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Patients with Osteoarthritis in all Three Knee Compartments and Patients with Medial Knee Osteoarthritis Have a Phenotype with High Bone Mass and High Fat Mass but Proportionally Low Lean Mass

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Abstract: *Background and Purpose:* Cross-sectional studies have shown that patients with primary hip osteoarthritis (OA) have higher bone mineral density (BMD), higher BMI, lower lean body mass, and higher fat content. But it is unknown if this phenotype is found also in patients with knee OA and if it precedes OA or manifests as a result of the disease.

Patients and Methods: We included 21 women and 18 men (mean age, 71 years; range, 48-85 years) with primary OA in all three knee compartments, 17 women and 56 men (mean age, 55 years; range, 34-74 years) with primary medial knee OA and 122 women and 121 men without OA as controls. We measured total body BMD (g/cm^2), fat and lean mass (%) by dual energy X-ray absorptiometry and also registered height and weight to calculate BMI (kg/m^2). Z-scores were calculated for each individual. Data are presented as means with 95% confidence intervals within brackets.

Results: Individuals with primary OA in all three knee compartments had the following Z-scores: total body BMD 0.4 (0.0, 0.9); BMI 1.2 (0.7, 1.6); proportion of lean mass -0.6 (-1.1, -0.1); proportion of fat mass 0.4 (0.0, 1.8). Individuals with medial knee OA had the following Z-scores: total body BMD 0.4 (0.3, 0.6); BMI 1.1 (0.8, 1.4); proportion of lean mass -0.8 (-1.3, -0.9); proportion of fat mass 0.9 (0.7, 1.1).

Interpretations: A phenotype with higher BMD, higher BMI, higher fat mass, and proportionally lower lean body mass is evident in individuals with primary OA in all three knee compartments and in patients with only medial knee OA.

Keywords: Generalized, knee, localized, men, osteoarthritis, women.

INTRODUCTION

Primary osteoarthritis (OA) is a condition that affects joint cartilage, the adjacent skeleton, and the surrounding soft tissue [1]. The disease could affect most joints [2, 3] and is associated with risk factors such as heredity, old age, female gender, ethnicity, and high body mass index (BMI) [4]. Additional local influences, such as chronic repeated loads, loads with high magnitude, ligament instability, neuromuscular impairment, and joint deformity may be additional unfavorable factors that accelerate the degenerative process [5]. A high prevalence of OA has also been found in obese patients and in weight-bearing joints [5, 6], partly referred to a high joint surface load [7]. Studies evaluating patients with hip OA have found gender differences in anthropometry and that the risk of prevalent hip OA is associated with the magnitude of the difference. If this applies also for patients with knee OA is debated [8, 9].

Primary OA results in local skeletal changes such as cysts, subchondral sclerosis, and osteophytes [8]. Patients with end-stage knee and hip OA have been found to have a phenotype with high bone mineral density (BMD) [9] and high BMI [9-11]. There are also reports indicating that high BMI precede the OA development [10, 11]. If also high BMD precede the disease, or follow as a result of OA, is unknown. If the described phenotype was found also in patients with localized knee OA, this would support that the phenotype itself could be involved in the pathogenesis. Since localized knee OA generally precede the development of OA in all three knee compartments [12-14], localized medial primary knee OA could be used as model for early knee OA. We hypothesized that men and women with primary OA in all three knee compartments and men and women with primary OA only in the medial knee compartment have different anthropometry compared to healthy individuals and that the risk of prevalent OA increases by the magnitude of the difference in the evaluated trait compared to healthy individuals, with similar pattern in women and men. We therefore evaluated if individuals with primary OA in all three knee compartments, as well as individuals with localized medial primary knee OA have a phenotype with higher BMD, higher BMI, proportionally lower lean (muscle) mass and proportionally higher fat.

MATERIAL AND METHODS

We included in this cross-sectional case control study 39 consecutively collected patients with primary OA in all three knee compartments and 73 patients with localized medial

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primary knee OA, during a two year period referred to our hospital for a decision on surgery and there scheduled for total knee arthroplasty or proximal tibial osteotomy. All patients were white and residents of Malmo, Sweden with disabling pain from the affected joint, both at rest and during activity, and typical clinical and radiographic features of knee OA. All had grade III to V of joint degeneration according to the classification of Ahlbäck [15]. The final classification of primary OA in all three knee compartments or localized medial OA for this study was done by the surgeon through cartilage inspection during open surgery. In the theatre the surgeon was aware of the results of the preoperative radiographs. The group classified as having primary OA in all three knee compartments, included patients with visual cartilage destruction that exposed the underlying bone in all the three knee compartments, and those classified as having localised medial OA group with visual cartilage destruction that exposed the underlying bone only in the medial compartment.

The control population was included separately from the cases. The control population has previously been described and reported [16] as a normative sample consisting of community based individuals randomly selected from the official population records (including all Swedes) of Statistics Sweden, a central government authority. The attendance rate was 50% resulting in 122 women and 121 men serving as controls. The patients and controls underwent the same study protocol and had measurements with the same dual energy X-ray absorptiometry (DXA) apparatus. There was no specific matching of controls and patients with knee 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, any food restrictions, diabetes or other diseases, use of any medication (yes/no), and for women also questions regarding menopause and birth control pills as well as if they had ever given birth to any children. Age and lifestyle factors stratified by sex for patients and controls are presented in Table **1**.

Body weight and body height were measured by standard equipment and BMI was calculated as weight/height squared (kg/m^2). BMD (g/cm^2) was measured by DXA (Lunar DPX-L® 1.3z, Lunar Corporation, Madison, WI, USA) in the femoral neck, Wards triangle and trochanter region by a hip scan. After inclusion of the first 24 patients we decided to add a total body scan to the study protocol measuring also total body, spine, leg, and arm BMD as well as total body lean mass and fat mass. Daily calibration of the apparatus was done with a Lunar® phantom. The coefficient of variation (CV) after repositioning 14 individuals was 0.4% for total body BMD, 1.6% for femoral neck BMD, 1.0% for spine BMD, 3.0% for arm and leg BMD, 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). Descriptive data are presented as numbers with proportions (%), means ± standard deviations (SD), or as means with 95% confidence interval (95% CI). We calculated the mean and SD in the control cohort. The Z score presented for the OA patients were derived from these calculations in that the individual Z scores, the number of SDs above or below the age-predicted

Table 1. Age, anthropometry and lifestyle factors in patients with osteoarthritis (OA) in all knee compartments or localized medial OA of the knee and controls.

Parameter	Women				Men			
	OA in All Compartments	Medial OA	Controls	p-Value	OA in All Compartments	Medial OA	Controls	p-Value
	(n=21)	(n=17)	(n=122)		(n=18)	(n=56)	(n=121)	
Age (years)	71.3 ± 8.3	53.4 ± 7.2	63.9 ± 14.4	<0.001 *	72.1 ± 9.9	55.9 ± 9.6	60.6 ± 15.4	<0.001 *
Height (cm)	161.4 ± 8.8	166.3 ± 4.1	163.3 ± 5.2	0.49	176.2 ± 5.5	177.9 ± 5.8	176.9 ± 6.5	0.79
Weight (kg)	78.8 ± 17.5	81.9 ± 11.3	63.9 ± 10.5 *	<0.001 *	86.2 ± 11.1	89.9 ± 12.0	79.4 ± 10.5*	<0.001 *
BMI (kg/m^2)	30.1 ± 5.9	29.6 ± 3.7	23.9 ± 3.8 *	<0.001 *	27.7 ± 3.3	28.2 ± 3.8	25.4 ± 3.0 *	<0.001 *
Blue collar worker	3/19 (16%)	13/17 (76%)	45/107 (42%)	<0.001 *	10/16 (63%)	38/54 (70%)	48/102 (47%)	0.02*
Smoker	2/20 (10%)	7/17 (41%)	18/106 (17%)	<0.001 *	0/16 (0%)	20/56 (36%)	28/101 (28%)	<0.001 *
Uses alcohol	8/12 (67%)	11/17 (65%)	75/94 (80%)	0.30	11/14 (79%)	46/56 (82%)	92/99 (93%)	0.07
Drinks coffee	20/20 /100%)	11/15 (73%)	99/105 (94%)	<0.01 *	14/15 (93%)	33/39 (96%)	85/88 (97%)	0.46
Any food restriction	0/7 (0%)	0/17 (0%)	2/105 (2%)	0.66	0/4 (0%)	0/56 (0%)	2/102 (2%)	0.39
Has given birth	18/20 (90%)	15/17 (88%)	91/102 (89%)	0.76	----	----	----	----
Menopause	18/21 (86%)	11/17 (65%)	83/122 (68%)	0.44	----	----	----	----
Diabetes	2/21 (10%)	1/17 (6%)	1/122 (1%)	0.08	1/18 (6%)	3/56 (5%)	4/121 (3%)	0.78
Other diseases	13/21 (62%)	9/17 (53%)	57/122 (47%)	0.41	10/18 (56%)	20/56 (36%)	58/121 (48%)	0.20
Currentmedication	16/20 (80%)	14/15 (93%)	55/107 (51%)	0.001 *	7/16 (44%)	37/55 (67%)	46/102 (45%)	0.02 *

Presented as mean values (SD) for continuous parameters and numbers with proportion (%) for categorical parameters, evaluations of group differences were done by Student´s t-test between means, Chi-square test or Fisher´s exact test. * statistically significant difference.

mean, were derived by linear regression using the control cohort as reference population. We estimated the association between age and evaluated trait and then calculated the deviation from this regression line for each specific individuals, as to achieve a Z score for each specific individual. Group differences, both in analyses of all individuals as well as in sex specific sub-groups were evaluated by Fisher's exact or chi-square tests for categorical variables and by student´s t-test between means or analysis of covariance (ANCOVA) for normally distributed continuous variables. Age or age and BMI were included as covariates in the ANCOVA analyses. Odds ratios (ORs) with 95% CI were calculated by logistic regression to estimate the risk of having OA with each SD higher total body BMD, higher BMI, higher proportion of fat mass, and each SD lower proportion of lean body mass. We did not address missing data in any way, no subgroup analyses or analyses of interaction were done and there was no specific matching of cases and controls.

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.

RESULTS

There were 21 women (mean ± SD) 71 ± 8 years old (range, 52 - 85 years) and 18 men 72 ± 10 years old (range, 48 - 85 years) with primary OA in all three knee compartments and 73 patients, 17 women (mean ± SD) 53 ± 7 years old (range, 46 - 68 years) and 56 men 56 ± 10 years old (range, 34 - 74 years) with primary localized medial knee OA (Table **1**). All patients were Caucasians and all had disabling pain from the affected joint, both at rest and during activity, and typical clinical and radiographic features of knee OA. One-hundred-twenty-two women 64 ± 14 years old (range, 40 - 87 years) and 121 men 61 ± 15 years (range, 34 - 85 years) served as controls.

Individuals with knee OA had a phenotype with higher BMD than controls (Table **2**), for primary OA in all three knee compartments with a total body BMD Z-score of 0.4 (95% CI, 0.0, 0.9) and for patients with primary localized medial knee OA of 0.4 (95% CI, 0.3, 0.6) (Table **3**).

Individuals with knee OA had a phenotype with higher BMI than controls (Table **2**), for primary OA in all three knee compartments with a Z-score of 1.2 (95% CI, 0.7, 1.6) and for patients with primary localized medial knee OA of 1.1 (95% CI, 0.8, 1.4) (Table **3**).

Individuals with knee OA had a phenotype with proportionally lower total body lean mass than controls (Table **2**), for primary OA in all three knee compartments with a Z-score of -0.6 (95% CI, -1.1, -0.1) and for primary localized medial knee OA of -0.8 (95% CI, -1.3, -0.9) (Table **3**).

Individuals with knee OA had a phenotype with proportionally higher fat mass than controls (Table **2**), for primary OA in all three knee compartments with a Z-score of 0.4 (95% CI, 0.0, 0.8), and for primary localized medial knee OA of 0.9 (95% CI 0.7, 1.1) (Table **3**).

When we adjusted for age and body size (BMI), all group differences between patients with primary OA in all three knee compartments, patients with localized knee OA, and controls remained (Table **2**). This was true also in sex specific analyses except for the proportion of lean and fat mass in women (Table **2**).

Each SD higher BMI was associated with a 2.4 higher probability of having primary OA in all three knee compartments or localized knee OA, each SD higher total body BMD with a 80% higher probability of having primary OA in all three knee compartments and a 2.6 higher probability of having primary localized medial OA and each SD lower proportional lean (muscle) mass with a more than doubled probability of having primary knee OA in all three knee compartments and almost 5 times higher probability of having primary localized medial knee OA (Table **4**).

DISCUSSION

In this study we found that both patients with OA in all knee compartments and with primary localized medial knee OA had higher BMD, higher BMI, higher fat mass and lower lean (muscle) mass than controls. Primary OA in all three knee compartments has previously been associated with a specific anthropometric and musculoskeletal phenotype [4, 6, 9-11,17-19]. The fact that we found the same phenotype in individuals with primary localized medial knee OA, supports, but does not prove, that this specific phenotype could be involved in the pathogenesis of the disorder

Studies suggest an association between OA in the hip and knee and high BMD [6, 9, 20-24]. It has been speculated that a higher 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 [25]. In our study we found higher BMD in both individuals with primary OA in all three knee compartments and primary localized medial knee OA, independently of the high BMI. Furthermore, the association between BMD and primary knee OA was strong, with each SD higher total body BMD associated with an 80% higher risk of having primary OA in all three knee compartments and 2.6 higher risk of having primary localized medial knee OA. That is, high BMD is found already early in the stage of the disease.

This is a cross-sectional study and we can therefore only examine associations. A higher BMD was associated with a higher risk for having both types of knee OA. This is somewhat unexpected, as most studies infer that high BMD is the result of strong muscle forces acting on the bone [26, 27], and we found a low proportion of lean (muscle) mass. In the clinical setting a normal or high BMD is probably beneficial for prosthesis fixation in joint replacement surgery [28]. Since knee OA is associated with this phenotype there seems no need for routine preoperative BMD assessment in joint replacement surgery, a strategy proposed by some [29].

High BMI is another risk factor for knee OA [10, 11, 30] and overweight has been found to precede the disease [31, 32]. High BMI is difficult to interpret since a high BMI could be the result of different bodily characteristics. The high BMI in our patients was the result of high fat mass, not high proportion of lean (muscle) mass or a short statue (Tables **2-4**). The proportionally low muscle mass may indicate a lower capacity to withstand joint trauma and the finding of low lean mass also in individuals with early knee OA suggests that the low muscle mass could be present early

Table 2. Anthropometry and bone mineral density (BMD) in patients with osteoarthritis (OA) in all knee compartments or localized medial OA of the knee and a control cohort.

	Women				
Parameter	**OA in all Compartments**	**Medial OA**	**Controls**	**p-Value (Adjusted for Age)**	**p-Value (Adjusted for Age and BMI)**
Antropometry	**(n=12)**	**(n=14)**	**(n=115)**		
Absolut fat mass (kg)	31.1 (24.0, 38.2)	37.0 (31.8, 42.2)	23.4 (21.9, 24.9)	<0.001 *	0.08
Absolut lean mass (kg)	38.4 (35.9, 47.6)	44.7 (41.5, 48.1)	39.1 (38.4, 39.9)	<0.001 *	0.05 *
Proportion fat mass(%)	41.7 (36.2, 47.1)	44.2 (40.6, 47.8)	35.5 (34.1, 36.9)	<0.001 *	0.66
Proportion lean mass (%)	55.1 (48.4, 61.7)	54.4 (51.3, 57.5)	61.9 (60.6, 63.3)	<0.001 *	0.53
BMD (g/cm^2)	**(n=12)**	**(n=14)**	**(n=115)**		
Total body	1.09 (1.02, 1.16)	1.18 (1.14, 1.22)	1.03 (1.01, 1.05)	<0.001 *	0.01 *
Spine	1.05 (0.97, 1.12)	1.27 (1.18, 1.35)	1.00 (0.97, 1.02)	<0.001 *	<0.01 *
Leg	1.08 (0.99, 1.18)	1.19 (1.14, 1.24)	1.06 (1.03, 1.09)	0.04 *	0.20
Arm	0.81 (0.74, 0.89)	0.89 (0.83, 0.94)	0.76 (0.74, 0.78)	<0.001 *	0.01 *
	(n=21)	(n=17)	(n=120)		
Hip femoral neck	0.81 (0.75, 0.87)	0.94 (0.88, 0.99)	0.83 (0.80, 0.86)	0.47	0.34
Hip WardsTriangle	0.67 (0.60, 0.73)	0.85 (0.78, 0.92)	0.72 (0.69, 0.76)	0.57	0.31
Hip trochanter	0.77 (0.70, 0.85)	0.86 (0.82, 0.91)	0.74 (0.71, 0.76)	0.01 *	0.47
	Men				
Parameter	**OA in all Compartments**	**Medial OA (n=56)**	**Controls (n=121)**	**p-Value (Adjusted for Age)**	**p-Value (Adjusted for Age and BMI)**
Antropometry	**(n=10)**	**(n=52)**	**(n=112)**		
Absolut fat mass (kg)	20.1 (18.3, 21.9)	24.9 (23.1, 26.7)	18.9 (17.7, 20.2)	<0.001 *	<0.01 *
Absolut lean mass (kg)	55.8 (52.1, 59.4)	59.4 (58.0, 60.8)	58.9 (57.5, 60.3)	<0.001 *	<0.001 *
Proportion fat mass(%)	25.3 (23.9, 26.6)	27.9 (26.3, 29.4)	23.4 (22.2, 24.6)	<0.001 *	0.01*
Proportion lean mass (%)	70.1 (67.9, 72.4)	67.7 (66.4, 69.0)	74.3 (73.0, 75.5)	<0.001 *	<0.001 *
BMD (g/cm^2)	**(n=10)**	**(n=52)**	**(n=112)**		
Total body	1.15 (1.06, 1.23)	1.24 (1.22, 1.26)	1.17 (1.15, 1.19)	<0.001 *	0.04 *
Spine	1.09 (0.99, 1.19)	1.18 (1.14, 1.23)	1.11 (1.08, 1.14)	<0.01 *	0.08
Leg	1.23 (1.12, 1.33)	1.36 (1.33, 1.29)	1.29 (1.27, 1.31)	<0.01 *	0.08
Arm	0.94 (0.88, 1.00)	0.98 (0.96, 1.00)	0.95 (0.93, 0.97)	0.26	0.66
	(n=18)	**(n=56)**	**(n=120)**		
Hip femoral neck	0.93 (0.82, 1.03)	1.01 (0.97, 1.05)	0.96 (0.92, 0.99)	0.51	0.81
Hip WardsTriangle	0.77 (0.65, 0.88)	0.92 (0.87, 0.97)	0.82 (0.78, 0.85)	0.03 *	0.47
Hip trochanter	0.92 (0.80, 1.03)	0.99 (0.95, 1.03)	0.91 (0.88, 0.95)	0.09	0.51

Data shown as unadjusted means with 95% CI within brackets; group comparison were made by ANCOVA adjusted for age and for age and body size (BMI) * statistical significant differences.

in the disease. Losing weight, as recommended for knee OA patients by most physicians, may still be good advice, but similar attention should perhaps be paid to building muscle by exercise. Another clinical aspect is that high BMI and fat content are both risk factors for perioperative and postoperative complications [7].

Inferior neuromuscular function has been identified as a risk factor for knee OA [10, 11, 30], as joint protection from trauma may be inadequate [33, 34]. Our data support this finding, showing that each SD lower proportion of lean (muscle) mass was associated with 2 times higher risk of having primary OA in all three knee compartments and almost 5 times higher risk of having primary localized medial knee OA. The findings of high BMD and low proportion of lean (muscle) mass indicate that these patients may have a specific phenotype unrelated to the forces the

Table 3. Z-scores data in patients with osteoarthritis (OA) inall knee compartments and localized medial OA of the knee.

	All		Women		Men	
Parameter	**OA in all Compartments**	**Medial OA**	**OA in all Compartments**	**Medial OA**	**OA in all Compartments**	**Medial OA**
Antropometry	**(n=39)**	**(n=73)**	**(n=21)**	**(n=17)**	**(n=18)**	**(n=56)**
Height	-0.0 (-0.5, 0.4)	0.1 (-0.1, 0.3)	-0.2 (-0.9, 0.6)	0.2 (-0.0, 0.7)	0.1 (-0.3, 0.6)	0.1 (-0.2, 0.3)
Weight	1.1 (0.6, 1.6) *	1.1 (0.8, 1.4) *	1.4 (0.7, 2.2) *	1.7 (1.2, 2.3) *	0.7 (0.2, 1.2) *	0.9 (0.6, 1.2) *
Body mass index	1.17 (0.7, 1.6) *	1.1 (0.8, 1.4) *	1.54 (0.85, 2.23) *	1.58 (1.06, 2.10) *	0.7 (0.2, 1.3) *	1.0 (0.6, 1.3) *
	(n=22)	**(n=66)**	**(n=12)**	**(n=14)**	**(n=10)**	**(n=52)**
Absolut fat mass	0.5 (0.0, 1.0) *	1.1 (0.9, 1.4) *	0.9 (0.0, 1.8) *	1.8 (1.1, 2.4) *	0.0 (-0.3, 0.4)	1.0 (0.8, 1.3) *
Absolut lean mass	-0.1 (-0.5, 0.2)	0.2 (-0.0, 0.5)	-0.1 (-0.7. 0.5)	1.24 (0.5, 2.0) *	-0.2 (-0.6, 0.3)	-1.0 (-1.23, -0.8) *
Proportion fat mass	0.4 (0.0, 0.8) *	0.9 (0.7, 1.1) *	0.7 (0.0, 1.5) *	1.3 (0.8, 1.8) *	0.0 (-0.3, 0.3)	0.8 (0.6, 1.1) *
Proportion lean mass	-0.6 (-1.1, -0.1) *	-0.8 (-1.3, -0.9) *	-0.8 (-1.8, 0.1)	-1.2 (-1.7, -0.8) *	-0.4 (-0.8, 0.0)	-1.0 (-1.3, -0.8) *
Bone Mineral Density	**(n=22)**	**(n=66)**	**(n=12)**	**(n=14)**	**(n=10)**	**(n=52)**
Total body	0.4 (0.0, 0.9) *	0.4 (0.3, 0.6) *	0.9 (0.4, 1.4) *	0.7 (0.4, 1.0) *	-0.1 (-0.9, 0.7)	0.6 (0.4, 0.8) *
Spine	0.3 (-0.1, 0.7)	0.7 (0.4, 1.0) *	0.6 (0.2, 1.1) *	1.4 (0.9, 1.9) *	-0.1 (-0.8, 0.6)	0.5 (0.2, 0.8) *
Leg	0.1 (-0.3, 0.6)	0.4 (0.2, 0.6) *	0.5 (0.0, 1.0)	0.3 (0.0, 0.6)	-0.3 (-1.1, 0.5)	0.4 (0.2, 0.7) *
Arm	0.5 (0.1, 1.0) *	0.3 (0.1, 0.5) *	0.9 (0.3, 1.5) *	0.5 (0.0, 0.9) *	0.1 (0.4, 0.7)	0.2 (0.0, 0.5) *
	(n=39)	**(n=73)**	**(n=21)**	**(n=17)**	**(n=18)**	**(n=56)**
Hip femoral neck	0.1 (-0.2, 0.3)	0.2 (0.0, 0.3) *	0.1 (-0.2, 0.4)	0.20 (0.0, 0.4) *	0.00 (-0.5, 0.5)	0.2 (0.0, 0.4) *
Hip Wards Triangle	0.1 (-0.3, 0.4)	0.4 (0.2, 0.6) *	0.0 (-0.4, 0.4)	0.3 (-0.1, 0.7)	0.1 (-0.5, 0.7)	0.4 (0.2, 0.1) *
Hip trochanter	0.2 (-0.2, 0.6)	0.4 (0.3, 0.6) *	0.4 (-0.1, 0.9)	0.6 (0.3, 0.9) *	0.0 (-0.656, 0.3)	0.3 (0.2, 0.5) *

Data shown as mean with 95% CI within brackets; * statistical significant differences.

Table 4. Odds ratio for having osteoarthritis (OA) in all knee compartments or localized medial OA of the knee.

	All		Women		Men	
Parameter	**OA in all Compartments**	**Medial OA**	**OA in all Compartments**	**Medial OA**	**OA in all Compartments**	**Medial OA**
For Each SD Higher						
BMI	2. 4 (1.7, 3.3) *	2.4 (1.9, 3.2) *	2.9 (1.8, 4.5) *	3.7 (2.1, 6.4) *	1.9 (1.2, 3.1) *	2.2 (1.6, 3.1) *
Total body BMD	1.8 (1.1, 3.0) *	2.6 (1.8, 3.8) *	4.2 (1.8, 9.7) *	3.5 (1.6, 7.8) *	0.9 (0.5, 1.8)	2.3 (1.5, 3.5) *
Absolute fat mass	1.6 (1.03, 2.4) *	2.7 (2.0, 3.7) *	2.1 (1.2, 3.7) *	4.2 (2.2, 8.1) *	1.0 (0.5, 2.0)	2.6 (1.7, 3.8) *
Proportion fat mass	1.6 (0.98, 2.7)	3.2 (2.2, 4.7) *	2.3 (1.1, 4.7) *	5.1 (2.1, 12.1) *	1.0 (0.5, 2.2)	3.0 (1.9, 4.8) *
For Each SD Lower						
Absolute lean mass	1.2 (0.7, 1.9)	0.8 (0.6, 1.02)	1.1 (0.6, 2.0)	0.3 (0.2, 0.7) *	1.2 (0.6, 2.6)	1.0 (0.7, 1.6)
Proportion lean mass	2.1 (1.2, 3.5) *	4.7 (3.0, 7.3) *	2.4 (1.2, 4.8) *	5.3 (2.2, 12.8) *	1.6 (0.7, 3.6)	5.0 (2.8, 9.1) *

BMD = bone mineral density; BMI= body mass index; data presented as means with 95% CI in brackets; 95% CI for odds ratio were calculated by logistic regression; *Statistical significant differences.

muscles exert on the skeleton [26, 27]. We also speculate that the lower lean (muscle) mass we found could be involved in the development of the disease, in that a lower muscle mass could represent a lower capacity to withstand joint trauma, that in addition to a the higher weight, giving a higher joint load, may be especial harmful to the joint.

The limitations include the cross-sectional design and the lack of data regarding the proportion of the invited patients who actually participated in the study. Furthermore, we cannot state that our subgroups reflect a true longitudinal progression of knee OA. Primary medial localized OA and primary knee OA in all three compartments may be completely different conditions as not all localized medial OA will result in knee OA in all three compartments and every knee OA in all three compartments has not been preceded by localized medial OA. It would have been advantageous to have a larger sample size facilitating subgroup analyses of women and men and a more thorough evaluation of life-style. That not all patients were subjected

to a total body scan is another weakness that could influence our inferences. It would also have been advantageous to have data on knee symptoms in the control group, as we could not exclude that there also are individuals with knee degeneration in the control group. The prevalence of reported diseases in the control group may seem high, but as this cohort was randomly selected from the official population records of Statistics Sweden the sample ought to be representative.

CONCLUSION

Individuals with both primary OA in all three knee compartments and primary localized medial knee joint OA have a phenotype with higher BMD, higher BMI, proportionally lower lean body mass, and proportionally higher fat mass than controls. The higher BMI may result in a higher joint load. The lower lean (muscle) mass may result in a lower capacity to withstand joint trauma. The higher BMD may provide a solid base for prosthesis fixation and the higher BMI an elevated risk of perioperative and postoperative complications. Since we could not find any difference between individuals with primary OA in all three knee compartments and primary localized medial primary knee OA in any of the evaluated traits, this supports the hypothesis that that described phenotype is found early in the natural course of the disease.

ABBREVIATIONS

ANCOVA	=	Analysis of covariance
BMD	=	Bone mineral density
BMI	=	Body mass index
CI	=	Confidence interval
CV	=	Coefficient of variation
DXA	=	Dual energy X-ray absorptiometry
OA	=	Osteoarthritis
OR	=	Odds ratios
SD	=	Standard deviation

CONFLICT INTEREST

The authors confirm that this article content has no conflict of interest.

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