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BASIC RESEARCH

Patients With Hip Osteoarthritis Have a Phenotype With High Bone Mass and Low Lean Body Mass

Magnus K. Karlsson MD, PhD, Håkan Magnusson MD, PhD, Maria C. Cöster MD, Tord vonSchewelov MD, PhD, Caroline Karlsson MD, PhD, Björn E. Rosengren MD, PhD

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Abstract

Background Although hip osteoarthritis (OA) is common, its etiology is poorly understood. Specifically, it is not known whether hip OA is associated with abnormal relationships among the anthropometric and musculoskeletal characteristics that are associated with OA in general.

Questions We asked whether patients with primary hip OA have a phenotype with higher bone mineral density (BMD), higher BMI, larger skeletal size, lower lean body mass, and higher fat content.

Material and Methods We included 30 women and 32 men (mean age, 66 years; range, 42–84 years) with primary hip OA and 96 women and 91 men as control subjects. Dual energy x-ray absorptiometry was used to measure total body BMD (g/cm^2), femoral neck width (cm), fat and lean mass (%), and BMI (kg/m^2). Z scores were calculated for each individual. Data are presented as means with 95% CI.

Results Women with hip OA had the following Z scores: total body BMD 0.6 (0.3, 1.0); BMI 0.6 (0.2, 1.0); femoral neck width 0.2 (−0.6, 1.0); percent total body lean mass −0.9 (−1.2, −0.5); and percent total body fat mass 0.6 (0.2, 0.9). Men with hip OA had the following mean Z scores: total body BMD 0.5 (0.0, 1.0); BMI 0.8 (0.3, 1.3); femoral neck width 0.4 (0.01, 0.9); percent total body lean mass −0.8 (−1.1, −0.5); and percent total body fat mass 0.5 (0.2, 0.8).

Conclusions Women and men with idiopathic hip OA have a phenotype with higher BMD, higher BMI, proportionally higher fat mass, and proportionally lower lean body mass. Men also have a larger skeletal size.

Clinical Relevance A higher BMD may lead to a stiffer bone and a proportionally lower lean body mass to lower joint-protective ability, both traits probably predisposing for hip OA.

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M. K. Karlsson (✉), H. Magnusson, M. C. Cöster, T. vonSchewelov, C. Karlsson, B. E. Rosengren
Clinical and Molecular Osteoporosis Research Unit, Departments of Orthopedics and Clinical Sciences, Skåne University Hospital, Lund University, 205 02 Malmö, Sweden
e-mail: magnus.karlsson@med.lu.se

Introduction

Primary osteoarthritis (OA) is a condition without a fully known etiology that affects joint cartilage, the adjacent skeleton, and the surrounding soft tissue [11]. It is a disease that could affect most joints [27, 33]. General risk factors for primary OA include heredity, old age, female gender, specific ethnicity, and high BMI [12]. This suggests that primary OA may include different pathophysiologic etiologies, therefore OA at different joints may require different surgical and nonsurgical treatment approaches. In addition to these general factors, local factors such as chronic repeated loads, loads with high magnitude, ligament

instability, neuromuscular impairment, and joint deformity may accelerate the degenerative process [6]. A high prevalence of OA also has been reported in obese patients and in weightbearing joints [4, 6], partly referred to a high joint surface load [31]. However, primary OA also has been seen in nonweightbearing joints such as the thumb base and fingers [33, 35]. Gender differences regarding the prevalence of primary OA were found for several joints [4, 6]. This further strengthens the view that primary OA may have different pathophysiologic etiologies [12].

Based on epidemiologic studies, a general primary OA phenotype includes local effects on the skeleton, with cysts, subchondral sclerosis, and osteophytes [14]. However, there also are studies inferring that patients with OA have a general high bone mineral density (BMD) [4, 9, 12, 13, 17, 24, 29, 30] and high BMI [17, 29]. If this phenotype could be found in all patients with OA, independent of the affected joint, is unclear. For example, the literature suggests that a high BMI is associated with incident knee OA but not with incident hip OA and that a high BMI is associated with progression of knee OA but not hip OA [17, 29], and that BMI and percent body fat and other measures of body mass are approximately twice as strongly associated with the risk of knee OA than with hip OA [22].

We therefore conducted this study to determine whether individuals, based on gender, with primary hip OA have a phenotype with (1) higher BMD, (2) higher BMI, (3) smaller bone size, (4) proportionally lower lean (muscle) mass, and (5) proportionally higher fat mass.

Patients and Methods

We included 62 patients, 30 women (mean ± SD) 68 ± 9 years old (range, 48–84 years) and 32 men 65 ± 10 years old (range, 42–81 years), referred to our hospital between 2005 and 2006 with severe radiographic verified OA for a decision on surgery owing to primary end-stage hip OA. All patients were Caucasians from Malmö in southern Sweden and all had disabling pain from the affected joint at rest and during activity, and typical clinical and radiographic features of hip OA. No exclusion criteria were used. Ninety-six women 68 ± 11 years old (range, 48–85 years) and 91 men 64 ± 12 years old (range, 42–83 years) were the control subjects [18]. The patients and control subjects received the same protocol and had measurements with the same dual energy x-ray absorptiometry (DXA) apparatus. The control subjects were selected randomly from the population register and were described in a report of normative BMD and body composition data in our region [18]. From this cohort we included individuals with the same age ranges as our patient group. There was no specific matching to each patient with hip OA. All participants answered the same questionnaire on lifestyle including questions on occupation (blue-collar or white-collar worker), recreational exercise (yes/no), smoking, alcohol and coffee consumption, avoiding anything in food, having children, diabetes or other diseases, use of any medication (yes/no), and questions regarding menopause and birth control pills for women. Age and lifestyle factors were stratified by sex for patients and control subjects (Table 1). The study was approved by the Ethics Committee of Lund University (LU 267-00), and conducted in accordance with the Helsinki Declaration. Informed written consent was obtained from all participants before the start of the study.

BMD (g/cm^2) was measured by DXA (Lunar DPX-L® 1.3z, Lunar Corporation, Madison, WI, USA) in total body, spine, leg, and arm with a total body scan. Femoral neck BMD was measured with a hip scan, as was the femoral neck width, a measurement often used as an estimate of bone size [1, 3]. Body weight and body height were measured by standard equipment and BMI then was calculated as weight/height squared (kg/m^2). Femoral neck width was calculated from the AP hip scan as the femoral neck area divided by the scan length. Total body lean mass and total body fat mass were evaluated from the total body scan. Daily calibration of the apparatus was done with a Lunar® phantom. The coefficient of variation after repositioning 14 individuals was 0.4% for total body BMD, 1.6% for femoral neck BMD, 1.0% for lumbar spine BMD, 3.0% for arm and leg BMDs, 1.5% for femoral neck width, 1.5% for total body lean mass, and 3.7% for total body fat mass.

Statistical calculations were done with Statistica®, 7.1 (StatSoft, Tulsa, OK, USA). All data and comparisons were done separately for men and women. Descriptive data are presented as numbers with proportions (%), means ± SD, or as means with 95% CI. Individual Z scores, the number of SDs above or below the age-predicted mean, were derived by linear regression using the control cohort as a reference population. Group differences were evaluated by Student's t-test as a parametric test, Fisher's exact and chi-square tests as nonparametric tests, and analysis of covariance when adjusting the group comparison for covariates. Odds ratios (ORs) were calculated by logistic regression to estimate the risk of having OA with each SD higher total body BMD, higher BMI, higher percent fat mass, and each SD lower percent lean body mass.

Results

Individuals with hip OA had a phenotype with higher BMD, for women with a total body BMD Z score of 0.6, (95% CI, 0.3, 1.0) and for men of 0.5 (95% CI, 0.01, 1.0) (Table 2).

Table 1. Age and lifestyle factors

Parameter	Women			Men		
	Patients with osteoarthritis (n = 30)	Control subjects (n = 96)	p value	Patients with osteoarthritis (n = 32)	Control subjects (n = 91)	p value
Age (years)	67.9 ± 8.8	67.6 ± 11.5	—	65.0 ± 9.5	64.2 ± 11.8	—
Height (cm)	163.4 ± 6.1	162.8 ± 5.3	0.60	175.9 ± 6.6	176.3 ± 6.0	0.77
Weight (kg)	70.5 ± 12.3*	64.1 ± 10.6*	< 0.01*	86.8 ± 13.5*	79.6 ± 10.7*	< 0.01*
BMI (kg/m^2)	26.4 ± 4.3*	24.2 ± 3.9*	< 0.01*	28.0 ± 4.0*	25.6 ± 3.0*	< 0.001*
Blue-collar worker	13/27 (48.1 %)	29/84 (34.5%)	0.20	17/31 (54.8%)	32/80 (40.0%)	0.16
Recreational exercise	13/26 (50.0%)*	22/84 (26.2%)*	0.02*	17/30 (56.7%)	35/80 (43.8%)	0.23
Smoker	6/29 (20.7%)	14/69 (20.2%)	0.83	8/32 (25.0%)	21/79 (36.6%)	0.86
Uses alcohol	22/24 (91.7%)	55/73 (75.3%)	0.14	26/28 (92.9%)	74/78 (97.4%)	0.65
Drinks coffee	27/29 (93.1%)	77/83 (92.8%)	0.53	27/30 (90.0%)	69/70 (98.6%)	0.36
Any food restriction	0/8 (0%)	1/82 (1.2%)	1.00	1/6 (16.7%)	1/80 (1.2%)	0.13
Has children	25/28 (89.3%)	73/79 (92.4%)	0.69	—	—	
Menopause	22/30 (73.3%)	77/96 (80.2%)	0.45	—	—	
Used birth control pills	4/23 (17.4%)	13/77 (16.9%)	1.00	—	—	
Diabetes	1/30 (3.3%)	1/96 (1.0%)	0.42	1/32 (3.1%)	4/91 (4.4%)	1.00
Other diseases	15/30 (50.0%)	49/96 (51.0%)	0.92	16/32 (50.0%)	51/91 (56.0%)	0.55
Present medication	15/29 (51.7%)	45/84 (53.6%)	0.86	15/32 (46.9%)	41/80 (51.3%)	0.68

Presented as mean values (SD) for continuous parameters and numbers with proportion (%) for categorical parameters; evaluations of group differences were done using Student's t-test between means, chi-square test and Fisher's exact test; * statistically significant difference.

Individuals with hip OA had a phenotype with higher BMI, for women with a Z score of 0.6 (95% CI, 0.2, 1.0) and for men of 0.8 (95% CI, 0.3, 1.3) (Table 2).

Men with hip OA had a phenotype with larger bone size with a femoral neck width Z score of 0.4 (95% CI, 0.01, 0.9) while women with hip OA had a normal bone size with a femoral neck width Z score of 0.2 (95% CI, −0.6, 1.0) (Table 2).

Individuals with hip OA had a phenotype with proportionally lower total body lean mass, for women with a Z score of −0.9 (95% CI, −1.2, −0.5) and for men of −0.8 (95% CI, −1.1, −0.5) (Table 2).

Individuals with hip OA had a phenotype with proportionally higher fat mass, for women with a Z score of 0.6 (95% CI, 0.2, 0.9), and for men of 0.5 (95% CI, 0.2, 0.8) (Table 2).

The only lifestyle factor that differed statistically between patients with OA and control subjects was the current level of physical activity in women. After adjustment for group differences in physical activity, all group differences reported above remained (data not shown). When we adjusted for body size (BMI), the group difference in BMD remained in women but not in men (Table 2). In addition, when we adjusted for group differences in body size (BMI), the absolute values and the proportion of fat mass were no longer higher in the patients with OA, while the absolute and the proportion of lean (muscle) were significantly lower in patients with OA than in control subjects (Table 2).

Each SD higher BMI in women was associated with a 66% higher risk of having hip OA, each SD higher total body BMD with a more than doubled risk, and each SD lower body size (BMI) adjusted proportion of lean (muscle) mass with close to five times higher risk (Table 3). Each SD higher BMI in men was associated with an 87% higher risk of having hip OA, each SD higher total body BMD with a 65% higher risk, each SD larger femoral neck bone width with a 50% higher risk, and each SD lower body size (BMI) adjusted proportion of lean mass with more than three times higher risk (Table 3).

Discussion

It is unclear if hip OA is associated with a specific musculoskeletal phenotype. If so, the phenotype could be involved in the pathogenesis of the disorder. We wished to examine differences in bone traits, lean mass, and fat mass by DXA between patients with OA and control subjects.

The limitations of this study include the cross-sectional design, therefore the study should be regarded as hypothesis generating only. We included only patients with end-stage hip OA, and if the same phenotype is evident in patients with early hip OA is not known. If this is true it would strengthen the view that the phenotype may be associated with the pathogenesis of OA. However, as the

Table 2. Anthropometry and BMD

Parameter	Women				Men			
	Patients with osteoarthritis (n = 30)	Control subjects (n = 96)	p unadjusted	p adjusted	Patients with osteoarthritis (n = 32)	Control subjects (n = 91)	p unadjusted	p adjusted
Anthropometry								
Total body fat mass (kg)	28.1 (24.7, 31.5)*	23.8 (22.1, 25.4)*	0.02*	0.08	22.8 (20.0, 25.7)*	19.1 (17.7, 20.6)*	0.02*	0.25
Total body lean mass (kg)	37.3 (35.3, 39.2)	38.8 (38.0, 39.7)	0.10	< 0.01*	56.6 (53.5, 59.6)	58.9 (57.3, 60.5)	0.17	< 0.01*
Proportion body fat (%)	40.2 (37.4, 42.9)*	36.1 (34.5, 37.6)*	< 0.01*	0.08	27.0 (24.7, 29.3)*	23.6 (22.2, 25.1)*	< 0.01*	0.18
Proportion lean mass (%)	55.0 (52.3, 57.7)*	61.1 (59.6, 62.6)*	< 0.001*	< 0.001*	68.3 (66.0, 70.6)*	74.2 (72.6, 75.7)*	< 0.001*	< 0.01*
BMD (g/cm^2)								
Total body	1.08 (1.04, 1.13)*	1.01 (0.99, 1.04)*	< 0.01*	0.03*	1.22 (1.17, 1.27*	1.17 (1.14, 1.19)*	0.03*	0.15
Spine	1.06 (1.00, 1.12)*	0.97 (0.94, 1.00)*	< 0.01*	0.02*	1.16 (1.10, 1.22)	1.10 (1.07, 1.14)	0.12	0.38
Leg	1.06 (1.01, 1.11)	1.04 (1.01, 1.07)	0.41	0.83	1.30 (1.24, 1.36)	1.28 (1.26, 1.31)	0.56	0.90
Arm	0.81 (0.77, 0.85)*	0.74 (0.72, 0.76)*	< 0.01*	0.02*	0.99 (0.95, 1.04)*	0.94 (0.92, 0.96)*	0.03*	0.10
Hip femoral neck	0.90 (0.84, 0.96)*	0.81 (0.78, 0.84)*	< 0.01*	0.03*	1.00 (0.93, 1.08)	0.95 (0.91, 1.00)	0.28	0.81
Bone size (cm)								
Femoral neck width	3.51 (3.30, 3.74)	3.46 (3.40, 3.52)	0.46	0.78	4.12 (3.98, 4.28)*	3.96 (3.89, 4.04)*	0.05*	0.14

BMD = bone mineral density; data shown as unadjusted means with 95% CI in brackets; group comparisons were made unadjusted and adjusted for body size (BMI); * statistically significant differences.

Table 3. Sex-specific odds ratio for having hip OA

Parameter	Women (n = 126)	Men (n = 123)
For each SD higher		
BMI	1.66 (1.12, 2.46)*	1.87 (1.28, 2.74)*
Total body BMD	2.28 (1.32, 3.93)*	1.65 (1.07, 2.59)*
Femoral neck bone size	1.13 (0.82, 1.54)	1.50 (1.01, 2.24)*
Absolute fat mass	1.67 (1.07, 2.62)*	1.69 (1.07, 2.66)*
Proportion body fat	1.87 (1.11, 3.15)*	1.87 (1.09, 3.21)*
Proportion body size (BMI) adjusted body fat	1.99 (0.96, 4.14)	1.60 (0.82, 3.14)
For each SD lower		
Absolute lean body mass	1.43 (0.92, 2.21)	1.39 (0.86, 2.27)
Proportion lean body mass	2.79 (1.55, 5.04)*	3.08 (1.61, 5.89)*
Proportion body size (BMI) adjusted lean body mass	4.77 (2.00, 11.50)*	3.23 (1.50, 6.99)*

BMD = bone mineral density; data presented as mean with 95% CI in brackets; *statistically significant differences.

data indicate a specific phenotype in individuals with OA, large prospective observational studies should be conducted following individuals from youth through old age with DXA to evaluate if the phenotype precedes the disease. The approach used in this study often is advocated in research. First a cross-sectional study is done, and if the forwarded hypothesis is verified, future more resource-demanding prospective trials should be done to verify or refute the hypothesis. Another weakness is the use of femoral neck width as an estimate of general bone and joint size, even if the same approach is being used by other researchers [1, 3]. However, the degenerative process of the hip could have influenced the width measurement and if the size of the femoral neck width reflects all other skeletal regions could be discussed. Further prospective studies that follow bone size from before the development of OA and studies with CT that measure bone size and the cartilage surface area in several skeletal regions in conjunction with volumetric BMD measurements should be done. The BMD measurement could have been compromised by differences in body composition, since it is reported that soft tissue composition influences the estimate of BMD [1, 3]. However, after adjusting for BMI, our inferences remained. It was advantageous to have access to the radiographs so that we could reevaluate and grade the OA and measure the actual joint space height. It also was advantageous to have a sample size so that women could be stratified as premenopausal or postmenopausal. More thorough evaluation of current and previous lifestyle would have been preferable. This is especially true for physical activity that should be evaluated as current activity, past and daily activities, and training by physiotherapists. All patients in our region with hip OA are referred for physical training by

physiotherapists before making a decision regarding surgery, and the higher level of recreational exercise in women with OA than in control subjects probably reflects this treatment strategy.

Studies suggest an inverse relationship between OA and osteoporosis in the hip [10] and an association between OA in the hip, knee, ankle, and feet and a high BMD [4, 5, 7, 15, 21, 26]. It also was speculated that a high BMD may result in a denser and stiffer skeleton with less load absorptive ability, a phenotype that may be involved in the pathogenesis of primary OA [28]. In our study women and men with hip OA had a high BMD; in women independently of their high BMI but not in men. Furthermore, the association between high BMD and primary hip OA was strong, with each SD higher BMD being associated with a more than doubled risk of OA in women and a 65% higher risk in men. However, this is a cross-sectional study and we cannot state that a higher BMD would confer an increased risk, only that a higher BMD was associated with a higher risk for having OA. This is unexpected, as some studies suggest that high BMD is the result of strong muscle forces acting on the bone [2, 19], whereas we found low lean mass in women and men with OA. In the clinical setting a normal or high BMD probably is beneficial for prosthesis fixation in joint replacement surgery [16]. Since hip OA is associated with this phenotype there seems to be no need for routine preoperative BMD assessment in joint replacement surgery, a strategy proposed by some [20].

High BMI is another risk factor for hip OA [17, 29, 34] and being overweight has been found to precede the disease [8, 23]. However, a high BMI is difficult to interpret since a high BMI could be the result of totally different phenotypes in different individuals. The high BMI in the patients with OA in our study was the result of a large fat mass, not a high lean (muscle) mass or short stature (Table 2). Furthermore, related to the larger body size, women and men with primary hip OA had a normal fat content but a marked deficit in lean mass (Table 2). In other words, for the higher BMI found in the patients with OA, a deficit in lean mass was more striking than an excess in fat mass. This would indicate a lower capacity to withstand joint trauma. However, even if there is evidence in the literature that overweight precedes the development of OA [8, 23], we cannot state whether the deficit in muscle mass existed before the development of OA. High BMI may be a risk factor for perioperative and postoperative complications [31]. Finally, one of the most important findings of this study may be the low BMI adjusted lean mass found in patients with hip OA, as this may have clinical implications. Weight loss often is encouraged in patients considered for THA, but our study suggests that the high fat content could be less of a problem than a proportionally low muscle mass. Therefore, losing weight may still be good advice, but more attention perhaps should be paid to building muscle by exercise.

The finding of a larger femoral neck width in men but not in women indicates that there could be different pathogenic pathways in women and men when primary hip OA develops. However, when adjusting the femoral neck width for body size (BMI), the width was similar in women and men with hip OA compared with in control subjects. A different phenotype may be associated with primary OA in different joints.

Inferior neuromuscular function also has been identified as a risk factor for hip OA [8, 17, 29, 34], as joint protection from trauma may be inadequate [25, 32]. Our data support this finding, showing that each SD deficit in body size adjusted lean mass was associated with five times higher risk in women and three times higher risk in men of having hip OA. The findings of high BMD, high BMI, and low relative lean mass in patients with primary hip OA indicate that these patients may have a specific phenotype unrelated to the force the muscles exert on the skeleton [2, 19]. The muscle mass deficit we found may be involved in the development of the disease in that the muscle mass deficit, in addition to a higher joint load attributable to the higher weight, may be harmful to the joint.

Women and men with idiopathic hip OA have a phenotype with higher BMD, higher BMI, proportionally lower lean body mass, and proportionally higher fat mass. Men also have a larger skeletal size. Even though the higher BMD may provide a solid base for prosthesis fixation, the higher BMI may result in a higher joint load and an elevated risk of perioperative and postoperative complications and the lower muscle mass in a low capacity to withstand joint trauma. The different skeletal phenotypes in our patients with hip OA and patients with OA in other joints indicate that separate pathophysiologic pathways may be responsible for primary OA in different joints. Future prospective studies must be done to verify or refute the hypothesis raised in this study.

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