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Rheumatoid Arthritis is Associated with Less Optimal Hip Structural Geometry

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Conflict of Interest: The hip structural analysis program used to ascertain the outcome was developed by Thomas Beck and licensed to Hologic Inc. by the Johns Hopkins University. Dr. Beck is also the founder of Quantum Medical Metrics LLC, a company dedicated to developing technology for measuring bone structural geometry. None of the other co-authors have conflicts of interests pertaining to this study.

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Abstract

The overall goal of this study was to assess the longitudinal changes in bone strength in women reporting rheumatoid arthritis (RA) (n=78) compared to non-arthritic control participants (n=4,779) of the Women's Health Initiative Bone Mineral Density sub-cohort. Hip structural analysis program was applied to archived dual energy X-ray absorptiometry scans (baseline, years 3, 6, and 9) to estimate bone mineral density (BMD) and hip structural geometry parameters in three femoral regions: narrow neck, intertrochanteric and shaft. The association between RA and hip structural geometry was tested using linear regression and random coefficient models (RCM). Compared to the non-arthritic control the RA group had a lower BMD ($p=0.061$) and significantly lower outer diameter ($p=0.017$), cross-sectional area ($p=0.004$), and section modulus ($p=0.035$) at the narrow neck region in the longitudinal models. No significant associations were seen at the intertrochanteric or shaft regions, and the association was not modified by age, ethnicity, glucocorticoid use, or time. Within the WHI-BMD, women with RA group had reduced BMD and structural geometry at baseline, and this reduction was seen at a fixed rate throughout the nine years of study.

Keywords

Rheumatoid Arthritis; Hip Structural Geometry; Osteoporosis; Epidemiology

INTRODUCTION

Rheumatoid Arthritis (RA) is a multi-system disorder characterized by chronic destructive synovitis, associated with substantial adverse health consequences (1). Osteoporosis, a major public health concern for aging populations, is one of the common adverse health consequences seen in RA (2). Osteoporosis is characterized by low bone mineral density (BMD), and significant decreases in BMD are correlated with increases in fracture risk (3–6). RA patients have lower BMD than non-arthritic comparison populations (7–9), and this decrease in BMD subsequently increases the risk for a variety of osteoporotic fractures (10, 11).

The mechanism of fracture in RA populations has been under investigation for several years. Molecular factors including inflammatory cytokines such as, interleukin (IL) – 1, IL-6, and tumor necrosis factor (TNF)-alpha, have direct and indirect effects on osteoclasts, increasing bone resorption (12). Glucocorticoids, a class of common therapeutic agents used in RA, have known effects on calcium absorption and bone remodeling (13, 14), and are associated with increased risk for fractures (15). General lifestyle and demographic osteoporosis risk factors, such as age, smoking, and physical activity play a significant role in fracture risk (16), and have been considered as covariates in a variety of RA and fracture studies.

As stated by Griffith and Genant, osteoporotic fractures occur “when bone strength is less than forces applied to the bone” (17). Bone strength is comprised of both the material properties, including mineralization density and collagen composition, and structural properties, including architecture and geometry (18). Because low BMD is strongly correlated with increased fracture risk, BMD is commonly measured as a marker of bone

strength; although it is not a direct measure of either structural geometry or tissue material properties.

Beck and colleagues developed a hip structural analysis (HSA) program that utilizes dual energy X-ray absorptiometry (DXA) images to extract limited structural parameters. This is particularly advantageous to clinical and research practice as DXA is the method routinely used in the assessment of BMD. The HSA program has been used in a variety of studies, and significant improvements in hip structure have been observed with the use of a variety of agents used in the treatment of osteoporosis such as raloxifene (19), teriparatide (20), postmenopausal hormone therapy (21, 22), bisphosphonates (23), and denosumab (24), and modest benefit from calcium and vitamin D supplementation (25, 26) when compared to age-matched control or placebo groups.

To date, there have been no hip structure studies in RA populations. It is possible that the risk factors associated with low BMD in RA also have a negative effect on structural geometry, which could further increase the risk for fracture in this population. Structural instability has been observed in hip fracture cases compared to controls using HSA (27, 28), and recently LaCroix and colleagues found that outer diameter width at the intertrochanteric region was independently associated with hip fracture risk (29), highlighting the importance of having structural measures in the examination of fracture risk, as there are no non-invasive methods for measuring bone material properties. This epidemiologic investigation assessing the structural dynamics of bone over time may provide information on the role of hip structure in fracture risk in postmenopausal women with RA. The objectives of this study are to: 1) assess the longitudinal changes in hip structural geometry in RA compared to non-arthritic controls, and 2) test if age, ethnicity, time, or glucocorticoid use alters the association between RA and hip structural geometry in a population of postmenopausal women from the Women's Health Initiative.

METHODS

Women's Health Initiative (WHI)

This study was performed in participants of the Women's Health Initiative Bone Mineral Density (WHI-BMD) centers. The WHI is a nationwide study that investigated the risk factors and preventive strategies of the major contributors to morbidity and mortality in postmenopausal women: including heart disease, breast and colorectal cancer, and osteoporotic fractures (30). The WHI recruited 161,808 postmenopausal women aged 50 to 79 from 40 centers across the country to participate in the clinical trials (CT) component; including the hormone therapy trials (HT), dietary modification trial (DM), and the calcium and vitamin D trial (CaD); or the observational study (OS). Details of recruitment strategies and baseline participant information have been previously published (31).

Three clinical centers (Tucson/Phoenix, AZ; Birmingham, AL; and Pittsburgh, PA) comprised the BMD sub-cohort. Women enrolled in these centers (n=11,020) had DXA scans on a Hologic QDR 2000 or 4500W machine (Bedford, MA) to measure bone density at the spine, areal hip, and total body; in addition to whole body and regional body composition. The scans were completed at baseline, years 3, 6, and 9 for participants of the OS; and baseline, years 1, 3, 6, 9, and closeout of the study for CT participants. All participants gave signed consent to participate in the WHI study, and the current study was approved by the University of Arizona Institutional Review Board.

Defining Rheumatoid Arthritis Status

The WHI health assessment form was used to identify arthritis status at baseline. The participants were asked, "Did your doctor ever tell you that you have arthritis?" with

responses of yes or no. The participants answering “no” were placed in the non-arthritis control group. Women responding “yes” were then asked “What type of arthritis do you have?” with responses of “rheumatoid arthritis” and “other” or “do not know”. Using the methodology of Walitt and colleagues (32), the RA group was defined to include those women who self-reported RA and one or more of the following commonly used anti-rheumatic agents at baseline including: methotrexate, gold, biologic anti-TNF agents, leflunomide, cyclophosphamide, azathioprine, cyclosporine, tacrolimus, hydroxychloroquine, minocycline, sulfasalazine, and glucocorticoids. Non-responders, those answering “other/do not know”, those self-reporting RA without medications, and those not responding to the follow-up arthritis question were excluded.

Assessing Hip Strength using Hip Structural Analysis

The outcome of this study, the structural geometry of the proximal femur, was ascertained using the hip structural analysis (HSA) program. The HSA program was applied to the archived DXA (baseline, years, 3, 6, and 9) scans to produce estimates of bone strength at three femur cross-sections; the narrow neck (NN), intertrochanteric (IT), and shaft (S). Details on the specifics of HSA have been previously published (33), but in summary, the HSA program computes at each of the 3 cross-sections: conventional BMD, bone cross-sectional area (CSA) bone outer diameter (OD), the center of mass of each cross-section, and the section modulus (SM). Section modulus is an index of bending strength of a cross-section. Femur neck length, and neck-shaft angle are measured, and estimates of cortical thickness at each cross-section is used for an estimate of buckling ratio. Buckling ratio is an index of susceptibility to local cortical buckling under compressive loads and has been shown to be elevated in hip fracture cases (27, 28).

DXA Quality Control

The WHI center at the University of California, San Francisco (UCSF Prevention Sciences, San Francisco, CA) served as the BMD quality control center, which included monitoring DXA operator performance, DXA machine performance, and managing DXA databases from the three WHI clinic centers. Three Hologic spine, hip, and linearity phantoms were exchanged among the centers to assess quality control and cross-calibration. For the structural measurements, a separate cross-calibration was conducted using a special phantom designed for the HSA method. Sensitivity of HSA was not examined in this study, however, previous studies using the program have found moderate to good reliability with coefficient of variations ranging from 0.8% to 7.2% (34, 35).

Covariates

Variables potentially related to RA, BMD or to hip structural geometry were assessed as covariates. These variables included: age, ethnicity, height, weight, body mass index (BMI), total body percent lean mass, smoking status, hormone use status, physical activity, physical function dietary energy, total calcium intake, total vitamin D intake, use of certain medications (thiazide diuretic, statins, anti-convulsants, thyroid drugs, proton pump inhibitors, bisphosphonates, calcitonin, parathyroid hormone, non steroidal anti-inflammatory drugs, estrogens, phenobarbital, and heparin), and variables relevant to the WHI (clinical center, participation in HT or CaD trial). Covariates were assessed at baseline using either questionnaire data (age, ethnicity, smoking, hormone use, physical activity, physical function, nutritional factors, and medications), physical measurements (height, weight, BMI), or DXA derived estimates (percent lean mass).

Statistical Analysis

Descriptive variables reported by the two groups (non-arthritic control vs. RA) were compared using t-tests for continuous variables and χ^2 -squared test for categorical variables. The association between RA and hip geometry was tested using both cross-sectional and longitudinal analyses. For the cross-sectional analysis, the mean age-adjusted BMD and hip structural geometry variables were compared at each time point between the groups using linear regression. Linear mixed effects models (LMM), which incorporate all time observations (baseline, year 3, 6, and 9) in one model, were used to analyze the association between RA and hip strength longitudinally. The random coefficient model (RCM), a type of LMM, was used to control for serial correlation in the data by allowing each subject to have a different slope and intercept estimate fitted as random effects. The base model included the hip geometry measure as the dependent variable and RA status, the baseline measure, and visit as the independent variables. Marginal analyses were performed for each of the covariates, and those with a p-value <0.20 were tested in the full model. Backwards elimination techniques were used to generate the final model, which included all variables p<0.05, any clinically or biologically important variables not meeting the significance level, and variables related to WHI design. The interaction between age, ethnicity, time, and GC use were tested. All analyses were performed in STATA v.10 (College Station, TX).

RESULTS

A total of 11,020 women were enrolled in the WHI-DXA cohort. The baseline health assessment questionnaire was completed by 10,858 participants of whom 5,253 women reported not having arthritis, and 5,605 responded yes to the initial arthritis question. Of the self-reported arthritis patients, 584 self-reported RA and 4,348 reported other types of arthritis. After reviewing baseline medication, 83 (14.2%) of the self-reported RA cases also reported at least one of the commonly used anti-rheumatic agents. Baseline hip structural geometry measurements were available for 4,779 of the non-arthritic controls and 78 of the RA cases. Sample size at each study visit and the number of observations used in modeling can be found in Table 1.

Baseline Characteristics

Significant differences were seen between the two groups in several baseline demographic variables. The RA cases were significantly older than the non-arthritic control group with mean (SD) values of 65.4 (7.5) years compared to 61.7 (7.4) years. The non-arthritic control group was slightly taller (0.60 cm on average) than the RA group, and the non-arthritic control group weighed less (2.5 kg less on average) than the RA group. Ethnicity also varied significantly (p<0.001) between the groups, with a higher percentage of African Americans in the RA group (29%) compared to the non-arthritic group (13%).

There were slight differences in lifestyle factors between groups. The RA group had a higher but non-significant percentage of women currently using postmenopausal hormone therapy (HT) than the control group (42.3% vs. 35.3%). There were no significant differences between reports of energy intake, energy expended through physical activity, and intake of vitamin D between groups. Physical function was significantly reduced by RA status (p<0.001). Non-arthritic controls had a mean (SD) physical function score of 85.9 (16.4), whereas RA group had a mean score of 53.8 (25.0). Complete information on baseline demographics by RA status can be found in Table 2.

The Association between RA and Hip Structural Geometry

A decrease in BMD and strength was observed over the nine years of study in all groups (Table 3). Though not statistically significant, after adjusting for age, the mean BMD and

the hip geometry variables was smaller at baseline and each year of study in the RA group compared to the non-arthritic control group (Table 3). This trend was observed at all regions; however, the mean difference between the two groups was greatest at the narrow neck.

For the longitudinal analysis, no differential effect in hip strength was seen by age or ethnicity, and there was no statistical difference in the rate of loss between three groups over time. No statistically significant glucocorticoid (GC) interaction was also found using traditional interaction methods (main effect of arthritis * main effect of GC use). The final RCM was adjusted for visit and the following baseline variables: baseline strength parameter, age, ethnicity, clinical center, BMI, total body percent lean mass, randomization status (not randomized, intervention or placebo) in the CaD and HT trial, HT use, anticonvulsant medication use, osteoporosis medication use, and physical function. With incorporation of all time points in one model, significant declines in BMD and hip structural geometry variables were seen in the RA group compared to the non-arthritic control group (Table 4 & Figure 1). The RA group had a significantly lower mean OD, CSA, and SM over the study period at the narrow neck region. Though not statistically significant, the mean BMD was lower in the RA group than the nonarthritic control group, and the mean BR was higher (indicating decreased ability to resist local buckling) in the RA group than the non-arthritic control group. The magnitude of the association between RA and hip strength in the intertrochanteric and the shaft regions was not as large as at the narrow neck resulting in non-statistically significant effects, but similar decreasing trends in strength were seen in the RA group. Results from the random coefficient models for each region can be found on table 4 and the longitudinal graphs for the predicted narrow neck region can be found in Figure 1.

DISCUSSION

Our study provides confirmation on the adverse effects of RA on hip BMD, and also showed that RA is associated with a decrease in structural integrity. Though small in number, the RA group within the WHI-BMD centers had reduced BMD and structural geometry at baseline, which further decreased throughout the nine years of study after adjustment for several variables. Inflammation, the primary driver of deteriorating bone health in RA patients, has been shown to be associated with markers of bone remodeling (36). Though not exclusively studied, one can hypothesize that inflammatory cytokines, such as TNF- α , IL-6, or other known inflammatory cytokine with adverse effects on osteoclasts, also have a negative effect on bone structure, providing molecular evidence for the declines in both bone quantity and quality in RA.

Although significant positive effects of various treatments on hip structure at all regions have been shown, our study only found significant results at the narrow neck region. For example, Bonnick and colleagues recently reported a significant effect at all regions with once weekly alendronate and risendronate therapy, with the treatment effect being the strongest at the intertrochanter (23). Our study showed similar trends in decreased strength in the intertrochanteric and shaft regions; however, the magnitude of the association between RA and hip structure was smaller in magnitude and unlike the narrow neck region, did not reach statistical significance. Systemic inflammation is a manifestation of RA, however, the joints are the primary region affected by the disease. Of the regions analyzed, the narrow neck is closest to the hip joint and its placement makes it either intracapsular or close to the capsule margin. This should make it more vulnerable to the erosive effects of the proliferative synovium of RA on bone mass and structure than the other regions, possibly explaining the findings of our study.

Though GC use has adverse effects on bone health, our study did not show any modification on the RA and hip geometry association by GC use. In the non-RA population, GC use slightly reduced the mean BMD and strength estimates to that of the GC negative RA population, and further slightly reduced BMD and strength estimates in the GC positive RA population. Studies on GC use and bone strength are limited. In 2007, Burnham and colleagues reported a study on the effects of glucocorticoid use on bone strength in a population of children with Crohn's disease and nephrotic syndrome (37). They found that cumulative glucocorticoid use was negatively correlated with and inversely associated with outer diameter and section modulus of the femur shaft region (37). Our study did not take into account dosage or cumulative use, which may alter the RA and geometry association, and the truncated sample size hindered statistical power.

Strengths and Limitations

The primary limitations of this study are related to the assessment of the RA. The WHI was not designed to be a RA specific study, and RA status is based solely on the respondent. Agreement estimates of self-reported RA to physician diagnoses range from 7–38% (38–42). The method used by Walitt and colleagues in a previous WHI study, showed that coupling medication information with self-report increased the positive predictive value (32). In the current study, only 14% of the self-reported RA cases indicated one of the medications of interest. The RA cases are probably true RA cases; however, these may represent the more severe cases, which could overestimate the effect of RA on hip strength. Using general RA population prevalence estimates, 1% or 114 women in the WHI-BMD centers should have an RA diagnosis. By using the baseline medication, we potentially captured only 60% of the cases, missing a significant number of likely RA cases. The addition of these unknown cases would provide more unbiased estimates of the associations between RA and hip strength. It is also possible that women with other rheumatologic conditions taking the medications of interest were misclassified as RA cases; however conditions such as systemic lupus erythematosus and Crohn's disease were ascertained in separate questions. The WHI also did not collect information on disease duration or severity, which potentially could modify the association between RA and hip strength.

There are also limitations associated with study outcome measurements. Three-dimensional hip structural geometry are being measured from a two-dimensional DXA scan, and several fundamental limitations have been noted (34). For example, it has been stated that DXA scanners are “optimized to measure mineral mass and not spatial dimensions”, hindering the machines ability to precisely measure structural parameters (34). The precision of femur geometry measurements is particularly dependent on subject positioning, much more than conventional BMD (34), making it more difficult to reliably detect small changes over time.

Though these limitations have been noted, the WHI ensured the quality of the data with a large number of quality control procedures. As previously stated, the DXA machines used at each of the centers were scanned using calibrated phantoms and any necessary corrections to the machine and clinic procedures were made over the study period. All DXA technicians were trained under manufacturer and WHI protocols, and there is no reason to suggest that the RA patients were positioned differently from the control group. Dedicated clinic staff also made sure the participants filled out all questionnaires so that complete information on covariates would be available. Examining the data longitudinally also provided the opportunity to increase the analytical power by including all time points in one model in addition to controlling for all other important covariates not examined in the cross-sectional analysis. The WHI is one of the largest and most diverse cohorts of postmenopausal women in the United States. There is a wealth of data within the WHI on longitudinal changes in bone strength and as well as information on important RA outcomes such as fractures,

making it a good resource to assess the longitudinal effect of RA on bone loss, alterations in structural stability, and fracture risk.

Conclusion

Osteoporosis is a significant public health problem for older populations, and highly prevalent in RA populations. Osteoporotic fractures are a result of reduced bone strength, and with the advent of HSA, material and structural properties can be measured, providing a more complete strength estimate. With incorporation to many Hologic machines, the HSA program is now widely being used in the clinical and research arena. This investigation on RA and its effect on bone strength and changes over time, contributes epidemiological data to the field of rheumatology, which can be used to improve fracture assessment in women with rheumatoid arthritis.

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Figure 1. Longitudinal Changes in BMD and Hip Structural Geometry by Arthritis Status

Longitudinal graph of predicted values from random coefficient model adjusted for mean value of the total population for continuous variables and mean proportion of total population for categorical variables.

A-Bone Mineral Density; B- Outer Diameter; C- Cross Sectional Area; D- Section Modulus; E-Buckling Ratio

Table 1

Sample Size and Observation Count by Arthritis Status

Sample Size at Each Study Visit		
	No Arthritis	RA
Baseline	4779	78
Year 3	3834	49
Year 6	3447	38
Year 9	1878	20
Number of Observations		
	No Arthritis	RA
1	741	25
2	903	19
3	2053	22
4	1308	14

Table 2

Baseline Demographics by Rheumatoid Arthritis Status

	No Arthritis	RA	
	N (%)	N (%)	p-value
Participant of Observational Study			<0.001
No	2078 (43.5)	18 (23.1)	
Yes	2701 (56.5)	60 (76.9)	
Participant of Hormone Trial			0.118
No	3929 (82.2)	68 (87.2)	
Yes	850 (17.8)	10 (12.8)	
Participant of CaD Trial			0.003
No	3676 (76.9)	71 (91.0)	
Yes	1103 (23.1)	7 (9.0)	
Participant of Dietary Modification Trial			<0.001
No	3277 (68.6)	69 (88.5)	
Yes	1502 (31.4)	9 (11.5)	
Baseline Age Group			<0.001
50–59	2039 (42.7)	19 (24.4)	
60–69	1917 (40.1)	29 (37.2)	
70–79	823 (17.2)	30 (38.5)	
Ethnicity			<0.001
American Indian or Alaskan Native	50 (1.1)	1 (1.3)	
Asian or Pacific Islander	20 (0.4)	0 (0.0)	
Black or African-American	618 (13.0)	22 (28.6)	
Hispanic/Latino	330 (7.0)	8 (10.4)	
White (not of Hispanic origin)	3728 (78.6)	46 (59.7)	
Baseline HT usage			0.214
Never used	2370 (49.6)	33 (42.3)	
Past user	719 (15.1)	12 (15.4)	
Current user	1688 (35.3)	33 (42.3)	
BMI Category			<0.001
Underweight (< 18.5)	43 (1.0)	1 (1.8)	
Normal (18.5 – 24.9)	1420 (34.1)	15 (26.8)	
Overweight (25.0 – 29.9)	1539 (37.0)	22 (39.3)	
Obesity i (30.0 – 34.9)	764 (18.4)	10 (17.9)	
Obesity ii (35.0 – 39.9)	283 (6.8)	6 (10.7)	
Extreme obesity iii (>= 40)	111 (2.7)	2 (3.6)	
Baseline Smoking Status			0.045
Never smoked	2608 (55.2)	34 (44.2)	
Past smoker	1695 (35.9)	39 (50.7)	
Current smoker	420 (9.0)	4 (5.2)	
	NoRA	RA	

	No Arthritis	RA	p-value
	N (%)	N (%)	
	Mean $\pm$ SD	Mean $\pm$ SD	p-value
Age (years)	61.7 $\pm$ 7.4	65.4 $\pm$ 7.5	<0.001
Height (cm)	161.9 $\pm$ 6.4	161.3 $\pm$ 5.7	0.395
Weight (kg)	72.2 $\pm$ 15.5	74.7 $\pm$ 15.8	0.160
BMI (kg/m ²)	27.4 $\pm$ 5.5	28.7 $\pm$ 5.5	0.055
Total Energy Expended per Week (METs)	12.3 $\pm$ 14.6	11.7 $\pm$ 16.4	0.697
Physical Function	85.9 $\pm$ 16.4	53.8 $\pm$ 25.0	<0.001
Dietary Energy (kcal)	1644.1 $\pm$ 836.3	1539.8 $\pm$ 717.2	0.274
Total Calcium (mg)	1087.7 $\pm$ 707.6	1198.1 $\pm$ 915.6	0.174
Total Vitamin D (IU)	315.6 $\pm$ 266.5	341.1 $\pm$ 291.1	0.402

Table 3

Age-Adjusted BMD and Hip Structural Geometry by RA Status at the Narrow Neck Region

	No Arthritis	RA	
	Mean $\pm$ SE	Mean $\pm$ SE	p-value
BMD (g/cm²)			
Baseline	0.717 $\pm$ 0.002	0.707 $\pm$ 0.013	0.468
Year 3	0.726 $\pm$ 0.002	0.695 $\pm$ 0.018	0.093
Year 6	0.716 $\pm$ 0.002	0.700 $\pm$ 0.021	0.457
Year 9	0.702 $\pm$ 0.003	0.667 $\pm$ 0.026	0.181
OD (cm)			
Baseline	2.998 $\pm$ 0.003	3.043 $\pm$ 0.024	0.067
Year 3	3.015 $\pm$ 0.004	3.025 $\pm$ 0.031	0.753
Year 6	3.026 $\pm$ 0.004	2.999 $\pm$ 0.038	0.480
Year 9	3.068 $\pm$ 0.005	3.002 $\pm$ 0.050	0.190
CSA (cm²)			
Baseline	2.041 $\pm$ 0.005	2.045 $\pm$ 0.039	0.917
Year 3	2.078 $\pm$ 0.006	2.002 $\pm$ 0.052	0.150
Year 6	2.057 $\pm$ 0.007	1.994 $\pm$ 0.063	0.318
Year 9	2.045 $\pm$ 0.008	1.907 $\pm$ 0.077	0.074
SM (cm³)			
Baseline	0.907 $\pm$ 0.003	0.923 $\pm$ 0.021	0.448
Year 3	0.936 $\pm$ 0.003	0.901 $\pm$ 0.030	0.243
Year 6	0.932 $\pm$ 0.004	0.918 $\pm$ 0.035	0.697
Year 9	0.934 $\pm$ 0.005	0.871 $\pm$ 0.043	0.143
BR			
Baseline	12.363 $\pm$ 0.038	12.766 $\pm$ 0.299	0.182
Year 3	12.318 $\pm$ 0.044	12.930 $\pm$ 0.389	0.118
Year 6	12.572 $\pm$ 0.049	12.943 $\pm$ 0.469	0.431
Year 9	13.018 $\pm$ 0.067	13.548 $\pm$ 0.619	0.394

BMD=Bone Mineral Density; OD=Outer Diameter; CSA=Cross- Sectional Area; SM=Section Modulus; BR=Buckling Ratio

Table 4

The Association between Rheumatoid Arthritis, BMD and Hip Structural Geometry based on Random Coefficient Model^A

	Narrow Neck	Intertrochanteric	Shaft
	coef. ^B (95%CI)	coef. ^B (95% CI)	coef. ^B (95% CI)
BMD	-0.013* (-0.027, 0.001)	-0.002 (-0.016, 0.011)	0.002 (-0.018, 0.022)
OD	-0.035** (-0.064, -0.006)	0.003 (-0.042, 0.047)	-0.008 (-0.029, 0.014)
CSA	-0.061*** (-0.102, -0.012)	-0.005 (-0.068, 0.058)	-0.003 (-0.055, 0.049)
SM	-0.027** (-0.052, -0.002)	-0.022 (-0.090, 0.046)	-0.015 (-0.050, 0.020)
BR	0.175 (-0.158, 0.508)	0.102 (-0.154, 0.358)	0.006 (-0.094, 0.107)

BMD=Bone Mineral Density; OD=Outer Diameter; CSA=Cross-Sectional Area; SM=Section Modulus; BR=Buckling Ratio

* p<0.1;

** p<0.05;

*** p<0.01;

^A All models adjusted for visit, baseline age, ethnicity, center, BMI, total body % lean mass, CaD Trial arm, HT trial arm, hormone use, physical function, anticonvulsant medication use, and osteoporosis medication usage

^B BMD and HSA coefficients of RA reference to the no arthritis group are presented.