine BMD, T-score, and Z-score were calculated as the mean values of the L1 through L4 spine. For premenopausal women, a race-adjusted Z-score ≤-2.0 was considered to be below the expected range for their age group and a Z-score >-2.0 as within the expected range for their age group. For postmenopausal women, osteoporosis was defined as a T-score ≤-2.5 in at least one of the lumbar spine, left femur neck, and total hip; osteopenia as a T-score >-2.5 and

<-1.0; normal as a T-score ≥-1.0.[15]

Statistical analysis

We presented continuous data as mean and standard deviation (SD) using the paired *t*-test for normally distributed variables and as medians and interquartile ranges (IQRs) using Wilcoxon-Mann-Whitney tests for non-normally distributed variables. Categorical data are presented as frequencies and percentages and were analyzed using chi-square or Fisher's exact tests for small case numbers. BMD values between the NORNS and KUMC cohorts were compared using Wilcoxon signed-rank tests. Correlations between BMD and demographic, gynecologic, and medical factors in the NORNS cohort were evaluated using a simple linear regression model. Finally, logistic regression analyses were used to investigate the risk factors for osteoporosis in postmenopausal women in the NORNS cohort. All reported *P*-values were two-sided and those <0.05 were considered statistically significant. All analyses were performed using IBM SPSS Statistics for Windows, version 20.0 (IBM Corp., Armonk, NY, USA) and GraphPad Prism version 7 (GraphPad Software, San Diego, CA, USA).

RESULTS

Baseline characteristics of the NORNS and KUMC groups

Among the 122 North Korean refugees, 70 were premenopausal women (57.4%) with a median age of 41 (IQR, 37 to 44) years and 52 were postmenopausal women (43.6%) with a median age of 62.5 (IQR, 55 to 68.5) years. The median duration of living in South Korea was 6.2 (IQR, 4.2 to 9.0) years. Their baseline characteristics in comparison with that of KUMC participants according to menopause status are described in Table 1. The NORNS

premenopausal women had a significantly lower mean height (155.0 ± 4.4 vs. 161.0 ± 5.2 cm, $P < 0.001$) and body weight (53.2 ± 6.7 vs. 58.0 ± 9.4 kg, $P < 0.001$) than the KUMC premenopausal women, whereas no difference in BMI (22.1 ± 2.3 vs. 22.4 ± 3.4 kg/m^2, $P = 0.514$) was observed between the two groups. However, the NORNS postmenopausal women had a lower height (153.1 ± 4.8 vs. 155.8 ± 5.3 cm, $P = 0.002$) and higher BMI (24.9 ± 3.2 vs. 23.4 ± 2.8 kg/m^2, $P = 0.002$) than the KUMC postmenopausal women. There was no difference in body weight (57.8 ± 7.5 vs. 56.7 6.8 kg, $P = 0.320$) between the two groups. The proportion of subjects engaged in physical activity for more than 5 hours per week was lower in both the NORNS pre- and postmenopausal women than in the KUMC pre- and postmenopausal women. All NORNS premenopausal women were never smokers, whereas 22 of 210 KUMC premenopausal women were ex-/current smokers ($P = 0.006$).

Serum vitamin D levels were obtained in 66 of 122 NORNS participants, with a mean level of 15.0 ± 4.3 ng/mL, and no subject had an adequate vitamin D level (25(OH)D ≥30 ng/mL). However, we could not assess the vitamin D level for KUMC participants, because their general health examination did not include a routine check for serum vitamin D level.

Comparison of osteoporosis prevalence and BMD between the NORNS and KUMC groups

All premenopausal participants in the NORNS group had normal Z-scores, whereas four premenopausal women in the KUMC group (1.9%, 4 of 210) had Z-scores below the expected range for their age group ($P = 0.575$). However, the prevalence of osteoporosis was significantly higher in the postmenopausal NORNS group than that in the postmenopausal KUMC group (48.1% vs. 17.3%) (Table 2). The proportion of participants with a normal T-score was more than two times higher in the KUMC postmenopausal group (20.5%, 32 of 156)

than that in the NORNS postmenopausal group (9.6%, 5 of 52). Figure 2 demonstrates the proportion of participants with osteoporosis and osteopenia in the postmenopausal NORNS and KUMC groups, stratified by 10-year age categories. The prevalence of osteoporosis in the postmenopausal NORNS group was 35% (7 of 20), 52% (10 of 19), and 67% (8 of 12) in participants aged 50–59, 60–69, and >70 years, respectively. For postmenopausal KUMC women, the prevalence of osteoporosis in each age group was higher than that of the respective NORNS group (5%, 3 of 60; 26%, 15 of 57; and 22%, 9 of 36 in those aged 50–59, 60–69, and >70 years, respectively). None of the participants over 60 years in the NORNS group had a normal T-score.

Table 3 shows the comparisons of BMD between the NORNS and KUMC groups. In premenopausal women, the lumbar spine BMD of the NORNS group was 0.952 ± 0.10, whereas that of the KUMC group was 1.001 ± 0.12, a significant difference ($P < 0.001$). Femur neck and total hip BMD did not differ significantly between the two groups. However, in postmenopausal women, the BMD of the lumbar spine, femur neck, and total hip was consistently lower in the NORNS group than in the KUMC group.

Risk factors associated with osteoporosis and low BMD in postmenopausal North Korean refugees

The risk factors associated with osteoporosis in the NORNS postmenopausal group, identified using logistic regression analysis, are shown in Table 4. Older age, lower body weight, and late menarche age were significantly related to osteoporosis in this group. However, the duration of living in South Korea as well as well-known risk factors such as smoking, alcohol consumption, and physical activity, were not. In addition, simple linear regression to determine

the factors correlated with lumbar spine BMD in the postmenopausal NORNS group revealed that old age, low vitamin D level, low body weight, and late menarche age were significantly associated with low BMD (Figure 3). There was no association between the duration of living in South Korea and BMD.

DISCUSSION

This cross-sectional case-control study demonstrated that the prevalence of osteoporosis in postmenopausal North Korean refugees was significantly higher than that in age-matched South Korean postmenopausal women of the general population. BMD values at the lumbar spine, femur neck, and total hip were significantly lower in postmenopausal North Korean refugees than those in South Korean postmenopausal women. Old age, low body weight, and late age of menarche were associated with osteoporosis and low BMD in the NORNS postmenopausal group.

Most of the postmenopausal women (92%, 48 of 52) in the NORNS group had endured the worst food shortage, the Arduous March, between 1996 and 2000, in which more than 600,000 people in North Korea died of starvation.[16] During this period, they could not obtain sufficient nutrients, including protein, calcium, and vitamin D, which have important roles in bone mineral acquisition. Moreover, the youngest age at the time of escape from North Korea in postmenopausal NORNS women was 35 years, indicating that all postmenopausal participants had reached their peak bone mass before leaving North Korea. Several studies have revealed that subjects who experience malnutrition during childhood and early adulthood are less likely to reach peak bone mass, leading to osteoporosis in later life.[17-19] Our results are also in line with previous cohort studies demonstrating the negative effects of malnutrition and famine on

bone health. Marcus et al. reported a high prevalence of osteoporosis and osteopenia (55% and 40%, respectively) among Holocaust survivors who had experienced malnutrition during their childhood.[20] Another study conducted in Hong Kong observed that past exposure to famine, especially in childhood, was associated with osteoporosis in postmenopausal women aged 65 years or older.[21]

Vitamin D has been well documented to play an important role in bone mineral metabolism via interactions with calcium and parathyroid hormone.[12] Our previous study with 366 North Korean refugees demonstrated that the prevalence of vitamin D deficiency (25(OH)D <20 ng/mL) was 87%.[11] In the present study, we also found that no participants had an adequate vitamin D level (25(OH)D ≥30 ng/mL) and that a low vitamin D level was associated with low BMD at the lumbar spine, even though we could not prove any correlation between vitamin D level and the risk of osteoporosis.

We did not evaluate the relationships between well-known risk factors, such as smoking and physical inactivity, and osteoporosis in this study. Among 110 subjects who provided information about smoking, only two subjects in this group were current/ex-smokers. The small proportion of subjects who were current/ex-smokers revealed no significant effect on osteoporosis. Because the level of physical activity was collected in a memory-recall questionnaire, it was difficult to obtain accurate data, particularly in the older age group.

Previous immigration studies showed that the duration of living in the migrated country was associated with BMD. Wang et al. reported that Chinese women who had migrated and lived in Denmark for more than 12 years had a significantly higher BMD than those who had lived there for less than 12 years.[6] Rajeev et al. also reported that Chinese women who had lived in New York for less than 10 years had a lower BMD than women who had lived in New York

for more than 20 years.[22] However, we did not observe a significant association between the duration of living in South Korea and osteoporosis. The median period of living in South Korea in postmenopausal North Korean refugees (7.3 years; IQR, 4.2 to 9.1 years) was relatively short compared with that in previous immigration studies, and less than 20% of postmenopausal North Korean refugees (10 of 52) had lived in South Korea for more than 10 years. Another explanation is that the duration of living in South Korea itself may not be a risk factor or indicator of acculturation, but may simply provide the circumstances in which other risk factors cause health problems. Our previous study based on the NORNS cohort identified that excess weight gain, but not duration of residence in South Korea, was an independent risk factor for metabolic syndrome,[23] making our hypothesis more plausible.

None of the premenopausal North Korean refugees had a Z-score below the expected range for their age group; however, the median BMD at the lumbar spine was significantly lower than that of the South Korean premenopausal women. A previous study reported that young North Korean refugees aged 12 to 24 years had a significantly lower daily intake of energy and most nutrients, including protein and calcium, than that of general age-/sex-matched South Koreans.[24] Our study also showed that premenopausal North Korean women had significantly lower body weight and less physical activity than did South Korean premenopausal women. These results imply that young North Korean refugees are at high risk for osteoporosis, indicating the importance of meticulous screening and follow-up.

Several limitations of this study need to be acknowledged. First, the relatively small number of participants may have reduced the power of the results and may not represent the entire population of female North Korean refugees living in South Korea. The NORNS study is based on the voluntary participation of North Korean refugees living in the Seoul metropolitan area,

and it has taken considerable time to recruit large sample sizes. Second, we collected information about their postmenopausal status using self-reported questionnaires, which may have led to inaccuracy in the perimenopausal age group. Finally, the association between serum vitamin D level and the lumbar BMD was not universal in this group because we could not check vitamin D levels in all participants.

Conclusions

This study reveals the high prevalence of osteoporosis in postmenopausal North Korean refugees living in South Korea compared with that in South Korean postmenopausal women. Outreach efforts are needed in this community to promote prevention, treatment, and access to care, especially among those of older age, with low body weight, and in late menarche. Further longitudinal studies are needed to evaluate changes in bone health in this group.

Declarations

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Author Contribution SGK designed the NORNS study and supervised the data collection and data entry. JHA and KJK conducted the statistical analysis and drafted the manuscript. KJK, NHK, and HYK coordinated the data collection. JHY, HJY, JAS, NHK, KMC, and SHB commented on and critically revised the manuscript. All authors read and approved the final manuscript.

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Competing interests All authors declare that they have no competing interests.

Consent for publication Not applicable.

Ethical approval and consent to participate All subjects provided written informed consent to participate. This study was approved by the Institutional Review Board (IRB) of Korea University's Anam Hospital (IRB No. ED08023).

Availability of data and material The dataset generated during the current study is available upon reasonable request from the corresponding author, Sin Gon Kim (k50367@korea.ac.kr).

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Figure legends

Figure 1 Study design.

Figure 2 Proportion of subjects with osteoporosis, osteopenia, and normal bone mineral density stratified by 10-year age groups in North Korean (A) and South Korean (B) postmenopausal women.

Figure 3 Simple linear regression between the lumbar spine bone mineral density (BMD) of postmenopausal North Korean women and age (A), vitamin D level (B), body weight (C), menarche age (D), and duration of living in South Korea (E).

Table 1 Baseline characteristics of North Korean women refugees according to menopausal status

	NORNS			KUMC		
	All†	Premenopausal	Postmenopausal	All†	Premenopausal	Postmenopausal
Total cases, n (%)	122	70 (57.4)	52 (42.6)	366	210 (57.4)	156 (42.6)
Age, median (years, IQR)	46.0 (40.0-60.0)	41.0 (37.0-44.0)	62.5 (55.0-68.5)	46.0 (40.0-60.0)	41.0 (37.0-44.0)	62.5 (55.0-68.5)
Height (mean ± SD), cm	154.2 ± 4.7	155.0 ± 4.4	153.1 ± 4.8	158.8 ± 5.8	161.0 ± 5.2*	155.8 ± 5.3**
Body weight (mean ± SD), kg	55.2 ± 7.4	53.2 ± 6.7	57.8 ± 7.5	57.5 ± 8.4	58.0 ± 9.4*	56.7 ± 6.8
BMI (mean ± SD), kg/m^2	23.3 ± 3.0	22.1 ± 2.3	24.9 ± 3.2	22.8 ± 3.2	22.4 ± 3.4	23.4 ± 2.8**
Age at menarche, median (years, IQR) (n=111)‡	17.0 (15.0-18.0)	16.0 (15.0-18.0)	17.0 (16.0-19.0)	14 (13-15)	14 (13-14)*	15 (14-17)**
Age at menopause (mean ± SD), years (n=43)‡	49.2 ± 4.0	—	49.2 ± 4.0	50.6 ± 4.3	—	50.6 ± 4.3
Alcohol, n (%)						
Never drinker	43 (37.4)	14 (20.6)	29 (61.7)	167 (46)	61 (29.0)	106 (69.3)
Ex-/current drinker	72 (62.6)	54 (79.4)	18 (38.3)	196 (54)	149 (71.0)	47 (30.7)
Smoking, n (%)						
Never smoker	103 (98.1)	65 (100)	38 (95)	326 (91.8)	186 (89.4)*	139 (95.2)
Ex-/current smoker	2 (1.9)	0	2 (5.0)	29 (8.2)	22 (10.6)*	7 (4.9)
Physical activity, n (%)						
Never	60 (56.6)	38 (56.7)	22 (56.4)	157 (43.7)	104(50.7)*	53 (34.4)**
<5 hours/week	37 (34.9)	26 (38.8)	11 (28.2)	117 (32.6)	64 (31.2)*	53 (34.4)**
≥5 hours/week	9 (8.5)	3 (4.5)	6 (15.4)	85 (23.7)	37 (18.0)*	48 (31.2)**
25(OH)D (mean ± SD), ng/mL (n=66)‡	15.0 ± 4.3	15.4 ± 4.2	14.1 ± 4.5	—		
OCP use, n (%) (n=110)‡	17 (15.5)	16 (24.6)	1 (2.2)	55 (15.9)	18 (9.0)*	37 (25.0)**
Number of pregnancies, median (IQR) (n=117)‡	3.0 (2.0-4.0)	2.0 (1.0-3.0)	3.0 (2.0-4.0)	2.0 (1.0-2.0)	2.0 (1.0-2.0)*	2.0 (2.0-3.0)**
Age at escape from North Korea, (mean ± SD), [min-max], years	37.9 ± 13.5 [17-69]	28.43 ± 6.2 [17-40]	51.0 ± 9.2 [35-69]	—		
Duration of living in South Korea, median (IQR), years	6.2 (4.2-9.0)	5.3 (4.1-8.0)	7.3 (4.2-9.1)	—		

Abbreviations: BMI, body mass index; IQR, interquartile range; KUMC, Korea University Medical Center; NORNS, North Korea Refugee Health in South Korea; OCP, oral contraceptive pill; 25(OH)D, 25-hydroxyvitamin D; SD, standard deviation.
*P-value < 0.05 compared with NORNS premenopausal women.
**P-value < 0.05 compared with NORNS postmenopausal women.
† Valid percentages were displayed in categorical variables.
‡ Available data number were described

Table 2 Prevalence of osteoporosis in North Korean women refugees and South Korean women

	Premenopausal, n (%)		
	NORNS (n = 70)	KUMC (n = 210)	*P*-value
Below the expected range (Z-score ≤ -2.0)	0	4 (1.9)	0.575
Within the expected range (Z-score > -2.0)	70 (100)	206 (98.1)	
	Postmenopausal, n (%)		
	NORNS (n = 52)	KUMC (n = 156)	*P*-value
Normal (T-score ≥ -1.0)	5 (9.6)	32 (20.5)	<0.001
Osteopenia (-2.5 < T-score < -1.0)	22 (42.3)	97 (62.2)	
Osteoporosis (T-score ≤ -2.5)	25 (48.1)	27 (17.3)	

Abbreviations: NORNS, North Korea Refugee Health in South Korea; KUMC, Korea University Medical Center.

Table 3 Comparisons of BMD at the lumbar spine, femur neck, and total hip between North Korean refugee women and South Korean women

	Lumbar spine BMD (g/cm^2)	*P*-value	Femur neck BMD (g/cm^2)	*P*-value	Total hip BMD (g/cm^2)	*P*-value
Premenopausal						
NORNS (n = 70)	0.952 ± 0.10	<0.001	0.735 ± 0.08	0.477	0.881 ± 0.13	0.737
KUMC (n = 210)	1.001 ± 0.12		0.741 ± 0.10		0.884 ± 0.10	
Postmenopausal						
NORNS (n = 52)	0.760 ± 0.11	<0.001	0.610 ± 0.10	<0.001	0.774 ± 0.11	0.002
KUMC (n = 156)	0.861 ± 0.12		0.653 ± 0.09		0.808 ± 0.10	

Abbreviations: BMD, bone mineral density; NORNS, North Korea Refugee Health in South Korea; KUMC, Korea University Medical Center.

Data are expressed as mean ± standard deviation.

Table 4 Risk factors for osteoporosis in postmenopausal North Korean women identified by univariate logistic regression analysis

Variables	OR	95% CI	*P*-value
Age	1.084	1.007-1.166	0.031
Alcohol (never vs. ex/current)	0.857	0.263-2.792	0.798
Smoking (never vs. ex/current)	0	0	0.999
Physical activity			
<5 hours/week vs. never	1.458	0.335-0.347	0.615
≥5 hours/week vs. never	3.5	0.52-23.559	0.198
Weight	0.869	0.788-0.959	0.005
Height	0.908	0.803-1.027	0.124
Years living in South Korea			
5-10 vs. <5	1.667	0.453-6.131	0.442
≥10 vs. <5	0.667	0.117-3.813	0.649
Age at menarche	1.473	1.043-2.081	0.028
Age at menopause	1.134	0.955-1.347	0.152

Abbreviations: CI, confidence interval; OR, odds ratio.

Fig. 1

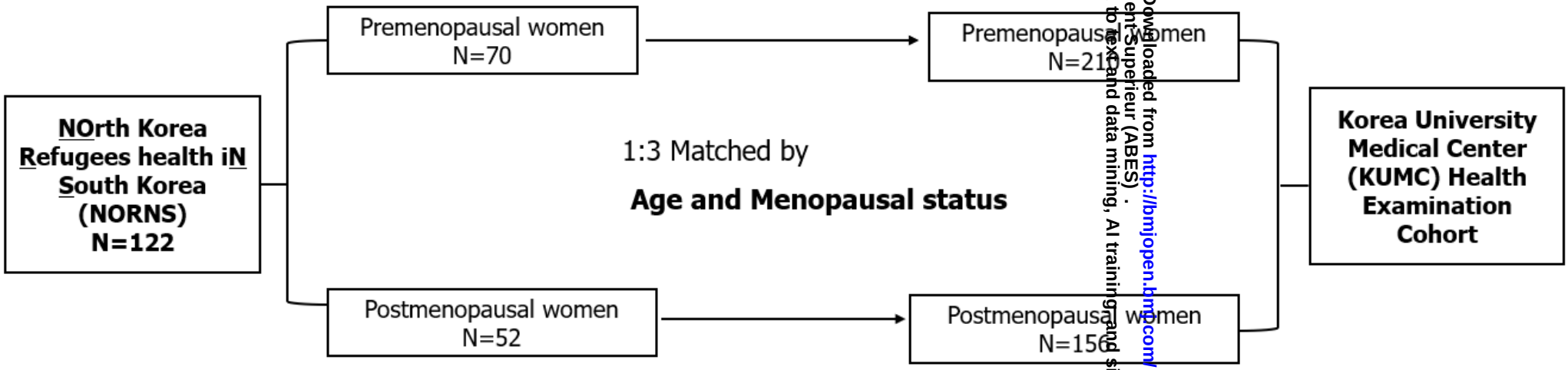


Fig. 2

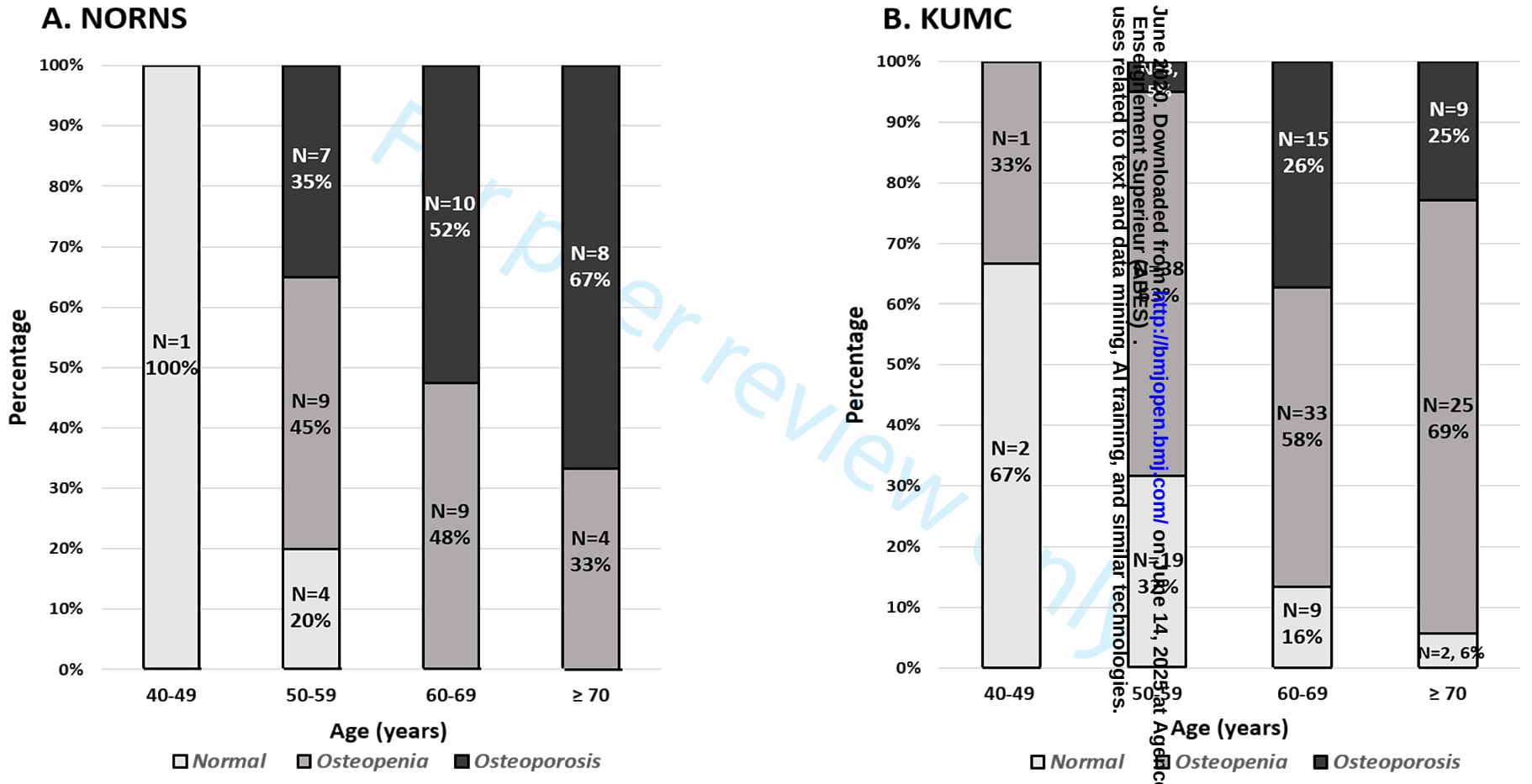
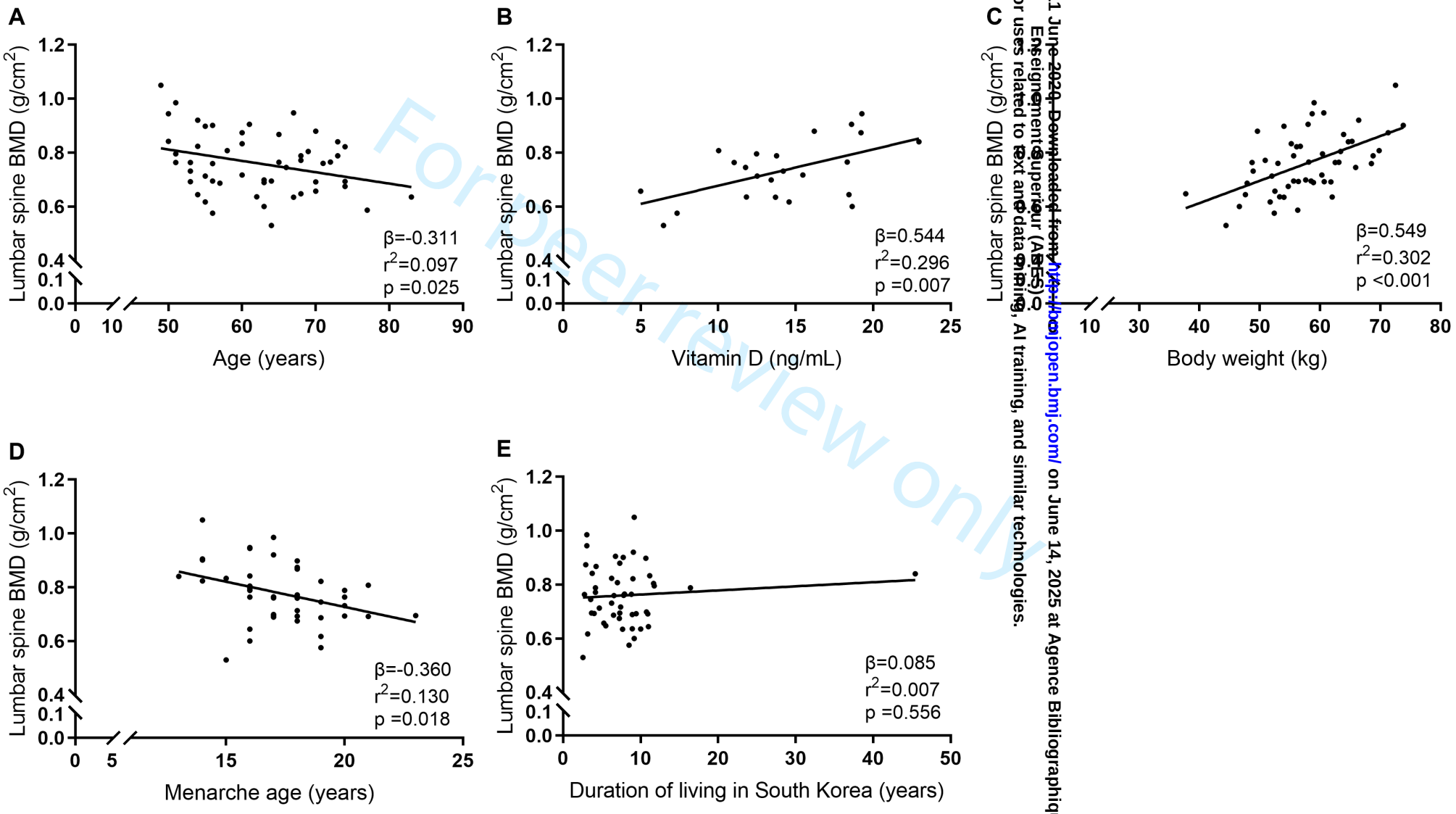


Fig. 3



Reporting checklist for case-control study.

Based on the STROBE case-control guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

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In your methods section, say that you used the STROBE case-controlreporting guidelines, and cite them as:

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		Reporting Item	Page Number
Title and abstract			
Title	#1a	Indicate the study's design with a commonly used term in the title or the abstract	1

Abstract	#1b	Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background / rationale	#2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	#3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	#4	Present key elements of study design early in the paper	6
Setting	#5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Eligibility criteria	#6a	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. For matched studies, give matching criteria and the number of controls per case	6
Eligibility criteria	#6b	For matched studies, give matching criteria and the number of controls per case	6
	#7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7

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. Give information separately for cases and controls.	7
Bias	#9	Describe any efforts to address potential sources of bias	n/a
Study size	#10	Explain how the study size was arrived at	6
Quantitative variables	#11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	8
Statistical methods	#12a	Describe all statistical methods, including those used to control for confounding	8
Statistical methods	#12b	Describe any methods used to examine subgroups and interactions	8
Statistical methods	#12c	Explain how missing data were addressed	7
Statistical methods	#12d	If applicable, explain how matching of cases and controls was addressed	6
Statistical methods	#12e	Describe any sensitivity analyses	n/a

Results

Participants	#13a	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. Give information separately for cases and controls.	8-9
Participants	#13b	Give reasons for non-participation at each stage	n/a
Participants	#13c	Consider use of a flow diagram	6
Descriptive data	#14a	Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. Give information separately for cases and controls	8-9
Descriptive data	#14b	Indicate number of participants with missing data for each variable of interest	20
Outcome data	#15	Report numbers in each exposure category, or summary measures of exposure. Give information separately for cases and controls	n/a
Main results	#16a	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	10
Main results	#16b	Report category boundaries when continuous variables were categorized	9-10

Main results	#16c	If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	#17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	n/a
Discussion			
Key results	#18	Summarise key results with reference to study objectives	11
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.	13
Interpretation	#20	Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.	13
Generalisability	#21	Discuss the generalisability (external validity) of the study results	13
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	14

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Prevalence of osteoporosis among North Korean women refugees living in South Korea: a comparative cross-sectional cohort study

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Abstract

Objective: To investigate the prevalence of osteoporosis among North Korean women refugees when compared with South Korean women, who have identical genetic backgrounds but experience different environments.

Design: Comparative cross-sectional cohort study.

Setting: North Korean Refugee Health in South Korea (NORNS) study in South Korea.

Participants: We evaluated 122 North Korean women who participated in NORNS study and 366 age-/menopausal status-matched South Korean women from the Korea University Medical Center (KUMC) health examination cohort. The median age of the NORNS participants was 46 years (interquartile range [IQR], 40–60 years) with 52 women (42.6%) being postmenopausal.

Results: Among the postmenopausal women, NORNS participants had a higher body mass index and number of pregnancies and lower physical activity than the KUMC participants. The overall prevalence of osteoporosis was 48% (25/52) and 17% (27/156) in NORNS and KUMC participants, respectively. The bone mineral density (BMD) values at the lumbar spine, femur neck, and total hip were significantly lower in postmenopausal NORNS women than in the postmenopausal KUMC women. Old age, low body weight, and late age of menarche were associated with low BMD among the postmenopausal North Korean refugees. In premenopausal participants, the NORNS women had lower body weight and physical activity than the KUMC women at baseline. All the NORNS women had normal Z-scores, although the BMD at the lumbar spine was significantly lower in NORNS women than in the KUMC women (0.952 vs. 1.002 g/cm^2, $P < 0.001$).

Conclusions: Osteoporosis is a prevalent health problem in postmenopausal North Korean women refugees living in South Korea. It is conceivable to prepare vigilant countermeasures for bone health deterioration in this growing population, especially for postmenopausal women. Further research is warranted to determine the cause of the differences between participants of the same ethnic group.

Keywords: Bone density, Osteoporosis, Democratic People's Republic of Korea, Republic of Korea, cross-sectional study

Strengths and limitations of this study

- We compared the prevalence of osteoporosis between North Korean women refugees and age-/menopausal status-matched South Korean women of same ethnicity but with different environmental factors.
- This is the first qualitative study using dual-energy x-ray absorptiometry to identify the bone health status of North Korea women refugees living in South Korea.
- All the confounding factors associated with osteoporosis were not included in this study.
- Our analysis, restricted to relatively small portion of North Korean women refugees, minimize the representativeness of the entire North Korean women population.

INTRODUCTION

Osteoporosis is one of the most common health problems in an aged society, particularly among older women, leading to fractures that are closely associated with morbidity and mortality.[1-3] Early detection and risk management can reduce the osteoporosis incidence and prevent fractures. Environmental factors, such as malnutrition, current smoking status, alcohol consumption, physical inactivity, and medications such as corticosteroids in addition to inherent factors like older age and female sex are well known risk factors for osteoporosis.[4-7] Moreover, recent epidemiological studies have demonstrated that Asian women immigrants have a high prevalence of osteoporosis and low bone mineral density (BMD). In a study of 73 premenopausal Chinese immigrant women living in Denmark, their BMD was significantly lower than that of the general population of premenopausal Danish women.[8] Similarly, Marquez et al. reported that immigrants from Southeast Asia had a lower BMD than that of white residents living in Minnesota, USA.[9] However, previous studies were not sufficient to distinguish whether the lower BMD between the two groups was due to the environmental factors, including immigration itself, or ethnicities. In this context, how the environmental factors influence the bone health in an immigration population of the same ethnicity has not been clearly elucidated.

The Korean peninsula has been the only divided country in the world since 1945. In the subsequent decades, South and North Korea have experienced stark differences in politics, economics, and culture. North Korea has experienced severe poverty due to its economic deterioration and global sanctions;[10] therefore, most North Korean refugees who left North Korea and resettled in South Korea have experienced penury and malnutrition.[11, 12] Moreover, we previously reported a high prevalence of vitamin D deficiency in North Korean refugees

that has been well documented for its role in the maintenance of bone health.[13, 14]

In the present study, we evaluated the prevalence of osteoporosis in North Korean women refugees compared with that in South Korean women, who are of the same ethnicity but who have encountered completely different socioeconomic environments. Furthermore, we analyzed the associated risk factors for osteoporosis in North Korean women refugees.

METHODS

Participants and study design

The North Korea Refugee Health in South Korea (NORNS) study, which started in October 2008 and is still ongoing, aimed to evaluate the medical health and disease status of North Korean refugees in South Korea. The NORNS study is a longitudinal study consisting of two parts, the first and the second surveys, which followed the same participants as the first survey approximately 3.5 years later. The NORNS study included interviews, structural surveys, physical examinations, and blood samples in both the first and second surveys, however, dual-energy x-ray absorptiometry (DXA) was only performed in the second survey. The entire study process was conducted in Anam Hospital at the Korea University Medical Center in Seoul. More specific details on the NORNS study design and general features have been published elsewhere.[13, 15]

Figure 1 illustrates the study design. Age- and menopausal status-matched control subjects were randomly selected at a 1:3 ratio of cases to controls from the Korea University Medical Center (KUMC) Anam Hospital Health Examination cohort to compare the prevalence of osteoporosis between North Korean women refugees (NORNS group) and South Korean women (KUMC group). Written informed consent was obtained from all participants, and this

study was approved by the Institutional Review Board (IRB) of Korea University's Anam Hospital under IRB process No. ED08023. We used the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines.[16]

Questionnaire and anthropometric measurements

General demographic data including age, sex, year of emigration from North Korea, year of entry into South Korea, menarche age, and menopausal status as well as health-related lifestyle behaviors including smoking, alcohol consumption, and physical activity were included in the questionnaire. Anthropometric measurements including height and body weight were conducted after an overnight fast. All the demographic and anthropometric measurements based on the results of the second survey were analyzed in this study. For handling the missing data of questionnaire and anthropometric measurements, available-case analyses (also known as pairwise deletion) were used without additional data handing.

BMD measurements

BMD at the lumbar spine, left femur neck, and total hip was measured in the NORNS and KUMC cohorts by DXA using the Hologic Discovery system (HOLOGIC Inc., Waltham, MA, USA). BMD was expressed as the total bone mineral content (g) divided by the area (cm^2). The lumbar spine BMD, T-score, and Z-score were calculated as the mean values of the L1 through L4 spine. For premenopausal women, a race-adjusted Z-score ≤-2.0 was considered to be below the expected range for their age group and a Z-score >-2.0 as within the expected range for their age group. For postmenopausal women, osteoporosis was defined as a T-score ≤-2.5 in at least one of the lumbar spine, left femur neck, and total hip; osteopenia as a T-score >-2.5 and

<-1.0; normal as a T-score ≥-1.0.[17]

Statistical analysis

We presented continuous data as mean and standard deviation (SD) using the paired *t*-test for normally distributed variables and as medians and interquartile ranges (IQRs) using Wilcoxon-Mann-Whitney tests for non-normally distributed variables. Categorical data are presented as frequencies and percentages and were analyzed using chi-square or Fisher's exact tests for small case numbers. BMD values between the NORNS and KUMC cohorts were compared using Wilcoxon signed-rank tests. Correlations between BMD and demographic, gynecologic, and medical factors in the NORNS cohort were evaluated using a simple linear regression model. Finally, logistic regression analyses were used to investigate the risk factors for osteoporosis in postmenopausal women in the NORNS cohort. All reported *P*-values were two-sided and those <0.05 were considered statistically significant. All analyses were performed using IBM SPSS Statistics for Windows, version 20.0 (IBM Corp., Armonk, NY, USA) and GraphPad Prism version 7 (GraphPad Software, San Diego, CA, USA).

Patient and public involvement

Participants of this study or members of the public were not directly and personally involved with study design, data provision, analysis and publication of the study.

RESULTS

Baseline characteristics of the NORNS and KUMC groups

Among the 122 North Korean refugees, 70 were premenopausal women (57.4%) with a median

age of 41.0 (IQR, 37.0 to 44.0) years and 52 were postmenopausal women (42.6%) with a median age of 62.5 (IQR, 55.0 to 68.5) years. The median duration of living in South Korea was 6.2 (IQR, 4.2 to 9.0) years. Their baseline characteristics in comparison with that of KUMC participants according to menopause status are described in Table 1. The NORNS premenopausal women had a significantly lower mean height (155.0 ± 4.4 vs. 161.0 ± 5.2 cm, $P < 0.001$) and body weight (53.2 ± 6.7 vs. 58.0 ± 9.4 kg, $P < 0.001$) than the KUMC premenopausal women, whereas no difference in BMI (22.1 ± 2.3 vs. 22.4 ± 3.4 kg/m^2, $P = 0.514$) was observed between the two groups. However, the NORNS postmenopausal women had a lower height (153.1 ± 4.8 vs. 155.8 ± 5.3 cm, $P = 0.002$) and higher BMI (24.9 ± 3.2 vs. 23.4 ± 2.8 kg/m^2, $P = 0.002$) than the KUMC postmenopausal women. There was no difference in body weight (57.8 ± 7.5 vs. 56.7 ± 6.8 kg, $P = 0.320$) between the two groups. The proportion of subjects engaged in physical activity for more than 5 hours per week was lower in both the NORNS pre- and postmenopausal women than in the KUMC pre- and postmenopausal women. All NORNS premenopausal women were never smokers, whereas 22 of 210 KUMC premenopausal women were ex-/current smokers ($P = 0.006$).

Comparison of osteoporosis prevalence and BMD between the NORNS and KUMC groups

All premenopausal participants in the NORNS group had normal Z-scores, whereas four premenopausal women in the KUMC group (1.9%, 4 of 210) had Z-scores below the expected range for their age group ($P = 0.575$). However, the prevalence of osteoporosis was significantly higher in the postmenopausal NORNS group than that in the postmenopausal KUMC group (48.1% vs. 17.3%) (Table 2). The proportion of participants with a normal T-score was more than two times higher in the KUMC postmenopausal group (20.5%, 32 of 156)

than that in the NORNS postmenopausal group (9.6%, 5 of 52). Figure 2 demonstrates the proportion of participants with osteoporosis and osteopenia in the postmenopausal NORNS and KUMC groups, stratified by 10-year age categories. The prevalence of osteoporosis in the postmenopausal NORNS group was 35% (7 of 20), 52% (10 of 19), and 67% (8 of 12) in participants aged 50–59, 60–69, and >70 years, respectively. For postmenopausal KUMC women, the prevalence of osteoporosis in each age group was lower than that of the respective NORNS group (5%, 3 of 60; 26%, 15 of 57; and 25%, 9 of 36 in those aged 50–59, 60–69, and >70 years, respectively). None of the participants over 60 years in the NORNS group had a normal T-score.

Table 3 shows the comparisons of BMD between the NORNS and KUMC groups. In premenopausal women, the lumbar spine BMD of the NORNS group was 0.952 ± 0.10, whereas that of the KUMC group was 1.001 ± 0.12, a significant difference ($P < 0.001$). Femur neck and total hip BMD did not differ significantly between the two groups. However, in postmenopausal women, the BMD of the lumbar spine, femur neck, and total hip was consistently lower in the NORNS group than in the KUMC group.

Risk factors associated with osteoporosis and low BMD in postmenopausal North Korean refugees

The risk factors associated with osteoporosis in the NORNS postmenopausal group, identified using multivariate logistic regression analysis, are shown in Table 4. Lower body weight was the only significant risk factor of osteoporosis in this group. Older age and late menarche tend towards osteoporosis but no statistical significance, and duration of living in South Korea was not a risk factor of osteoporosis in this group. In addition, simple linear regression to determine

the factors correlated with lumbar spine BMD in the postmenopausal NORNS group revealed that old age, low body weight, and late menarche age were significantly associated with low BMD (Figure 3). There was no association between the duration of living in South Korea and BMD.

DISCUSSION

This comparative cross-sectional cohort study demonstrated that the prevalence of osteoporosis in postmenopausal North Korean refugees was significantly higher than that in age-matched postmenopausal South Korean women of the general population. BMD values at the lumbar spine, femur neck, and total hip were significantly lower in postmenopausal North Korean refugees than those in South Korean postmenopausal women. Low body weight was associated with osteoporosis and low BMD in the NORNS postmenopausal group.

Most of the postmenopausal women (92%, 48 of 52) in the NORNS group had endured the worst food shortage, the Arduous March, between 1996 and 2000, in which more than 600,000 people in North Korea died of starvation.[18] During this period, they could not obtain sufficient nutrients, including protein, calcium, and vitamin D, which have important roles in bone mineral acquisition. Although the actual nutritional status immediately after entering South Korea could not be evaluated due to restricted access authority, the youngest age at the time of escape from North Korea in the postmenopausal NORNS women was 35 years. This means that all postmenopausal participants had experienced malnutrition during their childhood and early adulthood and reached their peak bone mass before leaving North Korea. We consider that this is one of the major reasons why postmenopausal women were more vulnerable to osteoporosis. Several studies have revealed that subjects who experience malnutrition during

childhood and early adulthood are less likely to reach peak bone mass, leading to osteoporosis in later life.[19-21] Our results are also in line with previous cohort studies demonstrating the negative effects of malnutrition and famine on bone health. Marcus et al. reported a high prevalence of osteoporosis and osteopenia (55% and 40%, respectively) among Holocaust survivors who had experienced malnutrition during their childhood.[22] Another study conducted in Hong Kong observed that past exposure to famine, especially in childhood, was associated with osteoporosis in postmenopausal women aged 65 years or older.[23]

Vitamin D has been well documented to play an important role in bone mineral metabolism via interactions with calcium and parathyroid hormone.[14] Our previous study with 366 North Korean refugees demonstrated that the prevalence of vitamin D deficiency (25(OH)D <20 ng/mL) was 87%.[13] In the present study, serum vitamin D levels were only obtained in 66 of 122 NORNS participants (mean level of 15.0 ± 4.3 ng/mL) and no subject had adequate vitamin D level (25(OH)D ≥30 ng/mL, data now shown). Further meticulous study regarding the vitamin D deficiency and osteoporosis is needed in the future.

We did not evaluate the relationships between well-known risk factors, such as smoking and physical inactivity, and osteoporosis in this study. Among 110 subjects who provided information about smoking, only two subjects in this group were current/ex-smokers. The small proportion of subjects who were current/ex-smokers revealed no significant effect on osteoporosis. Because the level of physical activity was collected in a memory-recall questionnaire, it was difficult to obtain accurate data, particularly in the older age group.

Previous immigration studies showed that the duration of living in the migrated country was associated with BMD. Wang et al. reported that Chinese women who had migrated and lived in Denmark for more than 12 years had a significantly higher BMD than those who had lived

there for less than 12 years.[8] Rajeev et al. also reported that Chinese women who had lived in New York for less than 10 years had a lower BMD than women who had lived in New York for more than 20 years.[24] However, we did not observe a significant association between the duration of living in South Korea and osteoporosis. The median period of living in South Korea in postmenopausal North Korean refugees (7.3 years; IQR, 4.2 to 9.1 years) was relatively short compared with that in previous immigration studies, and less than 20% of postmenopausal North Korean refugees (10 of 52) had lived in South Korea for more than 10 years. Another explanation is that the duration of living in South Korea itself may not be a risk factor or indicator of acculturation, but may simply provide the circumstances in which other risk factors cause health problems. Our previous study based on the NORNS cohort identified that excess weight gain, but not duration of residence in South Korea, was an independent risk factor for metabolic syndrome,[25] making our hypothesis more plausible.

None of the premenopausal North Korean refugees had a Z-score below the expected range for their age group; however, the median BMD at the lumbar spine was significantly lower than that of the South Korean premenopausal women. A previous study reported that young North Korean refugees aged 12 to 24 years had a significantly lower daily intake of energy and most nutrients, including protein and calcium, than that of general age-/sex-matched South Koreans.[26] Our study also showed that premenopausal North Korean women had significantly lower body weight and less physical activity than did South Korean premenopausal women. These results imply that young North Korean refugees are at high risk for osteoporosis, indicating the importance of scrupulous screening and follow-up.

It's worth noting that the prevalence of osteopenia in the postmenopausal KUMC group was high (62.2%). A recent report from the Korean Society for Bone and Mineral Research

demonstrated that the prevalence of osteopenia among women > 50 years old was 48.9%.[27] These results indicate that osteopenia is also not a minor problem in Korean postmenopausal women.

Several limitations of this study need to be acknowledged. First, the relatively small number of participants may have reduced the power of the results and may not represent the entire population of female North Korean refugees living in South Korea. The NORNS study is based on the voluntary participation of North Korean refugees living in the Seoul metropolitan area, and it has taken considerable time to recruit large sample sizes. Second, we collected information about their postmenopausal status using self-reported questionnaires, which may have led to inaccuracy in the perimenopausal age group. Third, there is limited information regarding prior disease history that may affect the bone health of the KUMC control group.

Conclusions

This study reveals the high prevalence of osteoporosis in postmenopausal North Korean refugees living in South Korea compared with that in South Korean postmenopausal women. Outreach efforts are needed in this community to promote prevention, treatment, and access to care, especially among those of older age, with low body weight, and in late menarche. Further longitudinal studies are needed to evaluate changes in bone health in this group.

Declarations

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Author Contribution SGK designed the NORNS study and supervised the data collection and data entry. JHA and KyeongJK conducted the statistical analysis and drafted the manuscript. KyoungJK, NamHK, and HYK coordinated the data collection. JHY, HJY, JAS, NanHK, KMC, and SHB commented on and critically revised the manuscript. All authors read and approved the final manuscript.

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Competing interests All authors declare that they have no competing interests.

Consent for publication Not applicable.

Ethical approval and consent to participate All subjects provided written informed consent to participate. This study was approved by the Institutional Review Board (IRB) of Korea University's Anam Hospital (IRB No. ED08023).

Availability of data and material The dataset generated during the current study is available upon reasonable request from the corresponding author, Sin Gon Kim (k50367@korea.ac.kr).

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Figure legends

Figure 1 Study design.

Figure 2 Proportion of subjects with osteoporosis, osteopenia, and normal bone mineral density stratified by 10-year age groups in North Korean (A) and South Korean (B) postmenopausal women.

Figure 3 Simple linear regression between the lumbar spine bone mineral density (BMD) of postmenopausal North Korean women and age (A), body weight (B), menarche age (C), and duration of living in South Korea (D).

Table 1 Baseline characteristics of North Korean women refugees according to menopausal status

	NORNS			KUMC		
	All†	Premenopausal	Postmenopausal	All†	Premenopausal	Postmenopausal
Total cases, n (%)	122	70 (57.4)	52 (42.6)	366	210 (57.4)	156 (42.6)
Age, median (years, IQR)	46.0 (40.0-60.0)	41.0 (37.0-44.0)	62.5 (55.0-68.5)	46.0 (40.0-60.0)	41.0 (37.0-44.0)	62.5 (55.0-68.5)
Height (mean ± SD), cm	154.2 ± 4.7	155.0 ± 4.4	153.1 ± 4.8	158.8 ± 5.8	161.0 ± 5.2*	155.8 ± 5.3**
Body weight (mean ± SD), kg	55.2 ± 7.4	53.2 ± 6.7	57.8 ± 7.5	57.5 ± 8.4	58.0 ± 9.4*	56.7 ± 6.8
BMI (mean ± SD), kg/m^2	23.3 ± 3.0	22.1 ± 2.3	24.9 ± 3.2	22.8 ± 3.2	22.4 ± 3.4	23.4 ± 2.8**
Age at menarche, median (years, IQR) (n=111)‡	17.0 (15.0-18.0)	16.0 (15.0-18.0)	17.0 (16.0-19.0)	14.0 (13.0-15.0)	14.0 (13.0-14.0)*	15.0 (14.0-17.0)**
Age at menopause (mean ± SD), years (n=43)‡	49.2 ± 4.0	—	49.2 ± 4.0	50.6 ± 4.3	—	50.6 ± 4.3
Alcohol, n (%)						
Never drinker	43 (37.4)	14 (20.6)	29 (61.7)	167 (46.0)	61 (29.0)	106 (69.3)
Ex-/current drinker	72 (62.6)	54 (79.4)	18 (38.3)	196 (54.0)	149 (71.0)	47 (30.7)
Smoking, n (%)						
Never smoker	103 (98.1)	65 (100.0)	38 (95.0)	326 (91.8)	186 (89.4)*	139 (95.2)
Ex-/current smoker	2 (1.9)	0	2 (5.0)	29 (8.2)	22 (10.6)*	7 (4.9)
Physical activity, n (%)						
Never	60 (56.6)	38 (56.7)	22 (56.4)	157 (43.7)	104(50.7)*	53 (34.4)**
<5 hours/week	37 (34.9)	26 (38.8)	11 (28.2)	117 (32.6)	64 (31.2)*	53 (34.4)**
≥5 hours/week	9 (8.5)	3 (4.5)	6 (15.4)	85 (23.7)	37 (18.0)*	48 (31.2)**
OCP use, n (%) (n=110)‡	17 (15.5)	16 (24.6)	1 (2.2)	55 (15.9)	18 (9.0)*	37 (25.0)**
Number of pregnancies, median (IQR) (n=117)‡	3.0 (2.0-4.0)	2.0 (1.0-3.0)	3.0 (2.0-4.0)	2.0 (1.0-2.0)	2.0 (1.0-2.0)*	2.0 (2.0-3.0)**
Age at escape from North Korea, (mean ± SD), [min-max], years	37.9 ± 13.5 [17.0-69.0]	28.43 ± 6.2 [17.0-40.0]	51.0 ± 9.2 [35.0-69.0]	—		
Duration of living in South Korea, median (IQR), years	6.2 (4.2-9.0)	5.3 (4.1-8.0)	7.3 (4.2-9.1)	—		

Abbreviations: BMI, body mass index; IQR, interquartile range; KUMC, Korea University Medical Center; NORNS, North Korea Refugee Health in South Korea; OCP, oral contraceptive pill; SD, standard deviation.
*P-value < 0.05 compared with NORNS premenopausal women.

**P-value < 0.05 compared with NORNS postmenopausal women.
† Valid percentages were displayed in categorical variables.
‡ Available data number were described

Table 2 Prevalence of osteoporosis in North Korean women refugees and South Korean women

	Premenopausal, n (%)		
	NORNS (n = 70)	KUMC (n = 210)	*P*-value
Below the expected range (Z-score ≤ -2.0)	0	4 (1.9)	0.575
Within the expected range (Z-score > -2.0)	70 (100.0)	206 (98.1)	
	Postmenopausal, n (%)		
	NORNS (n = 52)	KUMC (n = 156)	*P*-value
Normal (T-score ≥ -1.0)	5 (9.6)	32 (20.5)	<0.001
Osteopenia (-2.5 < T-score < -1.0)	22 (42.3)	97 (62.2)	
Osteoporosis (T-score ≤ -2.5)	25 (48.1)	27 (17.3)	

Abbreviations: NORNS, North Korea Refugee Health in South Korea; KUMC, Korea University Medical Center.

Table 3 Comparisons of BMD at the lumbar spine, femur neck, and total hip between North Korean refugee women and South Korean women

	Lumbar spine BMD (g/cm^2)	*P*-value	Femur neck BMD (g/cm^2)	*P*-value	Total hip BMD (g/cm^2)	*P*-value
Premenopausal						
NORNS (n = 70)	0.952 ± 0.10	<0.001	0.735 ± 0.08	0.477	0.881 ± 0.13	0.737
KUMC (n = 210)	1.001 ± 0.12		0.741 ± 0.10		0.884 ± 0.10	
Postmenopausal						
NORNS (n = 52)	0.760 ± 0.11	<0.001	0.610 ± 0.10	<0.001	0.774 ± 0.11	0.002
KUMC (n = 156)	0.861 ± 0.12		0.653 ± 0.09		0.808 ± 0.10	

Abbreviations: BMD, bone mineral density; NORNS, North Korea Refugee Health in South Korea; KUMC, Korea University Medical Center.

Data are expressed as mean ± standard deviation.

Table 4 Risk factors for osteoporosis in postmenopausal North Korean women identified by multivariate logistic regression analysis.

Variables	OR	95% CI	*P*-value
Age	1.35	0.98-1.86	0.063
Weight	0.84	0.74-0.95	0.007
Age at menarche	1.45	0.96-2.19	0.077
Age at escape from North Korea	0.82	0.64-1.06	0.129
Years living in South Korea	0.89	0.63-1.25	0.489

Abbreviations: CI, confidence interval; OR, odds ratio.

Fig. 1

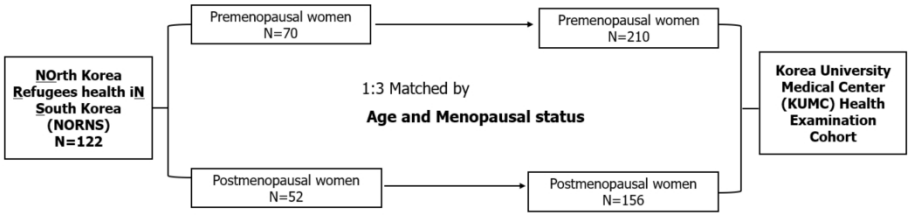

Figure 1 Study design.

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Fig.2

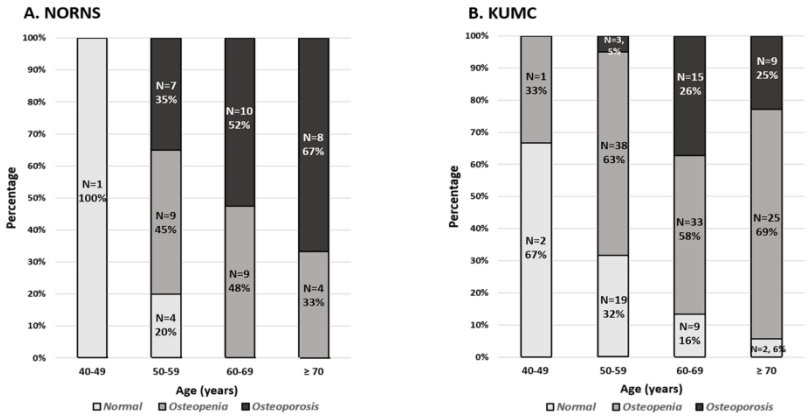

Figure 2 Proportion of subjects with osteoporosis, osteopenia, and normal bone mineral density stratified by 10-year age groups in North Korean (A) and South Korean (B) postmenopausal women.

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Fig.3

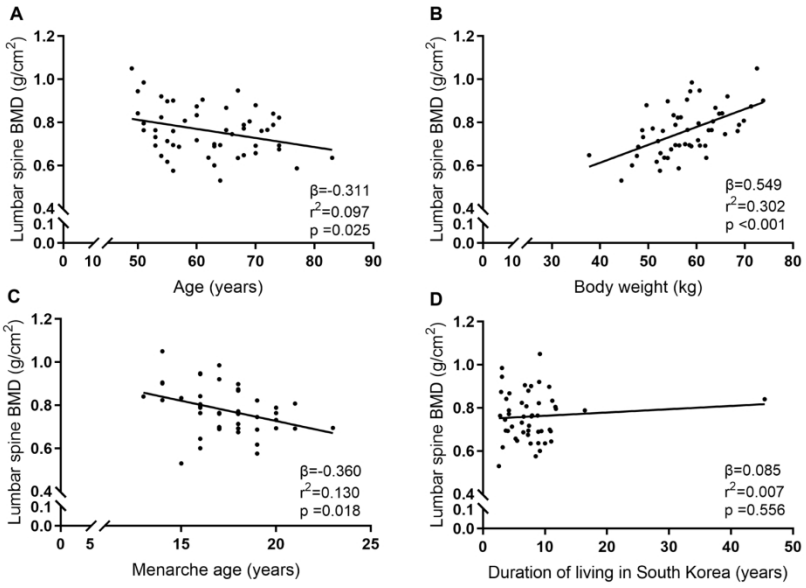

Figure 3 Simple linear regression between the lumbar spine bone mineral density (BMD) of postmenopausal North Korean women and age (A), body weight (B), menarche age (C), and duration of living in South Korea (D).

297x209mm (300 x 300 DPI)

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
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	7
Bias	9	Describe any efforts to address potential sources of bias	n/a
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8
		(*b*) Describe any methods used to examine subgroups and interactions	8
		(*c*) Explain how missing data were addressed	7
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	6
		(*e*) Describe any sensitivity analyses	n/a
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	8-9
		(b) Give reasons for non-participation at each stage	n/a
		(c) Consider use of a flow diagram	6
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8-9
		(b) Indicate number of participants with missing data for each variable of interest	20
Outcome data	15*	Report numbers of outcome events or summary measures	n/a
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	10

		(*b*) Report category boundaries when continuous variables were categorized	9-10
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	n/a
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
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	13
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13
Generalisability	21	Discuss the generalisability (external validity) of the study results	13
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	14

*Give information separately for exposed and unexposed groups.

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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Prevalence of osteoporosis among North Korean women refugees living in South Korea: a comparative cross-sectional study

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Abstract

Objective: To investigate the prevalence of osteoporosis among North Korean women refugees when compared with South Korean women, who have identical genetic backgrounds but experience different environments.

Design: Comparative cross-sectional study.

Setting: North Korean Refugee Health in South Korea (NORNS) study in South Korea.

Participants: We evaluated 122 North Korean women who participated in NORNS study and 366 age-/menopausal status-matched South Korean women from the Korea University Medical Center (KUMC) health examination cohort. The median age of the NORNS participants was 46 years (interquartile range [IQR], 40–60 years) with 52 women (42.6%) being postmenopausal.

Results: Among the postmenopausal women, NORNS participants had a higher body mass index and number of pregnancies and lower physical activity than the KUMC participants. The overall prevalence of osteoporosis was 48% (25/52) and 17% (27/156) in NORNS and KUMC participants, respectively. The bone mineral density (BMD) values at the lumbar spine, femur neck, and total hip were significantly lower in postmenopausal NORNS women than in the postmenopausal KUMC women. Old age, low body weight, and late age of menarche were associated with low BMD among the postmenopausal North Korean refugees. In premenopausal participants, the NORNS women had lower body weight and physical activity than the KUMC women at baseline. All the NORNS women had normal Z-scores, although the BMD at the lumbar spine was significantly lower in NORNS women than in the KUMC women (0.952 vs. 1.002 g/cm^2, $P < 0.001$).

Conclusions: Osteoporosis is a prevalent health problem in postmenopausal North Korean women refugees living in South Korea. It is conceivable to prepare vigilant countermeasures for bone health deterioration in this growing population, especially for postmenopausal women. Further research is warranted to determine the cause of the differences between participants of the same ethnic group.

Keywords: Bone density, Osteoporosis, Democratic People's Republic of Korea, Republic of Korea, cross-sectional study

Strengths and limitations of this study

- We compared the prevalence of osteoporosis between North Korean women refugees and age-/menopausal status-matched South Korean women of same ethnicity but with different environmental factors.
- This is the first qualitative study using dual-energy x-ray absorptiometry to identify the bone health status of North Korea women refugees living in South Korea.
- All the confounding factors associated with osteoporosis were not included in this study.
- Our analysis, restricted to relatively small portion of North Korean women refugees, minimize the representativeness of the entire North Korean women population.

INTRODUCTION

Osteoporosis is one of the most common health problems in an aged society, particularly among older women, leading to fractures that are closely associated with morbidity and mortality.[1-3] Early detection and risk management can reduce the osteoporosis incidence and prevent fractures. Environmental factors, such as malnutrition, current smoking status, alcohol consumption, physical inactivity, and medications such as corticosteroids in addition to inherent factors like older age and female sex are well known risk factors for osteoporosis.[4-7] Moreover, recent epidemiological studies have demonstrated that Asian women immigrants have a high prevalence of osteoporosis and low bone mineral density (BMD). In a study of 73 premenopausal Chinese immigrant women living in Denmark, their BMD was significantly lower than that of the general population of premenopausal Danish women.[8] Similarly, Marquez et al. reported that immigrants from Southeast Asia had a lower BMD than that of white residents living in Minnesota, USA.[9] However, previous studies were not sufficient to distinguish whether the lower BMD between the two groups was due to the environmental factors, including immigration itself, or ethnicities. In this context, how the environmental factors influence the bone health in an immigration population of the same ethnicity has not been clearly elucidated.

The Korean peninsula has been the only divided country in the world since 1945. In the subsequent decades, South and North Korea have experienced stark differences in politics, economics, and culture. North Korea has experienced severe poverty due to its economic deterioration and global sanctions;[10] therefore, most North Korean refugees who left North Korea and resettled in South Korea have experienced penury and malnutrition.[11, 12] Moreover, we previously reported a high prevalence of vitamin D deficiency in North Korean refugees

that has been well documented for its role in the maintenance of bone health.[13, 14]

In the present study, we evaluated the prevalence of osteoporosis in North Korean women refugees compared with that in South Korean women, who are of the same ethnicity but who have encountered completely different socioeconomic environments. Furthermore, we analyzed the associated risk factors for osteoporosis in North Korean women refugees.

METHODS

Participants and study design

The North Korea Refugee Health in South Korea (NORNS) study, which started in October 2008 and is still ongoing, aimed to evaluate the medical health and disease status of North Korean refugees in South Korea. The NORNS study is a longitudinal study consisting of two parts, the first and the second surveys, which followed the same participants as the first survey approximately 3.5 years later. The NORNS study included interviews, structural surveys, physical examinations, and blood samples in both the first and second surveys, however, dual-energy x-ray absorptiometry (DXA) was only performed in the second survey. The entire study process was conducted in Anam Hospital at the Korea University Medical Center in Seoul. More specific details on the NORNS study design and general features have been published elsewhere.[13, 15]

Figure 1 illustrates the study design. Age- and menopausal status-matched control subjects were randomly selected at a 1:3 ratio of cases to controls from the Korea University Medical Center (KUMC) Anam Hospital Health Examination cohort to compare the prevalence of osteoporosis between North Korean women refugees (NORNS group) and South Korean women (KUMC group). Written informed consent was obtained from all participants, and this

study was approved by the Institutional Review Board (IRB) of Korea University's Anam Hospital under IRB process No. ED08023. We used the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines.[16]

Questionnaire and anthropometric measurements

General demographic data including age, sex, year of emigration from North Korea, year of entry into South Korea, menarche age, and menopausal status as well as health-related lifestyle behaviors including smoking, alcohol consumption, and physical activity were included in the questionnaire. Anthropometric measurements including height and body weight were conducted after an overnight fast. All the demographic and anthropometric measurements based on the results of the second survey were analyzed in this study. For handling the missing data of questionnaire and anthropometric measurements, available-case analyses (also known as pairwise deletion) were used without additional data handing.

BMD measurements

BMD at the lumbar spine, left femur neck, and total hip was measured in the NORNS and KUMC cohorts by DXA using the Hologic Discovery system (HOLOGIC Inc., Waltham, MA, USA). BMD was expressed as the total bone mineral content (g) divided by the area (cm^2). The lumbar spine BMD, T-score, and Z-score were calculated as the mean values of the L1 through L4 spine. For premenopausal women, a race-adjusted Z-score ≤-2.0 was considered to be below the expected range for their age group and a Z-score >-2.0 as within the expected range for their age group. For postmenopausal women, osteoporosis was defined as a T-score ≤-2.5 in at least one of the lumbar spine, left femur neck, and total hip; osteopenia as a T-score >-2.5 and

<-1.0; normal as a T-score ≥-1.0.[17]

Statistical analysis

We presented continuous data as mean and standard deviation (SD) using the paired *t*-test for normally distributed variables and as medians and interquartile ranges (IQRs) using Wilcoxon-Mann-Whitney tests for non-normally distributed variables. Categorical data are presented as frequencies and percentages and were analyzed using chi-square or Fisher's exact tests for small case numbers. BMD values between the NORNS and KUMC cohorts were compared using Wilcoxon signed-rank tests. Correlations between BMD and demographic, gynecologic, and medical factors in the NORNS cohort were evaluated using a simple linear regression model. Finally, logistic regression analyses were used to investigate the risk factors for osteoporosis in postmenopausal women in the NORNS cohort. All reported *P*-values were two-sided and those <0.05 were considered statistically significant. All analyses were performed using IBM SPSS Statistics for Windows, version 20.0 (IBM Corp., Armonk, NY, USA) and GraphPad Prism version 7 (GraphPad Software, San Diego, CA, USA).

Patient and public involvement

Participants of this study or members of the public were not directly and personally involved with study design, data provision, analysis and publication of the study.

RESULTS

Baseline characteristics of the NORNS and KUMC groups

Among the 122 North Korean refugees, 70 were premenopausal women (57.4%) with a median

age of 41.0 (IQR, 37.0 to 44.0) years and 52 were postmenopausal women (42.6%) with a median age of 62.5 (IQR, 55.0 to 68.5) years. The median duration of living in South Korea was 6.2 (IQR, 4.2 to 9.0) years. Their baseline characteristics in comparison with that of KUMC participants according to menopause status are described in Table 1. The NORNS premenopausal women had a significantly lower mean height (155.0 ± 4.4 vs. 161.0 ± 5.2 cm, $P < 0.001$) and body weight (53.2 ± 6.7 vs. 58.0 ± 9.4 kg, $P < 0.001$) than the KUMC premenopausal women, whereas no difference in BMI (22.1 ± 2.3 vs. 22.4 ± 3.4 kg/m^2, $P = 0.514$) was observed between the two groups. However, the NORNS postmenopausal women had a lower height (153.1 ± 4.8 vs. 155.8 ± 5.3 cm, $P = 0.002$) and higher BMI (24.9 ± 3.2 vs. 23.4 ± 2.8 kg/m^2, $P = 0.002$) than the KUMC postmenopausal women. There was no difference in body weight (57.8 ± 7.5 vs. 56.7 ± 6.8 kg, $P = 0.320$) between the two groups. The proportion of subjects engaged in physical activity for more than 5 hours per week was lower in both the NORNS pre- and postmenopausal women than in the KUMC pre- and postmenopausal women. All NORNS premenopausal women were never smokers, whereas 22 of 210 KUMC premenopausal women were ex-/current smokers ($P = 0.006$).

Comparison of BMD and osteoporosis prevalence between the NORNS and KUMC groups

Table 2 shows the comparisons of BMD between the NORNS and KUMC groups. In premenopausal women, the lumbar spine BMD of the NORNS group was 0.952 ± 0.10, whereas that of the KUMC group was 1.001 ± 0.12, a significant difference ($P < 0.001$). Femur neck and total hip BMD did not differ significantly between the two groups. However, in postmenopausal women, the BMD of the lumbar spine, femur neck, and total hip was

consistently lower in the NORNS group than in the KUMC group.

All premenopausal participants in the NORNS group had normal Z-scores, whereas four premenopausal women in the KUMC group (1.9%, 4 of 210) had Z-scores below the expected range for their age group (P = 0.575). However, the prevalence of osteoporosis was significantly higher in the postmenopausal NORNS group than that in the postmenopausal KUMC group (48.1% vs. 17.3%) (Table 3). The proportion of participants with a normal T-score was more than two times higher in the KUMC postmenopausal group (20.5%, 32 of 156) than that in the NORNS postmenopausal group (9.6%, 5 of 52). Figure 2 demonstrates the proportion of participants with osteoporosis and osteopenia in the postmenopausal NORNS and KUMC groups, stratified by 10-year age categories. The prevalence of osteoporosis in the postmenopausal NORNS group was 35% (7 of 20), 52% (10 of 19), and 67% (8 of 12) in participants aged 50–59, 60–69, and >70 years, respectively. For postmenopausal KUMC women, the prevalence of osteoporosis in each age group was lower than that of the respective NORNS group (5%, 3 of 60; 26%, 15 of 57; and 25%, 9 of 36 in those aged 50–59, 60–69, and >70 years, respectively). None of the participants over 60 years in the NORNS group had a normal T-score.

Risk factors associated with osteoporosis and low BMD in postmenopausal North Korean refugees

The risk factors associated with osteoporosis in the NORNS postmenopausal group, identified using multivariate logistic regression analysis, are shown in Table 4. Lower body weight was the only significant risk factor of osteoporosis in this group. Older age and late menarche tend towards osteoporosis but no statistical significance, and duration of living in South Korea was

not a risk factor of osteoporosis in this group. In addition, simple linear regression to determine the factors correlated with lumbar spine BMD in the postmenopausal NORNS group revealed that old age, low body weight, and late menarche age were significantly associated with low BMD (Figure 3). There was no association between the duration of living in South Korea and BMD.

DISCUSSION

This comparative cross-sectional study demonstrated that the prevalence of osteoporosis in postmenopausal North Korean refugees was significantly higher than that in age-matched postmenopausal South Korean women of the general population. BMD values at the lumbar spine, femur neck, and total hip were significantly lower in postmenopausal North Korean refugees than those in South Korean postmenopausal women. Low body weight was associated with osteoporosis and low BMD in the NORNS postmenopausal group.

Most of the postmenopausal women (92%, 48 of 52) in the NORNS group had endured the worst food shortage, the Arduous March, between 1996 and 2000, in which more than 600,000 people in North Korea died of starvation.[18] During this period, they could not obtain sufficient nutrients, including protein, calcium, and vitamin D, which have important roles in bone mineral acquisition. Although the actual nutritional status immediately after entering South Korea could not be evaluated due to restricted access authority, the youngest age at the time of escape from North Korea in the postmenopausal NORNS women was 35 years. This means that all postmenopausal participants had experienced malnutrition during their childhood and early adulthood and reached their peak bone mass before leaving North Korea. We consider that this is one of the major reasons why postmenopausal women were more vulnerable to

osteoporosis. Several studies have revealed that subjects who experience malnutrition during childhood and early adulthood are less likely to reach peak bone mass, leading to osteoporosis in later life.[19-21] Our results are also in line with previous cohort studies demonstrating the negative effects of malnutrition and famine on bone health. Marcus et al. reported a high prevalence of osteoporosis and osteopenia (55% and 40%, respectively) among Holocaust survivors who had experienced malnutrition during their childhood.[22] Another study conducted in Hong Kong observed that past exposure to famine, especially in childhood, was associated with osteoporosis in postmenopausal women aged 65 years or older.[23]

Vitamin D has been well documented to play an important role in bone mineral metabolism via interactions with calcium and parathyroid hormone.[14] Our previous study with 366 North Korean refugees demonstrated that the prevalence of vitamin D deficiency (25(OH)D <20 ng/mL) was 87%.[13] In the present study, serum vitamin D levels were only obtained in 66 of 122 NORNS participants (mean level of 15.0 ± 4.3 ng/mL) and no subject had adequate vitamin D level (25(OH)D ≥30 ng/mL, data not shown). Further meticulous study regarding the vitamin D deficiency and osteoporosis is needed in the future.

We did not evaluate the relationships between well-known risk factors, such as smoking and physical inactivity, and osteoporosis in this study. Among 110 subjects who provided information about smoking, only two subjects in this group were current/ex-smokers. The small proportion of subjects who were current/ex-smokers revealed no significant effect on osteoporosis. Because the level of physical activity was collected in a memory-recall questionnaire, it was difficult to obtain accurate data, particularly in the older age group.

Previous immigration studies showed that the duration of living in the migrated country was associated with BMD. Wang et al. reported that Chinese women who had migrated and lived

in Denmark for more than 12 years had a significantly higher BMD than those who had lived there for less than 12 years.[8] Rajeev et al. also reported that Chinese women who had lived in New York for less than 10 years had a lower BMD than women who had lived in New York for more than 20 years.[24] However, we did not observe a significant association between the duration of living in South Korea and osteoporosis. The median period of living in South Korea in postmenopausal North Korean refugees (7.3 years; IQR, 4.2 to 9.1 years) was relatively short compared with that in previous immigration studies, and less than 20% of postmenopausal North Korean refugees (10 of 52) had lived in South Korea for more than 10 years. Another explanation is that the duration of living in South Korea itself may not be a risk factor or indicator of acculturation, but may simply provide the circumstances in which other risk factors cause health problems. Our previous study based on the NORNS cohort identified that excess weight gain, but not duration of residence in South Korea, was an independent risk factor for metabolic syndrome,[25] making our hypothesis more plausible.

None of the premenopausal North Korean refugees had a Z-score below the expected range for their age group; however, the median BMD at the lumbar spine was significantly lower than that of the South Korean premenopausal women. A previous study reported that young North Korean refugees aged 12 to 24 years had a significantly lower daily intake of energy and most nutrients, including protein and calcium, than that of general age-/sex-matched South Koreans.[26] Our study also showed that premenopausal North Korean women had significantly lower body weight and less physical activity than did South Korean premenopausal women. These results imply that young North Korean refugees are at high risk for osteoporosis, indicating the importance of scrupulous screening and follow-up.

It's worth noting that the prevalence of osteopenia in the postmenopausal KUMC group was

high (62.2%). A recent report from the Korean Society for Bone and Mineral Research demonstrated that the prevalence of osteopenia among women > 50 years old was 48.9%.[27] These results indicate that osteopenia is also not a minor problem in South Korean postmenopausal women.

Several limitations of this study need to be acknowledged. First, the relatively small number of participants may have reduced the power of the results and may not represent the entire population of female North Korean refugees living in South Korea. The NORNS study is based on the voluntary participation of North Korean refugees living in the Seoul metropolitan area, and it has taken considerable time to recruit large sample sizes. Second, we collected information about their postmenopausal status using self-reported questionnaires, which may have led to inaccuracy in the perimenopausal age group. Third, there is limited information regarding prior disease history that may affect the bone health of the KUMC control group.

Conclusions

This study reveals the high prevalence of osteoporosis in postmenopausal North Korean refugees living in South Korea compared with that in South Korean postmenopausal women. Outreach efforts are needed in this community to promote prevention, treatment, and access to care, especially among those of older age, with low body weight, and in late menarche. Further longitudinal studies are needed to evaluate changes in bone health in this group.

Declarations

Acknowledgements We especially thank the North Korean refugees who participated in the North Korea Refugee Health in South Korea (NORNS) study, as well as the medical doctors,

nurses, and volunteers who contributed to the health examinations of these refugees.

Author Contribution SGK designed the NORNS study and supervised the data collection and data entry. JHA and KyeongJK conducted the statistical analysis and drafted the manuscript. KyoungJK, NamHK, and HYK coordinated the data collection. JHY, HJY, JAS, NanHK, KMC, and SHB commented on and critically revised the manuscript. All authors read and approved the final manuscript.

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Competing interests All authors declare that they have no competing interests.

Consent for publication Not applicable.

Ethical approval and consent to participate All subjects provided written informed consent to participate. This study was approved by the Institutional Review Board (IRB) of Korea University's Anam Hospital (IRB No. ED08023).

Availability of data and material The dataset generated during the current study is available upon reasonable request from the corresponding author, Sin Gon Kim (k50367@korea.ac.kr).

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Figure legends

Figure 1 Study design.

Figure 2 Proportion of subjects with osteoporosis, osteopenia, and normal bone mineral density stratified by 10-year age groups in North Korean (A) and South Korean (B) postmenopausal women.

Figure 3 Simple linear regression between the lumbar spine bone mineral density (BMD) of postmenopausal North Korean women and age (A), body weight (B), menarche age (C), and duration of living in South Korea (D).

Table 1 Baseline characteristics of North Korean women refugees according to menopausal status

	NORNS			KUMC		
	All†	Premenopausal	Postmenopausal	All†	Premenopausal	Postmenopausal
Total cases, n (%)	122	70 (57.4)	52 (42.6)	366	210 (57.4)	156 (42.6)
Age, median (years, IQR)	46.0 (40.0-60.0)	41.0 (37.0-44.0)	62.5 (55.0-68.5)	46.0 (40.0-60.0)	41.0 (37.0-44.0)	62.5 (55.0-68.5)
Height (mean ± SD), cm	154.2 ± 4.7	155.0 ± 4.4	153.1 ± 4.8	158.8 ± 5.8	161.0 ± 5.2*	155.8 ± 5.3**
Body weight (mean ± SD), kg	55.2 ± 7.4	53.2 ± 6.7	57.8 ± 7.5	57.5 ± 8.4	58.0 ± 9.4*	56.7 ± 6.8
BMI (mean ± SD), kg/m^2	23.3 ± 3.0	22.1 ± 2.3	24.9 ± 3.2	22.8 ± 3.2	22.4 ± 3.4	23.4 ± 2.8**
Age at menarche, median (years, IQR) (n=111)‡	17.0 (15.0-18.0)	16.0 (15.0-18.0)	17.0 (16.0-19.0)	14.0 (13.0-15.0)	14.0 (13.0-14.0)*	15.0 (14.0-17.0)**
Age at menopause (mean ± SD), years (n=43)‡	49.2 ± 4.0	—	49.2 ± 4.0	50.6 ± 4.3	—	50.6 ± 4.3
Alcohol, n (%)						
Never drinker	43 (37.4)	14 (20.6)	29 (61.7)	167 (46.0)	61 (29.0)	106 (69.3)
Ex-/current drinker	72 (62.6)	54 (79.4)	18 (38.3)	196 (54.0)	149 (71.0)	47 (30.7)
Smoking, n (%)						
Never smoker	103 (98.1)	65 (100.0)	38 (95.0)	326 (91.8)	186 (89.4)*	139 (95.2)
Ex-/current smoker	2 (1.9)	0	2 (5.0)	29 (8.2)	22 (10.6)*	7 (4.9)
Physical activity, n (%)						
Never	60 (56.6)	38 (56.7)	22 (56.4)	157 (43.7)	104(50.7)*	53 (34.4)**
<5 hours/week	37 (34.9)	26 (38.8)	11 (28.2)	117 (32.6)	64 (31.2)*	53 (34.4)**
≥5 hours/week	9 (8.5)	3 (4.5)	6 (15.4)	85 (23.7)	37 (18.0)*	48 (31.2)**
OCP use, n (%) (n=110)‡	17 (15.5)	16 (24.6)	1 (2.2)	55 (15.9)	18 (9.0)*	37 (25.0)**
Number of pregnancies, median (IQR) (n=117)‡	3.0 (2.0-4.0)	2.0 (1.0-3.0)	3.0 (2.0-4.0)	2.0 (1.0-2.0)	2.0 (1.0-2.0)*	2.0 (2.0-3.0)**
Age at escape from North Korea, (mean ± SD), [min-max], years	37.9 ± 13.5 [17.0-69.0]	28.43 ± 6.2 [17.0-40.0]	51.0 ± 9.2 [35.0-69.0]	—		
Duration of living in South Korea, median (IQR), years	6.2 (4.2-9.0)	5.3 (4.1-8.0)	7.3 (4.2-9.1)	—		

Abbreviations: BMI, body mass index; IQR, interquartile range; KUMC, Korea University Medical Center; NORNS, North Korea Refugee Health in South Korea; OCP, oral contraceptive pill; SD, standard deviation.
*P-value < 0.05 compared with NORNS premenopausal women.

**P-value < 0.05 compared with NORNS postmenopausal women.
† Valid percentages were displayed in categorical variables.
‡ Available data number were described

Table 2 Comparisons of BMD at the lumbar spine, femur neck, and total hip between North Korean refugee women and South Korean women

	Lumbar spine BMD (g/cm^2)	*P*-value	Femur neck BMD (g/cm^2)	*P*-value	Total hip BMD (g/cm^2)	*P*-value
Premenopausal						
NORNS (n = 70)	0.952 ± 0.10	<0.001	0.735 ± 0.08	0.477	0.881 ± 0.13	0.737
KUMC (n = 210)	1.001 ± 0.12		0.741 ± 0.10		0.884 ± 0.10	
Postmenopausal						
NORNS (n = 52)	0.760 ± 0.11	<0.001	0.610 ± 0.10	<0.001	0.774 ± 0.11	0.002
KUMC (n = 156)	0.861 ± 0.12		0.653 ± 0.09		0.808 ± 0.10	

Abbreviations: BMD, bone mineral density; NORNS, North Korea Refugee Health in South Korea; KUMC, Korea University Medical Center.

Data are expressed as mean ± standard deviation.

Table 3 Prevalence of osteoporosis in North Korean women refugees and South Korean women

	Premenopausal, n (%)		
	NORNS (n = 70)	KUMC (n = 210)	*P*-value
Below the expected range (Z-score ≤ -2.0)	0	4 (1.9)	0.575
Within the expected range (Z-score > -2.0)	70 (100.0)	206 (98.1)	
	Postmenopausal, n (%)		
	NORNS (n = 52)	KUMC (n = 156)	*P*-value
Normal (T-score ≥ -1.0)	5 (9.6)	32 (20.5)	<0.001
Osteopenia (-2.5 < T-score < -1.0)	22 (42.3)	97 (62.2)	
Osteoporosis (T-score ≤ -2.5)	25 (48.1)	27 (17.3)	

Abbreviations: NORNS, North Korea Refugee Health in South Korea; KUMC, Korea University Medical Center.

Table 4 Risk factors for osteoporosis in postmenopausal North Korean women identified by multivariate logistic regression analysis.

Variables	OR	95% CI	*P*-value
Age	1.35	0.98-1.86	0.063
Weight	0.84	0.74-0.95	0.007
Age at menarche	1.45	0.96-2.19	0.077
Age at escape from North Korea	0.82	0.64-1.06	0.129
Years living in South Korea	0.89	0.63-1.25	0.489

Abbreviations: CI, confidence interval; OR, odds ratio.

Fig. 1

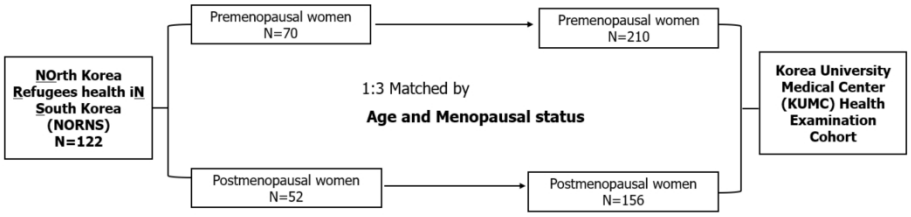

Figure 1 Study design.

297x209mm (300 x 300 DPI)

Fig.2

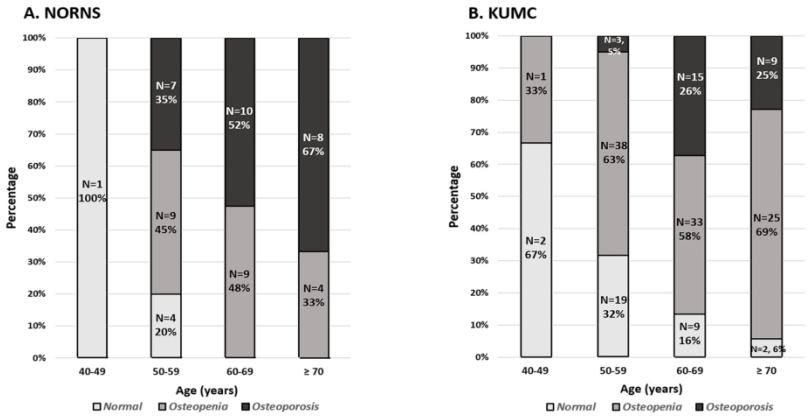

Figure 2 Proportion of subjects with osteoporosis, osteopenia, and normal bone mineral density stratified by 10-year age groups in North Korean (A) and South Korean (B) postmenopausal women.

297x209mm (300 x 300 DPI)

Fig.3

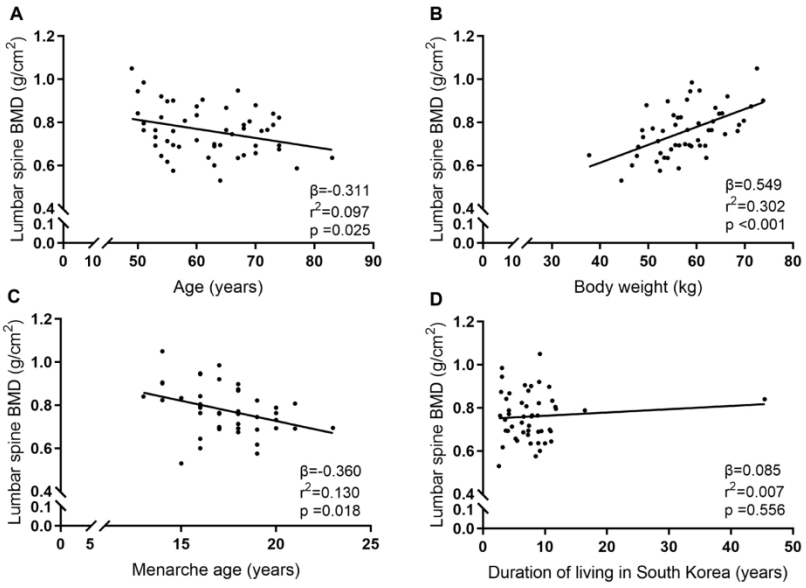

Figure 3 Simple linear regression between the lumbar spine bone mineral density (BMD) of postmenopausal North Korean women and age (A), body weight (B), menarche age (C), and duration of living in South Korea (D).

297x209mm (300 x 300 DPI)

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
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	7
Bias	9	Describe any efforts to address potential sources of bias	n/a
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8
		(*b*) Describe any methods used to examine subgroups and interactions	8
		(*c*) Explain how missing data were addressed	7
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	6
		(*e*) Describe any sensitivity analyses	n/a
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	8-9
		(b) Give reasons for non-participation at each stage	n/a
		(c) Consider use of a flow diagram	6
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8-9
		(b) Indicate number of participants with missing data for each variable of interest	20
Outcome data	15*	Report numbers of outcome events or summary measures	n/a
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	10

		(*b*) Report category boundaries when continuous variables were categorized	9-10
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	n/a
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
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	13
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13
Generalisability	21	Discuss the generalisability (external validity) of the study results	13
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	14

*Give information separately for exposed and unexposed groups.

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.