Waist circumference and the risk of lumbar and femur fractures: a nationwide population-based cohort study

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Abstract. – Although obesity is known to have an influence on fracture, the relationship between lumbar and femur fractures and weight or waist circumference is controversial. We investigated the incidence of fracture with regards to waist circumference using the customised database of the Korean National Health Insurance Service (NHIS). Among 8,922,940 adults who participated at least twice in the NHIS National Health Check-up Program in South Korea between 2009 and 2011, 1,556,751 subjects (780,074 men and 776,677 women) were extracted. Over a mean follow-up of 6.5 years, multivariate-adjusted logistic regression analysis demonstrated that higher waist circumference was associated with an increased risk of femur fractures in both males and females. Moreover, the incidence of lumbar fractures was also positively associated with an increased waist circumference in males and females. An increased waist circumference showed a positive linear relationship with the risk of lumbar and femur fractures in both males and females.

Key Words:
Waist circumference, Lumbar fracture, Femur fracture, BMI, Sex.

Introduction

The increased proportion of elderly populations worldwide has led to an increase in the incidence of osteoporotic fractures, and consequently increased the economic burden[1-5]. Especially, lumbar and femur fracture are associated with disability, morbidity, and mortality that needs socially and economically lots of supports[5-7]. Menopause, physical activity, alcohol drinking, smoking and habitual behaviours are known risk factors of osteoporotic fracture[8].

Fractures are considered to be related to body weight, but the research results are controversial. Several papers[9,10] have reported that lower body weight is correlated with the risk of femur fracture. However, it has been recently reported that the incidence of osteoporotic fractures are associated with metabolic disorders, such as diabetes and obesity[11-13]. The physiological burden of adipose tissue increases the strain on bones, and obesity makes bones stronger by improving the structural integrity of bones; however, the decreased muscle mass and hormonal changes increases the risk of osteoporotic fractures[14,15].

The majority of previous studies[16] have reported a negative correlation between body mass index and fracture, but few studies have analysed the correlation between the incidence of fracture and waist circumference. Since there are a limited number of studies on waist circumference and osteoporotic fractures in a large population in Korea, we aimed to determine the incidence of vertebral and femoral fractures according to waist circumference using a large cohort, derived from Korean Health Insurance Service data.

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Materials and Methods

Data Source

The customised research database of the Korean National Health Insurance Service (NHIS), a service provided by the Korean government, covering the 97% population of the Republic of Korea (approximately 50 million people), was used for the study. The NHIS database comprises information from all hospitals, including drug prescriptions, admission and outpatients visit records (using the Korean Standard Classification of Diseases [KCD] codes, which are similar to the International Classification of Disease [ICD] codes), and national health examination data. Korean adults older than 40 years, or employees older than 20 years, are required to undergo a health examination every one or two years for insurance purposes. The examination includes a self-reported questionnaire on health behaviours, measurements of height, weight, waist circumference (measured since 2009), blood pressure and laboratory tests for urine and blood. The NHIS provides a customised research database from the claims data, which includes all of the above-mentioned information, for research purposes. The customised research database refers to data that are extracted, summarised and processed according to the applicant's research purposes, such that data from health insurance and long-term care insurance that is collected, held and managed by the corporation can be used for policy development and academic research purposes. The customised research database is extracted randomly, and accurately reflects the characteristics of all Koreans. Furthermore, its data resources are validated and have been used in other studies[17,18]. This study was approved by the Institutional Review Board of the NHIS (NHIS-2019-1-447), Yonsei University Wonju College of Medicine (CR319321).

Study Design

The customised research database included 8,922,940 adults who underwent health examinations from 2009 to 2011. Patients who had cardiovascular events before 2011 (441,337), underwent health examination less than twice from 2009 to 2011 (1,134,965), were under 55 years old (8,778,456) and had missing data (11,431) were excluded. Finally, a total of 1,556,751 subjects (780,074 males and 776,677 females) were analysed, detailed inclusion and exclusion criteria are shown in Figure 1.

Variables

Waist circumference was measured at the middle point between the rib cage and the iliac crest by trained examiners. Blood pressure was measured according to the Korean Society Hypertension guideline[19]. Ex-smokers were people who smoked in the past but do not smoke at present. Heavy exercise was defined as moderate, or heavier regular physical exercise performed at least 30 minutes a day, on 3 or more days per week. Heavy drinking was defined as consuming seven or more drinks on the same occasion, more than 3 days per week.

Femur fractures were defined as those with ICD-10th codes of S72.0-S72.2, and a S72.9 diagnostic code at admission. Spine fractures were defined as those with an ICD-10th code of S22.1, S32.0, S32.7 and S32.8 at admission or outpatient appointment.

Statistical Analysis

Since osteoporotic fractures occur differently in males and females, the analysis is largely divided by sex. Chi-square test was used for categorical variables, and analysis of variance (ANOVA) was used for continuous variables. Post-hoc analysis was performed using the Bonferroni method. Waist circumference was divided by tertial values; the male waist circumference was divided into 82 cm and 87.5 cm, and the female waist circumference was divided into 77 cm and 83 cm. Incidences of fracture from 2013 to 2017 were divided by sex, such that the occurrence of femur factures and lumbar fractures according to the waist circumference was grouped by sex. The hazard ratio (HR) and 95% confidential interval (95% CI) for person years were determined, and

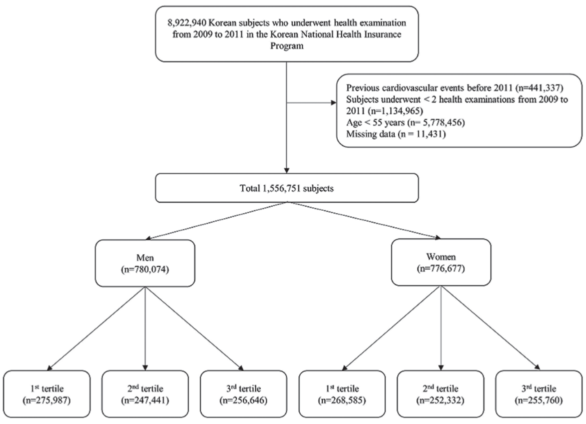

Figure 1. Study population.

three adjustment models were utilised. Model 1 was adjusted by age; model 2 was adjusted by adding smoking, alcohol drinking, regular physical exercise, and socioeconomic status (top 20% of insurance payments) to model 1; and model 3 was adjusted by adding osteoporosis medication, hypertension medication, diabetes medication and steroid and BMI to model 2. The *p*-value<0.05 is considered to be statistically significant. All statistical analysis was performed using SAS 9.1 Enterprise, which was provided by the National Health Insurance Corporation.

Results

Baseline Characteristics of Participants

The baseline characteristics of participants are shown in Table I. The BMI, systolic blood pressure, diastolic blood pressure, fasting blood sugar, ALT, triglyceride, incidence of heavy drinking, incidence of antihypertensive drug use, incidence of antidiabetic use, and incidence of steroid use increased as the waist circumference increase in both males and females. A total of 2,957 femur fractures and 13,638 lumbar fractures developed in males, and 4,160 femur fractures and 28,644 lumbar fractures developed in women. In females only, the proportion of femur and lumbar fractures increased as the waist circumference increased (Table I).

Number of Events, Person Years and Hazard Ratios for Fractures in Males

Over mean follow up of 6.5 years, model 1 and model 2 showed that increased waist circumference was negatively associated with femur and lumbar fracture in males. However, increased waist circumference was positively associated with femur fracture in model 3 (HR = 1.19; 95% CI, 1.07-1.32 in the 2nd tertial, and HR = 1.73; 95% CI, 1.51-1.99 in the 3rd tertial). Increased waist circumference was also positively associated with lumbar fracture in model 3 (HR = 1.06; 95% CI, 1.01-1.11 in the 2nd tertial, and HR = 1.33; 95% CI, 1.25-1.41 in the 3rd tertial) (Table II). The HR and 95% CIs for femur and lumbar fractures according to waist circumference were also expressed by cubic spline curves after adjustment for all variables (Figure 2A, B).

Number of Events, Person Years and Hazard Ratios for Fractures in Females

As the waist circumference increased, the femur fractures also increased in three models (HR = 1.19; 95% CI, 1.10-1.28 in the 3rd tertial in model 1; HR = 1.18; 95% CI, 1.09-1.74 in the 3rd tertial in model 2; HR = 1.41; 95% CI, 1.26-1.58 in the 3rd tertial in model 3). In lumbar fracture, all HRs increased significantly as the waist circumference increased (HR = 1.17; 95% CI, 1.14-1.21 in 2nd tertial; HR = 1.48; 95% CI, 1.42-1.54 in the 3rd tertial in model 3) (Table III). The HR and 95% CIs for femur and lumbar fractures according to waist circumference were also expressed by cubic spline curves after adjustment for all variables (Figure 2C, D).

Discussion

The incidence of femur and lumbar fractures by sex showed different properties as the waist circumference increased. In men, higher waist circumference was associated with a lower incidence of femur fractures in univariate analysis. However, after adjustment for BMI, waist circumference was associated with increased risk of femur fractures. In females, higher waist circumference was associated with an increased risk of femur fractures. In addition, higher waist circumference was associated with increased risk of lumbar fracture, both in males and females in all covariate adjusted models.

The relationship between obesity and bone health is complex. Obesity has a protective effect by absorbing energy that is imparted onto the bone; however, adipose tissue has negative effects on bone metabolism that obesity is associated with increased adipocyte formation in the bone marrow resulting increased risk for bone fractures[20,21]. In particular, visceral adipose tissue is associated with a number of hormones and cytokines that contribute to bone loss[20,22,23]. Furthermore, BMI, percentage of total body fat, skinfold thickness and waist circumference are measures of obesity. BMI seems to be not suitable for measuring obesity because it do not reflect age, the correlation between percentage of fat and BMI is not linear, and is gender dependent[24]. Waist circumference is used to predict visceral fat, whereas BMI is used to predict non-abdominal fat[23]. In addition, other studies also have shown that waist circumference, but not BMI is correlated with vertebral and hip fracture[25,26].

An inverse relationship between BMI and hip fracture has been demonstrated in cohort studies and meta-analyses[25,27,28]. Our study showed that after adjustment for BMI, higher waist circumference

Table I. Baseline characteristics of participants

Characteristics	Men		Women	*p*-value				*p*-value
	1st Tertile	2nd Tertile	3rd Tertile		1st Tertile	2nd Tertile	3rd Tertile	
Number (%)	275,987 (35.37)	247,441 (31.72)	256,646 (32.90)		268,585 (34.58)	252,332 (32.48)	255,760 (32.93)	
Waist circumference (cm)	< 82	≥ 82 and < 87.5	≥ 87.5	< 0.0001	< 77	≥ 77 and < 83	≥ 83	< 0.0001
Age (yrs)	61.01 ± 4.17	60.90 ± 4.13	61.10 ± 4.14	< 0.0001	60.52 ± 4.01	61.17 ± 4.04	61.76 ± 4.07	< 0.0001
BMI (kg/m^2)	21.66 ± 1.90	24.09 ± 1.56	26.47 ± 2.08	< 0.0001	21.89 ±1.90	24.27 ± 1.73	27.08 ± 2.55	< 0.0001
SBP (mmHg)	125.12 ± 12.69	128.01 ± 12.04	130.12 ± 11.80	< 0.0001	122.35 ± 12.92	125.79 ± 12.56	129.10 ± 12.51	< 0.0001
DBP (mmHg)	77.42 ± 7.98	79.05 ± 7.71	80.26 ± 7.65	< 0.0001	75.17 ± 8.12	76.90 ± 7.89	78.67 ± 7.89	< 0.0001
FBS (mg/dl)	101.18 ± 22.90	104.78 ± 24.19	108.35 ± 26.12	< 0.0001	96.07 ± 17.43	99.35 ± 19.63	103.56 ± 23.05	< 0.0001
AST (U/L)	27.77 ± 17.72	27.73 ± 25.62	29.40 ± 19.03	< 0.0001	25.08 ± 11.81	25.37 ± 14.48	26.57 ± 14.92	< 0.0001
ALT (U/L)	23.59 ± 16.37	26.79 ± 26.41	30.83 ± 19.93	< 0.0001	20.69 ± 13.39	22.95 ± 16.46	25.79 ± 17.13	< 0.0001
Total cholesterol (mg/dl)	191.07 ± 31.00	195.20 ± 31.68	195.41 ± 32.25	< 0.0001	205.50 ± 32.05	208.12 ± 32.95	208.63 ± 33.74	< 0.0001
Triglyceride (mg/dl)	122.03 ± 69.93	149.27 ± 81.84	167.17 ± 89.80	< 0.0001	114.75 ± 56.68	134.56 ± 66.63	147.31 ± 71.84	< 0.0001
HDL (mg/dl)	56.25 ± 18.43	52.15 ± 17.45	50.07 ± 16.46	< 0.0001	58.95 ± 19.20	55.86 ± 18.79	54.49 ± 17.84	< 0.0001
Heavy drinker, n (%)[a]	32,179 (11.66)	31,348 (12.67)	37,867 (14.75)	< 0.0001	927 (0.35)	1,011 (0.40)	1,448 (0.57)	< 0.0001
Smoking								
Never, n (%)	97,636 (35.38)	89,162 (36.03)	92,727 (36.13)	< 0.0001	260,688 (97.06)	245,702 (97.37)	247,884 (96.92)	< 0.0001
Ex-smoker, n (%)	79,720 (28.89)	84,553 (34.17)	91,796 (35.77)	< 0.0001	2,524 (0.94)	2,331 (0.92)	2,802 (1.10)	< 0.0001
Current smoker, n (%)	98,631 (35.74)	73,726 (29.80)	72,123 (28.10)	< 0.0001	5,373 (2.00)	4,299 (1.70)	5,074 (1.98)	< 0.0001
Heavy exercise, n (%)[b]	105,445 (38.21)	101,008 (40.82)	99,854 (38.91)	< 0.0001	83,689 (31.16)	75,641 (29.98)	68,493 (26.78)	< 0.0001
Medication history								
Antihypertensive drug, n (%)	113,081 (40.97)	131,402 (53.10)	163,622 (63.75)	< 0.0001	110,612 (41.18)	134,243 (53.20)	169,143 (66.13)	< 0.0001
Antidiabetic drug, n (%)	30,377 (11.01)	39,275 (15.87)	55,737 (21.72)	< 0.0001	20,980 (7.81)	30,910 (12.25)	49,362 (19.30)	< 0.0001
Steroid use, n (%)	169,383 (61.37)	160,236 (64.76)	170,389 (66.39)	< 0.0001	191,595 (71.33)	187,486 (74.30)	192,760 (75.37)	< 0.0001
Osteoporosis, n (%)	6,639 (2.41)	4,736 (1.91)	4,927 (1.92)	< 0.0001	99,057 (36.88)	86,920 (34.45)	80,837 (31.61)	< 0.0001
Femur fracture, n (%)	1,330 (0.48)	808 (0.33)	819 (0.32)	<0.0001	1,247 (0.46)	1,251 (0.50)	1,622 (0.63)	< 0.0001
Lumbar fracture, n (%)	5,059 (1.83)	4,019 (1.62)	4,605 (1.79)	<0.0001	8,171 (3.04)	9,040 (3.58)	11,433 (4.47)	< 0.0001

Table II. Multivariate-adjusted HR (95% CI) of lumbar and hip fracuture in males.

	Number of events	Person years	Model 1	Model 2	Model 3
Femur fracture	2,957				
1st Tertile	1,330	1,819,979	1	1	1
2nd Tertile	808	1,629,905	0.70 (0.64-0.77)	0.73 (0.66-0.80)	1.19 (1.07-1.32)
3rd Tertile	819	1,692,460	0.67 (0.61-0.73)	0.70 (0.63-0.76)	1.73 (1.51-1.99)
Lumbar fracture	13,683				
1st Tertile	5,059	1,810,682	1	1	1
2nd Tertile	4,019	1,624,975	0.90 (0.86-0.93)	0.91 (0.88-0.95)	1.06 (1.01-1.11)
3rd Tertile	4,605	1,682,974	0.97 (0.94-1.01)	0.99 (0.95-1.03)	1.33 (1.25-1.41)

Model 1 was adjusted for age. Model 2 was adjusted for the variables in model 2, plus smoking, alcohol drinking, regular physical exercise and top 20% of insurance payment.Model 3 was adjusted for the variables in model 3, plus osteoporosis medication, anti-hypertension, diabetes, steroid and Body Mass Index.

increased the risk of hip fracture; these findings are in line with those reported in other large cohort and prospective studies[25,29,30]. Different to other fat mass, abdominal fat might be differently associated with bone health[22]; for instance *via* the secretion of pro-inflammatory cytokines (such as, tumor necrosis factor α and interleukin-1) and hormones (such as, parathyroid hormone and insulin)[22,31,32].

In addition, visceral fat is harmful to both the structure and strength of bone[22,33]. The fat at the level of lumbar spine is the best predictive value to evaluate insulin resistance which is associated

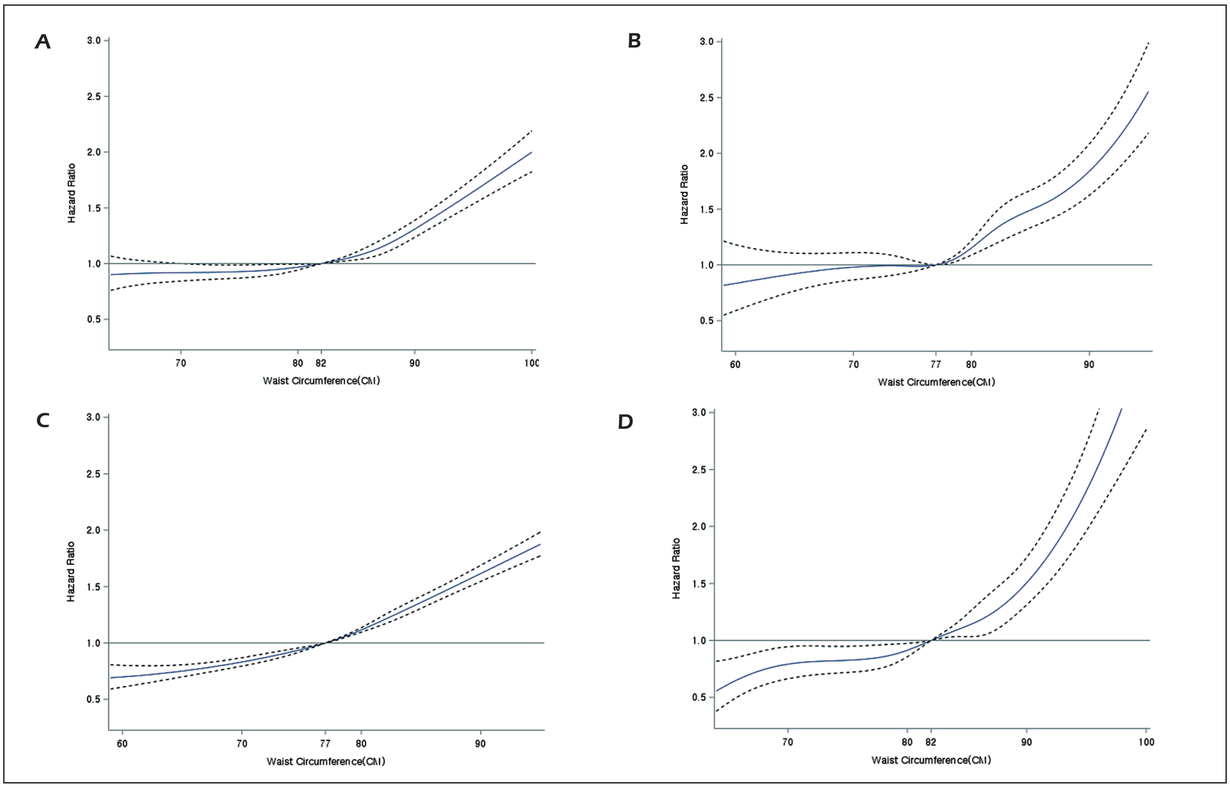

Figure 2. Hazard ratios with 95% confidence intervals for lumbar and hip fractures according to the distribution of waist circumferences in males and females. **A,** Hazard ratios (solid lines) with 95% confidence intervals (shaded area) for lumbar fracture according to waist circumference in males. **B,** Hazard ratios (solid lines) with 95% confidence intervals (shaded area) for hip fracture according to waist circumference in males. **C,** Hazard ratios (solid lines) with 95% confidence intervals (shaded area) for lumbar fracture according to waist circumference in females. **D,** Hazard ratios (solid lines) with 95% confidence intervals (shaded area) for hip fracture according to waist circumference in females.

Table III. Multivariate-adjusted HR (95% CI) of lumbar and hip fracuture in females.

	Number of events	Person years	Model 1	Model 2	Model 3
Femur fracture	4,160				
1st Tertile	1,247	1,771,263	1	1	1
2nd Tertile	1,251	1,666,509	0.98 (0.90-1.06)	0.98 (0.90-1.06)	1.06 (0.97-1.17)
3rd Tertile	1,622	1,692,282	1.19 (1.10-1.28)	1.18 (1.09-1.74)	1.41 (1.26-1.58)
Lumbar fracture	28,644				
1st Tertile	8,171	1,754,276	1	1	1
2nd Tertile	9,040	1,647,301	1.10 (1.07-1.14)	1.10 (1.07-1.14)	1.17 (1.14-1.21)
3rd Tertile	11,433	1,667,615	1.30 (1.26-1.34)	1.29 (1.25-1.33)	1.48 (1.42-1.54)

Model 1 was adjusted for age. Model 2 was adjusted for the variables in model 2, plus smoking, alcohol drinking, regular physical exercise and top 20% of insurance payment.Model 3 was adjusted for the variables in model 3, plus osteoporosis medication, anti-hypertension, diabetes, steroid and Body Mass Index.

with bone mass loss and bone fragility[34,35]. Finally, increased waist circumference impairs body balance, and increases the risk of fall.

Several studies[36,37] have shown that increased fat mass, especially visceral fat mass, is associated with an increased prevalence of vertebral fracture, mostly in females. The majority of previous studies have been conducted in females, and few studies have included both males and females. One study reported that increased waist circumference are associated with increased vertebral fracture in males[26]; however, other studies have shown opposite results[36]. The discrepancy between these results is likely due to the fact that the exact fracture sites were different between studies, the adjusted variables were inconsistent, and the criteria for subdividing the waist circumference were also different. Thus, it seems that more extensive research on visceral fat and vertebral fracture is necessary. However, previous studies, and our study, have demonstrated that waist circumference is associated with vertebral fracture.

Limitations

This study has some limitations. First, since the cohort data of the whole Korean population were obtained through a health examination, it was not possible to check that the waist circumference data were properly measured. However, waist circumference is a simple and affordable method for the measurement of abdominal obesity, and it have easily and widely been used in clinical practice. Second, the diagnosis of fracture was not acquired through actual patient visits, but through the ICD-10 code of the diagnoses. Therefore, there is potential for misdiagnosis. Third, the examination of smoking, alcohol, and exercise was only assessed by a self-report questionnaire sheet. In addition, the information was obtained at once that it is unavailable to show the influence of change of exercise, drinking, and smoking on bone fracture for follow up period. Fourth, since although this is a nationwide retrospective observational cohort study, data was mostly composed of one ethnicity. Nevertheless, this study utilized a large-scale population-based cohort to present evidence that increased waist circumference was associated with an increased risk of vertebral and hip fracture in both males and females.

Conflict of Interest

The Authors declare that they have no conflict of interests.

Acknowledgements

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