Published in final edited form as:

Ann Rheum Dis. 2012 October ; 71(10): 1698–1701. doi:10.1136/annrheumdis-2012-201659.

The association between erosive hand osteoarthritis and subchondral bone attrition of the knee: the Framingham Osteoarthritis Study

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Abstract

Objective—To examine whether erosive hand osteoarthritis (OA) is associated with knee subchondral bone attrition (SBA) and systemic bone mineral density (BMD).

Methods—Associations of MRI-defined knee SBA with radiographic erosive hand OA were evaluated in 1253 Framingham participants using logistic regression with generalised estimating equations. We also examined the association between the number of erosive OA finger joints and SBA adjusted for the number of non-erosive OA finger joints. Associations between erosive hand OA and femoral neck BMD were explored in 2236 participants with linear regression. Analyses were adjusted for age, sex and body mass index.

Results—Participants with erosive hand OA had increased odds of knee SBA (OR=1.60, 95% CI 1.07 to 2.38). The relation between the number of erosive OA finger joints and SBA became non-significant when adjusted for the number of non-erosive OA joints as a proxy for the burden of disease. There was a non-significant trend towards higher BMD in erosive hand OA compared with participants without hand OA.

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Contributors IKH: Study design, data collection, interpretation of results, drafting the manuscript, final approval of manuscript. DTF, ME and TN: Study design, interpretation of results, critical revision of manuscript, final approval of manuscript. KW: Performing statistical analyses, critical revision of manuscript, final approval of manuscript. PA, AG and FWR: Data collection, critical revision of manuscript, final approval of manuscript

Competing interests F Roemer is a shareholder in Boston Imaging Core Lab (BICL) and a consultant to Merck-Serono and NIH. A Guermazi is a shareholder in BICL and a consultant to Merck-Serono, Novartis, Genzyme, AstraZeneca and Stryker.

Patient consent Obtained.

Ethics approval Ethics approval provided by the Boston University Medical Center Institutional Review Board.

Provenance and peer review Not commissioned; externally peer reviewed.

Conclusions—Erosive hand OA was associated with knee SBA, but the relation might be best explained by a heightened burden of disease. No significant relation of erosive hand OA with BMD was found.

INTRODUCTION

Erosive hand osteoarthritis (OA) is characterised by radiographic central erosions and is most common in older women.¹ The pathogenesis is unclear, and inflammatory and biomechanical factors have been suggested.^{2–4}

Subchondral bone attrition (SBA) in the knee (flattening/depression of the articular bone surface) has a similar appearance as the central finger joint erosions and is believed to be the result of bone remodelling due to biomechanical stress.^{5,6} Hence, the underlying pathogenic processes may be similar in erosive hand OA and knee OA with SBA. It is currently unknown whether only local biomechanical influences are important or whether there exists an underlying susceptibility of bone damage in OA.

One such underlying bone abnormality may be related to systemic bone mineral density (BMD), and we hypothesise that there exist systemic BMD alterations that predispose to the development of central finger joint erosions. The association between BMD and hand OA has varied across previous studies,^{7–10} and the only study on erosive hand OA showed lower BMD in these patients compared with non-erosive hand OA and controls.¹¹

Therefore, the study objectives were first to examine whether erosive hand OA is associated with knee SBA, and second to examine whether BMD, as a proxy for systemic bone alterations, is associated with erosive hand OA.

MATERIAL AND METHODS

Participants

Participants were selected from the Framingham Offspring and Community cohorts. The Offspring cohort included children of participants in the Framingham Heart Study and their spouses,¹² whereas the Community cohort was recruited from the general population of Framingham.¹³ In 2002–2005, 1293 and 1039 participants from the Offspring and Community cohorts, respectively, were examined.

In this study, we included 1253 participants with hand radiographs and knee MRIs (subsample 1) and 2236 participants with hand radiographs and femoral neck BMD measurement (subsample 2).

The Boston University Medical Center Institutional Review Board approved both studies, and written informed consent was obtained.

Hand radiographs

The bilateral 2nd–5th distal interphalangeal (DIP), 2nd–5th proximal interphalangeal (PIP), 1st–5th metacarpophalangeal (MCP), thumb interphalangeal, thumb base and wrist joints (posteroanterior view) were scored by two readers (IKH, PA) according to a modified Kellgren–Lawrence (KL) scale¹ and the Osteoarthritis Research Society International (OARSI) atlas for presence of central erosions.¹⁴ Inter-reader reliability was good (KL grades (KLG): weighted $\kappa=0.76$, erosions: $\kappa=0.79$).¹

Erosions were present in DIP and PIP joints only. Participants were therefore classified as having erosive hand OA if they had ≥ 1 DIP/PIP joint(s) with OA (KLG ≥ 2) and erosion in

the same joint. In order to have comparable groups, we classified participants as having non-erosive hand OA if they had ≥ 1 DIP/PIP joint(s) with OA (KLG ≥ 2) and no erosions. Our referent group constituted those with no OA in DIP/PIP joints.

Knee MRIs

Offspring members with knee pain/aching/stiffness in the past month underwent MRI of the painful knee(s). Both knee MRIs were read when acquired. All Community members had bilateral knee MRIs independent of knee symptoms, but only the right knee was read due to funding limitations.

Sagittal/axial/coronal fat-suppressed intermediate-weighted turbo spin-echo and sagittal T1-weighted spin-echo images were obtained by a phase-array knee coil using a 1.5T system (Siemens, Mountain View, California, USA).¹³

The MRIs were read by two musculoskeletal radiologists (AG and FR) according to the Whole Organ MRI Score (WORMS).¹⁵ SBA was scored in 14 articular knee subregions on a 0–3 scale. We defined ‘any SBA’ as WORMS score ≥ 1 in ≥ 1 knee subregion(s) and counted the number of subregions with SBA. Inter-reader agreement for presence of SBA was moderate ($\kappa=0.45$).

Dual-energy x-ray absorptiometry

Femoral neck BMD (g/cm^2) was assessed using dual-energy x-ray absorptiometry (Lunar Prodigy; Lunar, Madison, Wisconsin, USA) and categorised into age-/sex-specific tertiles.

Statistics

We evaluated the association between erosive hand OA and presence of any SBA using logistic regression with generalised estimating equations. In our first model, we calculated the odds of having any SBA in participants with erosive and non-erosive hand OA, respectively, compared with our referent group (no DIP/PIP OA). In our second model, we examined the association between the number of erosive DIP/PIP joints and presence of any SBA, adjusting for the number of DIP/PIP joints with non-erosive OA in the same model, as a proxy for the burden of radiographic hand OA.

We also evaluated the association between erosive hand OA and the number of knee subregions with SBA in each knee using Poisson regression with generalised estimating equations (the same two models as described above). All analyses were repeated with the second definition of SBA (grade ≥ 2).

Least-squares mean BMD was calculated for participants with erosive and non-erosive hand OA and the referent group. We examined whether BMD (as continuous variable or age-/sex-specific tertiles) was associated with the presence of hand OA (both erosive and non-erosive) as our dependent variable using logistic regression. In order to explore potential differences between erosive and non-erosive hand OA, we also examined the relation between presence of erosive and non-erosive OA, respectively, and BMD (as the continuous dependent variable) using linear regression (one model). We repeated the analyses with the number of erosive and non-erosive DIP/PIP joints as independent variables (one model).

All analyses were adjusted for age, sex and body mass index. We also repeated the analyses with exclusion of those with isolated MCP, thumb base and/or wrist OA from the referent group.

RESULTS

Participants with erosive hand OA were more severely affected than participants with non-erosive hand OA with a higher number of OA finger joints (table 1). Erosive OA participants were older than non-erosive OA participants and the referent group (mean (SD) age 71.9 (8.3), 66.6 (8.3) and 60.5 (7.6) years, respectively) and were more often women (78.7%, 58.8% and 55.5%, respectively).

Associations between erosive hand OA and knee SBA

Participants with erosive and non-erosive hand OA had significantly higher odds of knee SBA compared with those without DIP/PIP OA, and the strongest association was observed for erosive hand OA (table 2; Model 1). When we adjusted for the number of non-erosive OA joints, there was no significant association between the number of erosive OA joints and knee SBA (table 2; Model 2). Hence, the stronger association between erosive hand OA and knee SBA was confounded by the higher amount of radiographic OA in those with erosive disease. Poisson regression analyses showed similar results (table 2).

Isolated MCP, thumb base and/or wrist OA were present in 224 of 658 (34.0%) subjects in our referent group. The sensitivity analyses (including n=434 without OA in any joint in the referent group) yielded essentially the same results. Analyses in which SBA presence was defined as WORMS score ≥ 2 did not alter the associations noted (data not shown).

Associations between erosive hand OA and BMD

Adjusted least-squares mean (SD) BMD was 0.93 (0.02), 0.93 (0.01) and 0.92 (0.01) in participants with erosive, non-erosive hand OA and the referent group, respectively. Higher BMD (continuous independent variable) was associated with higher odds of any hand OA (OR=1.90, 95% CI 0.91 to 3.98), although not statistically significant. However, the odds of any OA were significantly higher in those with the highest BMD tertile (OR=1.37, 95% CI 1.08 to 1.73) compared with those in the lowest tertile.

We found higher adjusted BMD in participants with erosive and non-erosive hand OA compared with the referent group, but the associations were non-significant (table 3).

Sensitivity analyses with participants without any OA in the referent group (n=863) did not appreciably change the results (data not shown).

DISCUSSION

Participants with erosive hand OA had the highest likelihood of knee SBA. However, the number of erosive joints was not associated with knee SBA after adjustment for the number of non-erosive OA finger joints as a proxy for the burden of disease. On the other hand, the number of non-erosive OA finger joints was significantly associated with knee SBA, suggesting that the burden of disease was driving the apparent association between erosive hand OA and knee SBA.

Although SBA may occur in joints without radiographic knee OA, it is most common in severe OA.¹⁶ Hence, our results support an association between hand and knee OA^{17–19} and perhaps a stronger association between severe disease in both joint areas, but they do not support a generalised susceptibility of erosions and attrition per se. Hence, we believe that finger joint erosions are more likely related to local biomechanical factors, as observed for knee SBA.⁵⁶ These results are also in support of previous longitudinal studies of erosive hand OA.^{3–4}

Femoral neck BMD was similar in participants with non-erosive and erosive hand OA in contrast to a previous small case-control study.¹¹ The conflicting results may be due to different study designs, selection bias in case-control studies and sample size. Although not investigated in this study, erosive hand OA may rather be related to local bone changes, which are not captured by systemic BMD measurements.

Our study is limited by BMD measurement of femoral neck only, MRI of painful knees for some participants and moderate reliability for SBA assessments.

Taken together, our results support a generalised OA susceptibility, while development of erosive hand OA may be a reflection of a mechanical load through the finger joints associated with more severe disease, similar to knee SBA.

Acknowledgments

The authors thank the participants of the Framingham Offspring and Community Cohorts for helping them to perform the study.

Funding Supported by grants from the National Institutes of Health (AG18393, AR47785, AR055127), the Swedish Research Council, the Faculty of Medicine at Lund University, the OARSI scholarship and South-Eastern Norway Regional Health Authority.

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Table 1

Demographic and clinical variables of the study participants

	Subsample 1 (n=1253)	Subsample 2 (n=2236)
Women, n (%)	740 (59.1)	1281 (57.3)
Age, mean (SD) years	63.9 (8.8)	64.5 (9.0)
Body mass index, mean (SD) kg/m ²	29.0 (5.8)	28.6 (5.5)
Knee OA (KLG 2) (n=1695 knees), n (%)	392 (23.1)	NA
Erosive DIP/PIP OA [*] n (%)	134 (10.7)	221 (9.9)
-Number of erosive OA joints, median (IQR) (0–16)	3 (1–6)	3 (1–5)
-Number of non-erosive OA joints, median (IQR) (0–16)	5 (3–8)	5 (3–8)
Non-erosive DIP/PIP OA [†] n (%)	461 (36.8)	761 (34.0)
-Number of non-erosive OA joints, median (IQR) (0–16)	2 (1–4)	2 (1–5)
Any subchondral bone attrition (n=1709 knees) [‡] n (%)	646 (37.8)	NA
-Number of affected knee subregions, median (IQR) (0–14)	2 (1–4)	
Femoral neck bone mineral density, mean (SD) g/cm ²	NA	0.91 (0.14)

^{*} One or more DIP and/or PIP joint(s) with OA (KLG 2) and erosion in the same joint.

[†] One or more DIP and/or PIP joint(s) with OA and no erosions.

[‡] One or more knee subregions with subchondral bone attrition grade 1.

DIP, distal interphalangeal; KLG, Kellgren–Lawrence grade; NA, not applicable; OA, osteoarthritis; PIP, proximal interphalangeal.

Table 2

The association between erosive and non-erosive hand osteoarthritis (OA) and the presence of subchondral bone attrition (SBA) of the knee (logistic regression) and the number of knee subregions with SBA (Poisson regression)

	Presence of any SBA (logistic regression)		Number of subregions within a knee with SBA (Poisson regression)	
	Crude OR (95% CI)	Adjusted OR* (95% CI)	Crude RR (95% CI)	Adjusted RR* (95% CI)
Model 1 (comparison of three groups of participants)				
No DIP/PIP OA (ref)	1.00	1.00	1.00	1.00
Erosive OA	2.19 (1.52, 3.14)	1.60 (1.07, 2.38)	2.43 (1.84, 3.22)	1.71 (1.25, 2.32)
Non-erosive OA	1.77 (1.40, 2.24)	1.44 (1.11, 1.86)	1.60 (1.30, 1.96)	1.25 (1.00, 1.57)
Model 2 (number of affected DIP/PIP joints) (all participants, one model)				
Erosive joints	1.02 (0.95, 1.10)	1.00 (0.92, 1.08)	1.06 (1.00, 1.12)	1.03 (0.98, 1.09)
Non-erosive joints	1.10 (1.06, 1.15)	1.07 (1.02, 1.12)	1.08 (1.05, 1.11)	1.04 (1.01, 1.07)

* Adjusted for age, sex and BMI.

BMI, body mass index; DIP, distal interphalangeal; PIP, proximal interphalangeal; RR, rate ratio.

Table 3

The association between erosive and non-erosive hand osteoarthritis (OA) and bone mineral density of the femoral neck (linear regression analyses)

	Crude B (95% CI)	Adjusted B (95% CI)*
Model 1 (comparison of three groups of participants)		
No DIP/PIP OA (ref)	0.00	0.00
Erosive OA	-0.06 (-0.08, -0.03)	0.01 (-0.01, 0.03)
Non-erosive OA	-0.02 (-0.03, -0.01)	0.01 (-0.001, 0.02)
Model 2 (number of affected DIP/PIP joints) (all participants, one model)		
Erosive joints	-0.007 (-0.011, -0.003)	-0.001 (-0.005, 0.003)
Non-erosive joints	-0.005 (-0.007, -0.003)	0.002 (-0.001, 0.004)

* Adjusted for age, sex and BMI.

B, regression coefficient (unstandardised β); BMI, body mass index; DIP, distal interphalangeal; PIP, proximal interphalangeal.