

Osteoarthritis of the Distal Interphalangeal and First Carpometacarpal Joints is Associated with High Bone Mass in Women and Small Bone Size and Low Lean Mass in Men

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Abstract: *Objective:* To determine if primary hand osteoarthritis (OA) is associated with abnormal bone and anthropometric traits.

Methods: We used DXA to measure total body bone mineral density (BMD), femoral neck width (bone size) and total body lean and fat mass in 39 subjects with hand OA (primary DIP and/or CMC I) and 164 controls. Data are presented as mean Z-scores or Odds Ratios (OR) with 95% confidence intervals.

Results: Women with hand OA had (compared to controls) higher BMD (0.5(0.1,0.9)) but similar bone size (-0.3(-0.8,0.2)), lean mass (0.3(-0.3,0.9)), fat mass (-0.1(-0.6,0.5)) and BMI (0.0(-0.6,0.6)). Men with hand OA had (compared to controls) similar BMD (-0.1(-0.7,0.6)), smaller bone size (-0.5(-1.1,-0.01)), lower lean mass (-0.6(-1.1,-0.04)), and similar fat mass (-0.2(-0.7,0.4)) and BMI -0.1(-0.6,0.6). In women, each SD higher BMD was associated with an OR of 1.8 (1.03, 3.3) for having hand OA. In men each SD smaller bone size was associated with an OR of 1.8 (1.02, 3.1) and each SD lower proportion of lean body mass with an OR of 1.9 (1.1, 3.3) for having hand OA.

Conclusion: Women with primary DIP finger joint and/or CMC I joint OA have a phenotype with higher BMD while men with the disease have a smaller bone size and lower lean body mass.

Keywords: Anthropometry, BMD, bone mineral density, BMI, bone size, carpometacarpal I joint, CMC I, distal interphalangeal joints, DIP, fingers, osteoarthritis.

INTRODUCTION

Osteoarthritis (OA) affects joint cartilage and the surrounding tissues [1]. Without any apparent causing factors, such as intra-articular fractures or rheumatoid arthritis, the disease is classified as primary. But also primary OA is associated with risk factors, such as old age, female gender, and obesity [2-10]. Heredity and genetics also seem important and associated genes have been identified [11]. Ethnicity may influence primary OA risk, with an increased risk in Afro American women but results are conflicting [2]. The degenerative process may be accelerated by local unfavourable factors such as frequent monotonous high magnitude repeated loads, ligament instability and joint deformity [5]. Therefore it is not surprising to find a high prevalence of OA in weight loaded joints such as the hip and knee [3-8], especially in overweight individuals [9, 10] and in those with low neuromuscular function with impaired joint protective ability [12, 13]. But primary OA is also found in unloaded joints such as in the fingers [14, 15]. This has raised the hypothesis

that primary OA may be the result of different pathophysiological pathways depending on the affected joint and also associated with different musculoskeletal phenotypes [2].

OA affects the skeleton and cysts, subchondral sclerosis and osteophytes are commonly found close to the affected joint [16]. Individuals with OA have also been found to have high bone mineral density (BMD) [17, 18]. A high BMD may result in a dense and stiff skeleton with less load absorptive ability with the result that mechanical load is directed to the cartilage [19, 20]. Also a small skeleton would result in a higher mechanical load since basic mechanics infer that the Pressure = Force/Area (N/m²). High BMD and obesity have been associated with OA of the hip, knee and ankle [2, 6-10, 12, 13, 21-24] and a small skeleton with OA of the ankle [12]. Furthermore, OA of the hip, knee and ankle have all been associated with low lean body mass [9, 10, 12, 13, 21, 25] and as lean mass is similar to muscle mass this may represent inferior muscular ability, which could result in inadequate joint protective capability and susceptibility to joint damage also from minor trauma [26, 27].

Some publications have examined hand OA and associations to a specific anthropometric or musculoskeletal trait most commonly weight and/or body mass index and in a few instances BMD [28-34] but not to our knowledge bone

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size or overall musculoskeletal and anthropometric phenotype.

To gain a more comprehensive description of the overall, musculoskeletal and anthropometric phenotype of patients with hand OA we conducted this hypothesis generating study to determine whether women and men with primary DIP finger joint and/or CMC I joint OA have a phenotype with (1) higher BMD, (2) higher BMI, (3) smaller bone size, (4) lower lean mass and (5) higher fat mass.

MATERIAL AND METHODS

We included 39 patients, 20 women (mean \pm SD) 64 ± 8 years old (range 47-75 years) and 19 men 69 ± 11 years old (range 49-88 years), referred to our department for decision on surgery for primary radiographically verified end-stage DIP finger joint and/or CMC I joint OA. 28 individuals had DIP finger joint OA, 6 CMC I joint OA and 5 both DIP finger joint and CMC I joint OA. All patients were Caucasians from the city of Malmö in southern Sweden and all had disabling pain from the affected joint, both at rest and during activity, and typical clinical and radiographic features of DIP finger joint and/or CMC I joint OA. No exclusion criteria were used. Seventy-four women 63 ± 10 years old (range 47-77 years), and 90 men 68 ± 11 years (range 49-87 years) were included as control subjects [35]. The control subjects were randomly selected from the population register for a report of normative BMD and body composition data in our region [35]. From this cohort we included individuals within the same age range as our patient group. There was no specific matching for each patient with DIP finger joint and/or CMC I joint OA.

All participants underwent measurements with the same dual energy X-ray absorptiometry (DXA) apparatus and answered the same non-validated general questionnaire on lifestyle including questions on occupation (blue-collar or white-collar worker), recreational exercise (yes/no), current physical activity (hours/week), smoking, alcohol and coffee consumption, food restrictions, diabetes or other diseases, use of any medication (yes/no), and for women also on menopause, birth control pills and if they had given birth to any children. The study was approved by the Ethics Committee of Lund University (LU 267-00), and conducted in accordance with the Declaration of Helsinki 1975, as revised 2008. Informed written consent was obtained from all participants prior to study start.

We measured body weight and body height by standard equipment and calculated body mass index (BMI) as weight/height squared (kg/m^2). We measured BMD (g/cm^2) by DXA (Lunar DPX-L[®] 1.3 z, Lunar Corporation, Madison, WI, USA) in total body, spine and arm with a total body scan. Femoral neck width was estimated from an anterior-posterior hip scan as the femoral neck area divided by the scan length, a measurement often used as an estimate of bone size [36, 37]. Total body lean and fat mass were evaluated from the total body scan. Daily calibration of the apparatus was done with a Lunar[®] phantom. The coefficient of variation (CV) after repositioning of 14 individuals was 0.4% for total body BMD, 1.0% for spine BMD, 3.0% for arm BMD, 1.5% for femoral neck width, 1.5% for total body lean mass, and 3.7% for total body fat mass. Studies in

animals, where chemical measurements can be utilized as gold standard, have indicated high accuracy of body composition measurements by DXA [38, 39]

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 \pm SD, or as means with 95% confidence intervals (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 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 (ANCOVA) when adjusting for age and current physical activity (hours per week). Odds ratios (OR) with 95% CI were calculated by logistic regression to estimate differences in prevalence of OA with each standard deviation (SD) change in the evaluated traits. By the included sample size and the known distribution of BMD and bone size values in the controls, a difference in total body BMD of 0.4 standard deviations (SD) in women and 0.5 SD in men and in femoral neck width 0.5 SD in women and 0.5 SD in men would be detected as a statistical significant difference ($p < 0.05$) with a power of 80%.

RESULTS

Age and lifestyle factors stratified by gender in individuals with DIP finger joint and/or CMC I joint OA and controls are presented in Table 1.

Women with DIP finger joint OA and/or CMC I joint had a phenotype with higher BMD with a total body BMD Z-score of 0.5 (95% CI 0.1, 0.9) while men with DIP finger joint and/or CMC I joint OA had normal BMD with a total body BMD Z-score of -0.1 (95% CI -0.7, 0.6) (Table 2).

Both women and men with DIP finger joint and/or CMC I joint OA had a phenotype with normal BMI, for women with a Z-score of 0.0, (95% CI -0.6, 0.6) and for men of -0.1, (95% CI -0.7, 0.6) (Table 2).

Women with DIP finger joint OA and/or CMC I joint had a normal bone size with a femoral neck width Z-score of -0.3 (95% CI -0.8, 0.2) while men had a phenotype with smaller bone size with a femoral neck width Z-score of -0.5 (95% CI -1.1, -0.01) (Table 2).

Women with DIP finger joint OA and/or CMC I joint had normal lean mass, with a total body lean mass Z-score of 0.3 (-0.3, 0.9) while men had a phenotype with lower lean mass, with a total body lean mass Z-score of -0.6 (-1.1, -0.04) (Table 2).

Both women and men with DIP finger joint and/or CMC I joint OA had a phenotype with normal fat mass, for women with a Z-score of -0.1 (-0.6, 0.5) and for men of -0.2 (-0.7, 0.4) (Table 2).

The only lifestyle factor that differed significantly between OA patients and controls in both women and men was current physical activity (both $p < 0.01$) (Table 1). After adjustment for group differences in physical activity, all reported group differences above remained (data not shown).

Table 1. Age and lifestyle in 20 women and 19 men with osteoarthritis (OA) in finger distal interphalangeal (DIP) joint and/or carpometacarpal (CMC) I joint and in 74 women and 90 men in a normative cohort within the same ages. Data are presented as means with standard deviations (SD) within brackets for continuous parameters and numbers with proportions (%) for categorical parameters. Significant group differences are bolded.

	Women			Men		
	Osteoarthritis	Controls	p-Value	Osteoarthritis	Controls	p-Value
Number	20	74	---	19	90	---
Age (years)	63.7 ± 8.2	62.5 ± 10.0	---	68.5 ± 11.4	67.9 ± 11.5	---
Blue collar worker	8/20 (40%)	28/70 (40%)	1.00	8/18 (44%)	25/72 (35%)	0.44
Current recreational exercise	13/20 (65%)	22/70 (31%)	0.007	14/18 (78%)	29/72 (40%)	0.004
Smokes	3/20 (15%)	13/70 (19%)	0.71	8/18 (44%)	18/71 (25%)	0.11
Uses alcohol	18/20 (90%)	53/63 (84 %)	0.72	14/16 (88%)	66/70 (94%)	0.31
Drinks coffee	20/20 (100%)	64/69 (93%)	0.58	17/18 (94%)	61/62 (98%)	0.35
Food Restrictions	0/8 (0%)	5/74 (7%)	0.59	0/3 (0%)	0/72 (0%)	1.00
Given birth to children	18/20 (90%)	60/65 (92%)	0.67	---	---	---
Menopause	3/20 (15%)	11/74 (15%)	1.00	---	---	---
Used birth control pills	4/20 (20%)	15/64 (23%)	0.74	---	---	---
Diabetes	1/20 (5%)	1/74 (1%)	0.38	1/19 (5%)	3/90 (3%)	0.54
Other diseases	10/20 (50%)	37/74 (50%)	1.00	12/19 (63%)	50/90 (56%)	0.54
Current medication	13/20 (65%)	35/70 (50%)	0.24	10/18 (56%)	41/72 (57%)	0.92

Table 2. Anthropometry and bone mineral density (BMD) in 20 women and 19 men with osteoarthritis (OA) in distal interphalangeal (DIP) finger joints and/or first carpometacarpal (CMC) joint and in 74 women and 90 men in a population based control cohort within the same age range. Data are presented as means with 95% confidence intervals within brackets. Significant group differences are bolded.

	Women			Men		
	Osteoarthritis	Controls	p-Value	Osteoarthritis	Controls	p-Value
Number	20	74	---	19	90	---
Age (years)	63.7 (59.9, 67.5)	62.5 (60.2, 64.8)	---	68.5 (63.0, 74.1)	67.9 (65.5, 70.3)	---
Anthropometry						
Height (cm)	165.1 (162.0, 168.1)	163.1 (161.9, 164.4)	0.12	173.4 (169.2, 177.6)	175.7 (174.4, 177.0)	0.18
Weight (kg)	67.5 (60.6, 74.4)	65.4 (63.1, 67.7)	0.44	75.9 (69.6, 82.1)	78.7 (76.5, 80.8)	0.32
Body mass index (kg/m ²)	24.7 (22.6, 26.8)	24.6 (23.7, 25.4)	0.91	25.2 (23.3, 27.2)	25.5 (24.8, 26.1)	0.77
Total body lean mass (kg)	40.1 (37.6, 42.8)	39.1 (38.2, 40.0)	0.26	53.7 (49.9, 57.5)	57.8 (56.3, 59.4)	0.02
Total body fat mass (kg)	24.1 (19.7, 28.5)	24.4 (22.6, 26.2)	0.85	18.3 (14.5, 22.2)	19.5 (18.0, 20.9)	0.52
Bone Mineral Density (g/cm²)						
Total body	1.09 (1.03, 1.14)	1.04 (1.02, 1.07)	0.03	1.15 (1.09, 1.22)	1.16 (1.13, 1.18)	0.88
Spine	1.04 (0.98, 1.11)	1.00 (0.96, 1.03)	0.11	1.07 (0.99, 1.14)	1.10 (1.07, 1.14)	0.36
Arm	0.82 (0.75, 0.88)	0.77 (0.75, 0.79)	0.02	0.93 (0.86, 0.99)	0.93 (0.91, 0.96)	0.82
Bone Size (cm)						
Femoral neck width	3.38 (3.24, 3.52)	3.45 (3.39, 3.52)	0.32	3.77 (3.59, 3.95)	3.95 (3.88, 4.02)	0.04

In women, each SD higher total body BMD was associated with an OR of 1.8 (95% CI 1.03, 3.3) for having DIP finger joint and/or CMC I joint OA (Table 3). In men each SD smaller femoral neck width was associated with an

OR of 1.8 (95% CI 1.02, 3.1) and each SD lower proportion of lean body mass with an OR of 1.9 (95% CI 1.08, 3.3) for having DIP finger joint and/or CMC I joint OA (Table 3).

Table 3. Gender-specific odds ratio (OR) for having distal interphalangeal (DIP) joint OA and/or first carpometacarpal (CMC) joint OA with each higher or lower standard deviation (SD) of body mass index (BMI), bone mineral density (BMD) or bone size evaluated in 94 women and 109 men. Data are presented as means with 95% confidence intervals within brackets. Significant group differences are bolded.

	Women (n=94)	Men (n=109)
For Each SD Higher		
Body mass index	1.02 (0.64, 1.63)	0.93 (0.58, 1.50)
Total body BMD	1.84 (1.03, 3.30)	0.96 (0.59, 1.57)
Absolute fat mass	0.95 (0.58, 1.54)	0.84 (0.50, 1.42)
Proportion body fat	0.82 (0.50, 1.34)	0.95 (0.58, 1.57)
For Each SD Lower		
Femoral neck bone size	1.31 (0.78, 2.22)	1.78 (1.02, 3.10)
Absolute lean body mass	0.95 (0.84, 1.06)	1.09 (1.00, 1.18)
Proportion lean body mass	0.78 (0.50, 1.22)	1.89 (1.08, 3.31)

DISCUSSION

Women with DIP finger joint and/or CMC I joint OA had higher BMD but similar lean mass, fat mass and bone size compared to the general population while men with the disease had lower proportion of lean mass and smaller bone size. As the reported gender specific group differences in BMD, bone size and lean mass remained after adjusting for life style factors and as there were no group differences in anthropometrics, this indicates that lifestyle and anthropometry could not explain the gender specific phenotypes. We have to emphasize that this study was initiated in order to be hypothesis generating. We hence only included patients with severe DIP finger joint and/or CMC I joint OA, patients referred to us for decision on surgery, and with these inclusion criteria, our sample could not be regarded as representative for all patients with DIP finger joint and/or CMC I joint OA in the general population.

Studies suggest an inverse relationship between OA of the hip and osteoporosis [40] and an association between OA of the hip, knee and ankle with high BMD has also been found [8, 12, 13, 29, 41-44]. This has raised the hypothesis that high BMD may result in a denser and stiffer skeleton with lower load absorptive capability, directing more mechanical load to the cartilage, possibly involved in the pathogenesis of primary OA [19]. For hand OA results are conflicting as some studies have found no association to BMD [28], others association to higher BMD [29] and yet others to lower BMD [30, 32]. In our study we found higher BMD only in women with the disease where each SD higher BMD was associated with 84% higher risk of having DIP finger joint and/or CMC I joint OA. Since no such association was found in men with primary DIP finger joint and/or CMC I joint OA, it seems likely that different phenotypes predispose for the disease in women and men.

Since this is a cross-sectional study we cannot state that a higher BMD in women resulted in an increased risk, only that a higher BMD was associated with a higher risk for having DIP finger joint and/or CMC I joint OA. As other studies infer that high BMD is the result of strong muscle forces acting on the bone [45, 46], our finding of a normal

lean mass in women with primary DIP finger joint and/or CMC I joint OA is unexpected. The fact that women with DIP finger joint and/or CMC I joint OA have higher BMD and men normal BMD is of clinical importance. A normal or higher BMD is regarded as beneficial for internal fixation of the skeleton [47, 48] but also for the fixation of prosthesis in finger joint replacement surgery [49]. Some researchers have inferred that an assessment of BMD should be included in the pre-operative routine for internal fixation or joint replacement [47]. Since both arthrodesis and joint replacement are surgical procedures for treatment of DIP finger joint and/or CMC I joint OA the same concerns could be valid for surgery in the fingers. However, our study indicates that low BMD is not a particular concern for this group of patients.

High BMI has been regarded as a general risk factor for primary OA, shown in the hip and knee [9, 10, 21, 25, 50]. For hand OA a recent meta-analysis [34] found a moderate association but advocated more quality research. In a recent study Visser *et al.* [33] found rather strong association between BMI and hand OA (Odds ratio 1.3 per standard deviation higher BMI) while Magnusson *et al.* [31] similarly to our study found no association between current BMI and hand OA. We however found that men with DIP finger joint OA had lower lean body mass than expected (Table 2). Since lean mass predominantly represents muscle mass, this may indicate inferior muscular function and suggests that joint protection from trauma may be inadequate [26, 27]. The association is rather strong giving that each SD lower proportion of lean mass was associated with 89% higher risk of having DIP finger joint and/or CMC I joint OA. Inferior neuromuscular function and low lean mass have also been identified as risk factors for OA of other joints [9, 10, 12, 13, 21, 25]. The finding of normal BMI and normal fat content in patients with DIP finger joint and/or CMC I joint OA may also have clinical implications, as high BMI and adiposity are risk factors for complications during and after surgery. Our study indicates that this is not a particular concern for this group of patients.

The relationship between BMI, body composition and hand OA however needs further exploration. Important leads

may be found in longitudinal rather than cross-sectional assessment of risk traits as evident in the above referenced study by Magnusson *et al.* [31] where they found no association between current BMI and Hand OA but an association between BMI in younger ages and the risk for hand OA later in life. Different measures of fat and lean body composition associated to hand OA including lean mass as found in our study and fat mass, waist hip ratio and visceral and subcutaneous abdominal fat found by Visser *et al.* [33] also need to be further explored.

The finding of a smaller femoral neck width in men but not in women with DIP finger and/or CMC I joint OA also indicates that there could be different pathogenic pathways responsible in women and men during the development of primary DIP finger joint and/or CMC I joint OA. This association is also strong giving that each SD smaller femoral neck width in men was associated with 78% higher probability of having DIP finger joint and/or CMC I joint OA. A smaller bone size has also been found in patients with ankle and foot OA [11] but not in patients with hip OA [13]. A phenotype with a smaller skeleton (and smaller joints) could be of importance as a small skeleton with a small joint area is exposed to a higher pressure by a given strain following the basic mechanical formula $\text{Pressure} = \text{Force}/\text{Area} (\text{N}/\text{m}^2)$.

The limitations of this study include the cross-sectional design and the study should hence be regarded as hypothesis-generating only. We included only patients with end-stage primary DIP finger joint and/or CMC I joint OA, and if the same phenotype is evident in patients with early OA is not known. Prospective observational studies should be conducted, following individuals from young years into old age, with DXA to evaluate if the phenotype precedes the disease. The approach used in this study is however often advocated in research. First a cross-sectional study is done, and if the forwarded hypothesis is verified, future more resource-demanding prospective studies 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 this approach is used by other researchers [36, 37]. It would have been advantageous to have data on bone size of the hand and finger joints and direct measurements of cartilage surface area. This ought to be done in future studies by computed tomography (CT) or magnetic resonance imaging (MRI). It would also have been advantageous with a larger sample facilitating sub-group analyses of pre- and postmenopausal women. It would have been interesting to evaluate the same traits in patients with OA of other joints in the fingers and the hand. The strengths of our study include measurements by the same apparatus in patients and controls that were all living in the same region and the strict definition of finger and/or CMC I joint OA through both clinical and radiological findings.

CONCLUSION

Women with primary DIP finger joint and/or CMC I joint OA have a phenotype with higher BMD and men with the disease a smaller bone size and lower lean body mass, indicating, but not proving, that gender specific pathophysiological pathways may be present. This view is supported in literature, indicating that anthropometric and

musculoskeletal phenotype in patients with primary OA may be joint and gender specific.

ABBREVIATIONS

BMD	=	Bone mineral density
BMI	=	Body mass index
CI	=	Confidence interval
CMC	=	Carpometacarpal
CT	=	Computer tomography
CV	=	Coefficient of variation
DIP	=	Distal interphalangeal
DXA	=	Dual energy X-ray absorptiometry
FN	=	Femoral neck
MRI	=	Magnetic resonance
OA	=	Osteoarthritis
OR	=	Odds ration
SD	=	Standard deviation

CONFLICT OF INTEREST

None of the authors have any conflict of interests. The funding sources had no part in the design or conduction of the study and not in interpretation of data or writing the manuscript.

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