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Osteoarthritis and Cartilage

Bone marrow lesions and collateral ligament lesions are associated in interphalangeal joints with osteoarthritis: The Hand OSTeoArthritis in Secondary care cohort

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SUMMARY

Objectives: To investigate whether bone activity adjacent to collateral ligaments is present and results in collateral ligament lesions (CLLs) of the proximal and distal interphalangeal joints in patients with hand osteoarthritis (OA), and vice versa.
Methods: We used data measured on baseline, year two and year four from the Hand OSTeoArthritis in Secondary care cohort. MR images of the right hand were scored at the radial and ulnar 1/3rd of each joint ("=joint side") for bone marrow lesions (BMLs) and CLLs (=non-visible or non-continuous ligament). Odds ratios (ORs) with 95% confidence intervals were used to quantify longitudinal associations at the same joint side, adjusted for patient effect.
Results: In 261 patients (mean age 61 years, 84% women), BMLs were present at baseline in 113/4169 joint sides (3%), and at year four in 89/3356 (3%). Any CLL was present at baseline in 500/4169 joint sides (12%), and at year four in 559/3356 (17%). The presence of BMLs and CLL was cross-sectionally associated.

In baseline joint sides without CLLs, BMLs were positively associated with CLL development in the corresponding joint side at year two and four (OR 3.7 (1.5;9.1) and 4.9 (2.3;10.7), respectively), compared with no BMLs.

In baseline joint sides without BMLs, CLLs were positively associated with BMLs at the same side at year two and four (9.2 (3.9;22.1) and 11.0 (5.8;20.9) respectively), compared with no CLLs.
Conclusions: BMLs are rare yet associated with CLLs that are more common, both cross-sectionally and longitudinally, both adding to the OA process.

Introduction

Osteoarthritis (OA) is a musculoskeletal disorder that affected almost 600 million persons worldwide in 2020. Its prevalence is expected to have risen by more than 48% in 2050.[1] In that year, 289 million patients are expected to have hand OA, which is one of the most prevalent forms of OA. Hand OA burdens patients and health care resources as it has a significant impact on hand pain, participation in society, and quality of life.[2–5] The etiology of hand OA is not fully known. Therefore, no disease-modifying drugs exist. However, mechanical factors, through micro- and macro trauma, are considered triggers of the osteoarthritic process.[6] The degree of OA-related damage has been hypothesized to be related to the amount of mechanical stress on the finger ligaments due to work or physical tasks an individual performs and the duration of this work.[7,8] The collateral ligaments provide stability to the joint and can rupture in case of trauma or excessive force.[9] The degree of OA-related damage has been hypothesized to be related to the degree of mechanical stress on the finger ligaments during locomotion.[10] An earlier study

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in 20 patients with early hand OA has reported that these ligaments are affected by hand OA in the form of thickening on magnetic resonance imaging (MRI), and in some cases even disruption, suggesting involvement of the ligaments in the hand OA process.[10] At the insertion sites of these ligaments, bone marrow lesions (BMLs) can be seen on MRI, which are lesions within the trabecular bone with signal characteristics consistent with increased water content.[10] Although it is not precisely clear what BMLs represent in osteoarthritic finger joints, since histological studies are lacking, BMLs in the finger joint as a whole are associated with local pain and radiographic progression.[11–13]

Based on MRI data, it has been suggested that BMLs of the interphalangeal joints can originate from the entheses, which are the connective tissues between the collateral ligaments and the bone.[10,14] Enthesitis or inflammatory bone activity around the ligament insertion site might therefore influence lesions of collateral ligaments. Alternatively, collateral ligament lesions lead to joint instability, resulting in abnormal joint loading and increased stress on the joint,[15] possibly leading to BMLs at the sites of bone-on-bone contact (known as “kissing contusion” or “kissing edema”).[16,17] Whether BMLs and collateral ligament lesions are associated is not known, while this knowledge is crucial for further understanding of the underlying mechanisms of the development of hand OA. Also, this knowledge could provide prognostic value, help develop new treatment options, and might help to prevent malalignment of the finger joints (a possible consequence of collateral ligament lesions).

Therefore, we aimed to investigate 1) to what extent bone activity (in the form of BMLs) adjacent to collateral ligaments and collateral ligament lesions of the proximal interphalangeal (PIP) and distal Interphalangeal (DIP) finger joints are present over time on MRI in patients with hand OA and 2) the longitudinal association between these BMLs and collateral ligament lesions.

Materials and methods

Study population

Data from the Hand OSTeoArthritis in Secondary care were used, an ongoing prospective cohort study investigating primary hand OA defined by the treating rheumatologist.[18] Patients with secondary hand OA (e.g. due to an intra-articular fracture) were excluded.[18] Variables were measured at baseline, year two and year four of follow-up (due to feasibility, not more often), including in the present study patients, who had an MRI of the right hand at least at baseline and year two. The right hand was chosen for MRI as this is the dominant hand for most persons. Written informed consent was obtained from all participants. The study was approved by the Leiden University Medical Center Ethical Committee (number P09.004).

Patient characteristics were collected with questionnaires. Self-reported hand pain and function were assessed with the Australian Canadian Hand OA Index (range for pain: 0–20, range for function: 0–36).[19] Comorbid diseases were recorded with a modified Charlson index (including osteoporosis, range 0–18).[20] Fulfillment of the American College of Rheumatology criteria for hand OA was defined based on questionnaire and physical examination by trained research nurses. Baseline dorsal-volar radiographs of the hands were scored according to the Kellgren-Lawrence (KL) system (DIP, PIP, first interphalangeal, metacarpophalangeal (MCP) and first carpometacarpal (CMC)), and according to the Verbruggen-Veys (VV) system (DIP and PIP),[18,21] all with good reliability.[18] Erosive hand OA was defined as at least one interphalangeal joint in VV anatomical phases E (“erosive”) or R (“remodelling”).[22,23]

MRI

From January 2011 to August 2015, MRI of the fingers of the right hand was performed as part of the baseline examination, with a repeated MRI after two and four years. The last follow-up MRI was completed in September 2019. Coronal and axial T1-weighted and T2-weighted fat-suppressed images were acquired with a slice thickness of 2–3 mm) (ONI-MSK-Extreme 1.5 Tesla (T) extremity MR imaging scanner (GE, Wisconsin, USA) (protocol in Supplementary File 1).

MRI scoring procedure

BMLs and collateral ligament lesions were scored on MRI. Scoring was done separately for the radial and ulnar side of each PIP and each DIP joint (n=16 joint sides per patient). BMLs were scored using the definition from the Hand Osteoarthritis Magnetic Resonance Scoring System (HOAMRIS) scoring method (“A lesion within the trabecular bone with signal characteristics consistent with increased water content (i.e., high signal intensity on short tau inversion recovery (STIR) images or T2w fat suppression images) and with ill-defined margins”).[24] Scores were as follows: 0 = Normal; 1 = 1–33% of bone volume; 2 = 34–66% of bone volume; 3 = Severe 67–100% of bone volume. BMLs were scored separately for the radial, ulnar and middle one-third of the joint (0–3 scale) and were regarded “adjacent to the collateral ligament” if situated in the ulnar or radial one-third of the joint BMLs not adjacent to a collateral ligament were excluded from the regression analyses, and radial and ulnar BMLs were dichotomized. An example of a joint with a BML on MRI is shown in Fig. 1.

Collateral ligament lesions were scored according to the Oslo scoring method,[25] which assigns the following scores: 0 = visible, continuous collateral ligament on T1w FS images, 1 = non-visible or non-continuous collateral ligament. The ulnar and radial collateral ligaments were scored separately. Examples of intact collateral ligaments and collateral ligament lesions on MRI are shown in Fig. 2. In case of doubt between two values, the lowest score was chosen.

Cross-sectional reliability

MRI scoring was performed by one dedicated, well-trained reader (S. Terpstra), supervised by a musculoskeletal radiologist (M. Reijnierse) with more than 20 years of experience. Scoring was performed blinded for demographic and clinical data, and in random time order, with knowledge of the current study aim. In order to evaluate intra-reader reliability, a random sample of 25 MRIs was rescored for BMLs and collateral ligament lesions after three weeks by the same reader (ST), blinded to the scores of the first assessment. To evaluate inter-reader reliability, a random sample of 25 MRIs was scored by two observers (Wendy Damman, MD PhD and ST, MD). Single and average measure intraclass correlation coefficient (mixed-effect models, absolute agreement) were calculated to assess intra-reader and inter-reader reliability, respectively.[26] Kappa scores for BMLs and collateral ligament lesions (intra-reader reliability and inter-reader reliability) exceeded 0.85. Details on these scores can be found in Supplementary File 2.

Statistical analysis

For none of the variables the number of missing values exceeded 5% per variable, except for “hand OA symptom duration” (6%). For analyses on patient level, scores of the eight PIP and DIP joints were summated (range 0–8 or 0–24). We calculated odds ratios (ORs) (95% confidence interval (CI) for the association between BML adjacent to collateral ligament (yes/no) and collateral ligament lesions at the same joint side (yes/no) at baseline and at follow-up. Generalized estimating equations (GEE) were used to quantify the association between BML adjacent to collateral ligament at baseline (yes/no) and collateral ligament lesion

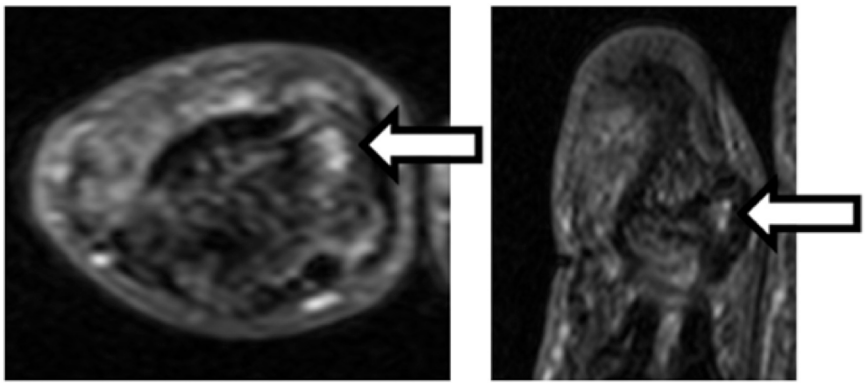

Fig. 1 Osteoarthritis and Cartilage

An example of a bone marrow lesion, adjacent to the collateral ligament (transversal and coronal plane, same joint) (DIP 2 joint, T2 setting).

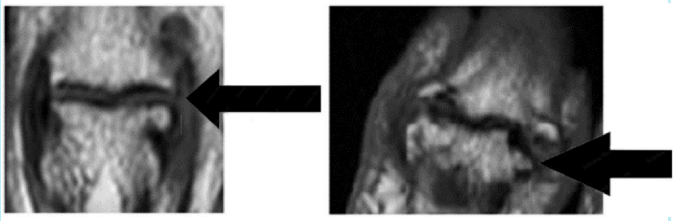

Fig. 2 Osteoarthritis and Cartilage

An example of an intact collateral ligament (left) and a collateral ligament lesion (right), as the ligament is absent on both sides (DIP 2 joint, T1 setting).

(yes/no) at two and four years of follow-up, and between collateral ligament lesion at baseline and BML adjacent to collateral ligament at two and four years, adjusted for patient effect. These GEEs were estimated crude, as well as adjusted for potential confounders (age, sex and BMI) if group sizes allowed (= at least ten events per predictor variable).[27] Full specification for all models, including coefficients and adjustment for KL and erosive hand OA is available in Supplementary File 2. Patients with complete follow-up data were compared with patients without follow-up data regarding potential confounders as well as the presence of any BMLs and collateral ligament lesions. R Studio Version 2022.02.3 was used for all analyses.

Results

261 patients had an MRI at baseline and year two and were included in our study. Baseline characteristics of the study population are shown in Table I. Of these patients, 213 (81%) had data on year four, as 48 patients (19%) were lost to follow-up/refused follow-up. Patients without data on year four (n=50, 19%) were older at baseline (mean age 62.6 versus 60.0) than those who completed follow-up. At baseline, 4169 joint sides (of 2088 joints) were scored and were therefore in our GEE analyses, as seven joint sides could not be scored due to technical reasons. Of these 4169 joint sides, we were able to score and analyze 4149 joint sides at year two and 3356 at year four.

Any BML adjacent to a collateral ligament of a PIP or DIP joint was present in 63 patients at baseline (24%), who had a median (interquartile range) number of affected joint sides of 1 (1;2). Any collateral ligament lesion was present in 129 patients (49%), with a median of 4 (2;6) joint sides affected. A BML at the same joint side as a collateral ligament lesion was present in 39 patients (15%). Baseline abnormalities on MRI on patient level as well as on joint level are reported in Table II. For BMLs as well as collateral ligament lesions, the DIP joints were more frequently affected than the PIP joints (Table III). The number of joint sides affected by BML and collateral ligament lesions for each joint side (ulnar/radial, each PIP and DIP joint) is shown in Supplementary File 3.

On joint side level (ulnar and radial for each joint PIP2 – DIP 5), 113/4169 joint sides (3%) were affected by BMLs at baseline. This proportion was similar at year four (89/3356 (3%)). Presence of these BMLs fluctuated over time, as only 48/133 (36%) of joint sides with a BML at baseline were also affected at year two (Table IV). Any collateral ligament lesion was present in 129 patients at baseline (49%), for whom 500/4169 joint sides (12%) were affected. Collateral ligament lesions remained present once there (Table IV), and increased in prevalence over time, with 559/3356 (17%) of joint sides affected at year four. A combination of a BML and a collateral ligament lesion was present in 64/4169 joint sides (2%) at baseline and 62/3356 (2%) at year four. BMLs were cross-sectionally associated with collateral ligament lesions at baseline (OR adjusted for patient effect 7.4 (CI 4.5;12.0), year two (OR 7.7 (4.5;13.2)) and at year four (7.0 (4.2;11.7)). Adjustment for patient effect, age, sex and BMI did not materially affect these estimates (Table V), as well as adjustment for erosive hand OA and KL grade (Supplementary File 2).

In joint sides with no collateral ligament lesion at baseline (n=3669), BML at baseline had an increased risk for a collateral ligament lesion at year two and year four (ORs 3.7 (CI 1.5;9.0) and 4.9 (2.0;10.8), respectively) compared with those without a BML at baseline (adjusted for patient effect, Table VI). Adjustment for age, sex and BMI was not done due to insufficient group size.

In joint sides with no BML at baseline (n=4056), collateral ligament lesion at baseline had an increased risk for BML at year two and year four (OR of 9.2 (CI: 3.9;22.1) and 11.0 (5.8;20.9), respectively), compared with those without a collateral ligament lesion at baseline (adjusted for patient effect) (Table VI).

There was a graded relationship between BMLs and collateral ligament lesions. Among joint sides with no collateral ligament lesion at baseline, a BML at one follow-up moment (=baseline, year two or year four) had an OR of 3.8 for collateral ligament lesion at year four compared with no BML. A BML at two or three follow-up moments had an even more increased risk for collateral ligament

General patient characteristics	
Age, years	60.5 (8.2)
Sex, women, *n (%)*	218 (84%)
BMI, kg/m^2	27.5 (4.9)
Any comorbidity present, *n (%)*	133 (53%)
Hand OA characteristics	
Fulfilling ACR hand OA criteria, *n (%)*	238 (91%)
Symptom duration, years*	5.7 (2.3;12.9)
AUSCAN hand pain(0–20)	9.4 (4.2)
AUSCAN hand function(0–36)	15.7 (8.1)
KL summated score (0–120)†	16 (8;27)
Erosive hand OA, *n (%)*‡	80 (31%)

Numbers represent mean (SD) unless otherwise specified.
Abbreviations: SD = standard deviation, IQR = interquartile range, BMI = Body Mass Index, ACR = American College of Rheumatology, AUSCAN = Australian Canadian Osteoarthritis Hand Index, OA = osteoarthritis, KL = Kellgren Lawrence.
* Median (IQR).
† Scored on conventional dorsal-volar radiographs according to the KL system with good reliability.[15,18]
‡ Defined as a hand joint in Verbruggen-Veys (VV) anatomical phases E ("erosive") or R ("remodelling").[18]

Table I

Osteoarthritis and Cartilage

Characteristics of the HOSTAS study population (n=261).

lesion compared with no BML (OR 9.9 (CI 4.2;23.6)) (Supplementary File 4). Similarly, among joint sides with no BML at baseline, a collateral ligament lesion at one or two follow-up moments had an increased risk for BML at year four, compared with no collateral ligament lesion (OR 10.2 (CI 4.2;25.1)). A collateral ligament lesion at all three follow-up moments had an even more increased risk for a BML at the same joint side at year four (OR adjusted for patient effect: 16.0 (7.6;33.6)).

Discussion

We investigated to what extent BMLs adjacent to the collateral ligaments and collateral ligament lesions of the finger joints are present over time in patients with hand OA, and the longitudinal association between these. We found that BMLs were rare and fluctuated in presence over time, while collateral ligament lesions were more common and remained present during follow-up. A consistent, strong association between both types of lesions was found over time.

BMLs were less frequent than collateral ligament lesions, which may be partially explained by the fluctuation of the presence of BMLs over time (only 36% of joint sides with BML at baseline were also affected at year two), while collateral ligament lesions remain present once there. It is not known for how long BMLs generally persists in hand OA. However, in patients with knee OA more than 48% of BMLs on MRI showed a change in volume > 50% at either six or twelve weeks of follow-up.[28] This is in line with our study on hand OA, as BMLs often disappeared over time. Also, it is therefore likely that between follow-up moments, joints have been affected by BMLs, which we did not detect, leading to an underestimation of the presence of BMLs.

We hypothesized that bone activity adjacent to collateral ligament, visualized as BMLs at that side, would associate with future collateral ligament lesions, which was indeed the case. Subchondral bone activity in the finger joints has been described to result from the entheses of the collateral ligaments, which could result in damage typical for hand OA.[10] BMLs in finger joints have earlier been shown in longitudinal studies to result in radiographic structural damage, as joint space narrowing and central erosions.[29] Our alternative hypothesis that collateral ligament lesions at baseline would be associated with future BMLs in our study was also met. As aforementioned, this could be due to collateral ligament lesions leading to BMLs at the sites of bone-on-bone contact ("kissing edema"). However, literature on this topic for hand OA was not found. Another explanation could be that ligament injuries impact the blood supply to the joint, resulting in changes in the vascular environment.[30] These changes in the vascular environment are associated with the occurrence of BMLs in knee OA.[31] However, whether these processes also play a role in hand OA has not been investigated.

Our study is one of the first to quantify BMLs and collateral ligament lesions in PIP and DIP joints of patients with hand OA. An earlier cross-sectional study investigated 85 patients with symptomatic hand OA (mean age 69, 91% women, mean BMI 26.0).[32] An 1.0 T extremity MRI unit and the same scoring definitions were used as in our study. That study found that out of all 678 PIP/DIP joints, 65 (10%) had a BML at the collateral ligament insertion side on MRI, and 400 out of 674 (59%) had a collateral ligament lesion. In our study, BMLs at the collateral ligament insertion side were less common (80/2.085 joints (4%) at baseline), and collateral ligament lesions were far less common (274/2.085 joints (13%) had any collateral ligament lesion at baseline). An explanation could be a higher age and therefore longer disease duration in the Norwegian study (mean age 69 versus 61). Another cross-sectional study investigated BMLs and collateral ligament lesions in one single PIP or DIP joint of 30 patients with symptomatic hand OA (17 DIPs and 13 PIPs in total).[33] Using a 1.5 T scanner and a 23-mm diameter surface coil with T2 images, and gadolinium diethylenetriaminepentaacetic acid (DTPA)-enhanced images, BMLs adjacent to collateral ligaments were found for 9/30 joints (30%), and disruptions of a collateral ligament for 14 joints (47%). This is more frequent than in our study (8% and 13% of joints at baseline, respectively). However, due to small group sizes in this study and a lack of information on how the selection of single joints per patient was done, it is difficult to interpret this difference.

The course of BMLs adjacent to collateral ligaments and collateral ligament lesion development over time has not been reported in earlier studies, so comparison with our data cannot be made.

Several aspects of our study suggest that there is a causal relation between BMLs and the development of collateral ligament lesions and of collateral ligament lesions with the development of BMLs. Whether an association is causal is difficult to prove. However, our findings fulfill several criteria for causality.[34] First, there is

	Number of patients with any joint affected (n=261)	Number of joints affected, joint level (n=2085)	Median of summated score, in patients with >0 joints affected (IQR)
Any BML, anywhere in the joint (0–8)	99 (40%)	168 (8%)	1 (1;2)
Any BML, middle of joint* (0–8)	70 (28%)	138 (7%)	1 (1;3)
BML adjacent to collateral ligament			
Any BML, radial or ulnar (0–16)	63 (24%)	80 (4%)	1 (1;2)
Radial, any (0–8)	46 (17%)	52 (3%)	1 (1;2)
Radial: grade 1 (0–8)	37 (14%)	43 (2%)	1 (1;1)
Radial: grade 2 (0–8)	12 (5%)	12 (1%)	1 (1;1)
Radial: grade 3 (0–8)	0 (0%)	0 (0%)	n/a (insufficient data)
Ulnar (0–8)	46 (17%)	59 (3%)	1 (1;2)
Ulnar: grade 1 (0–8)	38 (14%)	49 (2%)	1 (1;1)
Ulnar: grade 2 (0–8)	14 (5%)	9 (0%)	1 (1;1)
Ulnar: grade 3 (0–8)	3 (1%)	3 (0%)	1 (1;1)
Collateral ligament lesion			
Radial or ulnar (0–16)	129 (49%)	274 (13%)	4 (2;6)
Radial (0–8)	112 (43%)	250 (12%)	2 (1;3)
Ulnar (0–8)	117 (45%)	251 (12%)	2 (1;3)
BML adjacent to a collateral ligament lesion	39 (15%)	63 (3%)	1 (1;2)

Numbers represent n (%).
Adjacent to collateral ligament = in the ulnar or radial one-third of the joint.
Abbreviations: IQR = Interquartile range, BML = bone marrow lesion.
* Middle of joint = in the middle one-third of the joint space, assessed from radial to ulnar.

Table II Osteoarthritis and Cartilage

Baseline abnormalities scored on magnetic resonance imaging on patient level and on joint level.

	Bone marrow lesion	Bone marrow lesion, adjacent to collateral ligament*	Collateral ligament lesion, ulnar or radial
DIP 2	48 (18%)	27 (10%)	86 (33%)
DIP 3	27 (10%)	13 (5%)	58 (22%)
DIP 4	15 (6%)	9 (3%)	29 (11%)
DIP 5	13 (5%)	6 (2%)	55 (21%)
PIP 2	24 (10%)	13 (5%)	8 (3%)
PIP 3	20 (8%)	5 (2%)	10 (4%)
PIP 4	11 (4%)	4 (2%)	14 (5%)
PIP 5	10 (4%)	3 (1%)	15 (6%)

Numbers represent number (%).
* Adjacent to collateral ligament = in the ulnar or radial one-third of the joint space.

Table III Osteoarthritis and Cartilage

Baseline abnormalities for each DIP and PIP joint (n=261 patients).

Baseline, number of joint sides (%) (total = 4169)		Year two, number of joint sides (%) (total = 4149)		Year four, number of joint sides (%) (total = 3356)	
BML					
Yes	113 (3%)	Yes	48 (42%)	Yes	39 (44%)
		No	65 (58%)	No	50 (56%)
No	4056 (97%)	Yes	37 (1%)	Yes	50 (2%)
		No	3999 (99%)	No	3217 (98%)
Collateral ligament lesion					
Yes	500 (12%)	Yes	482 (99%)	Yes	400 (99%)
		No	6 (1%)	No	6 (1%)
No	3669 (88%)	Yes	125 (4%)	Yes	159 (6%)
		No	3536 (96%)	No	2791 (94%)

Numbers represent number (%). Percentages are based on baseline status ("yes" or "no"), out of those with information on the concerning follow-up moment available.
Abbreviation: BML = bone marrow lesion.

Table IV Osteoarthritis and Cartilage

Description at joint side level (ulnar and radial) of BMLs and collateral ligament lesions at baseline, year two and year four.

consistency; for all associations investigated, a strong, positive (statistically significant) association was found, even when adjusting for potential confounders. Second, there is a longitudinal association in line with the criterion of temporality. BMLs at baseline are associated with collateral ligament lesions at follow-up, and collateral ligament lesions at baseline were associated with BMLs at follow-up. Third, there is a graded effect, as longer exposure leads to a higher chance of the outcome. Fourth, our findings are analogous to other findings with regard to BMLs at baseline and other structural OA features than collateral ligament lesions at follow-up.[10] For example, BMLs at baseline are associated with future KL score, osteophytes or joint space narrowing at joint level.[35] Fifth, we regard the associations we found as plausible, because as mentioned earlier, there are biological explanations for our findings (BMLs of the interphalangeal joints have been described to origin from the entheses of the collateral ligaments,[10,14] and lesions of the collateral ligaments lead to joint instability, possibly resulting in abnormal joint loading and increased stress on the joint.[15,30]

Our study has multiple strengths. It is the first to quantify the association of BMLs and collateral ligament lesions, cross-sectionally as well as longitudinally. We did this in a large cohort containing most stages of hand OA, using validated scoring procedures with good reliability. Also, although patients were not included from the start of their disease, due to the fact that within a patient both affected and normal joints were present, still all stages of disease on joint level could be investigated. However, our study also has some limitations. First, BMLs on MRI were used as a proxy to investigate

Baseline (n=4169)				
BML	Collateral ligament lesion at baseline no, n (%)	Collateral ligament lesion at baseline yes, n (%)	Odds ratio* (95%CI)	Odds ratio† (95%CI)
No	3620 (87%)	436 (10%)	1 (reference)	1 (reference)
Yes	49 (1%)	64 (2%)	7.3 (4.6;11.6)	7.2 (4.4;11.8)
Year two (n=4149)				
BML	Collateral ligament lesion at baseline no, n (%)	Collateral ligament lesion at baseline yes, n (%)	Odds ratio* (95%CI)	Odds ratio† (95%CI)
No	3511 (85%)	553 (13%)	1 (reference)	1 (reference)
Yes	31 (1%)	54 (1%)	7.8 (4.6;13.3)	8.3 (4.7;14.7)
Year four (n=3356)				
BML	Collateral ligament lesion at baseline no, n (%)	Collateral ligament lesion at baseline yes, n (%)	Odds ratio* (95%CI)	Odds ratio† (95%CI)
No	2770 (83%)	497 (15%)	1 (reference)	1 (reference)
Yes	27 (1%)	62 (1%)	7.0 (4.2;11.7)	7.9 (4.8;13.1)

Percentages displayed are percentages out of all joints at the concerning follow-up moment.
* Adjusted for patient effect.
† Adjusted for patient effect, sex, baseline age and BMI.

Table V Osteoarthritis and Cartilage

Cross-sectional associations between BML and collateral ligament lesions at joint side level (ulnar and radial).

BML at baseline and collateral ligament lesion at follow-up (in joint sides without collateral ligament lesion at baseline)			
Collateral ligament lesion at year two			
	No	Yes	Odds ratio (95%CI)*
BML at baseline			
No	3492 (85%)	120 (13%)	1 (reference)
Yes	44 (1%)	5 (0%)	3.7 (1.5;9.1)
Collateral ligament lesion at year four			
	No	Yes	Odds ratio (95%CI)*
BML at baseline			
No	2799 (84%)	151 (15%)	1 (reference)
Yes	29 (1%)	8 (0%)	4.9 (2.3;10.7)
Collateral ligament lesion at baseline and BML at follow-up(in joint sides without BML at baseline)			
BML at year two			
	No	Yes	Odds ratio (95%CI)*
Collateral ligament lesion at baseline			
No	3594 (89%)	18 (0%)	1 (reference)
Yes	405 (10%)	19 (0%)	9.2 (3.9;22.1)
BML at year four			
	No	Yes	Odds ratio (95%CI)*
Collateral ligament lesion at baseline			
No	2891 (88%)	22 (1%)	1 (reference)
Yes	326 (10%)	28 (1%)	11.0 (5.8;20.9)

* Adjusted for patient effect.

Table VI Osteoarthritis and Cartilage

Longitudinal associations between BMLs and collateral ligament lesions, at joint side level (ulnar or radial).

bone activity. However, studies, such as histological studies, on what BMLs at the insertion site of a collateral ligament exactly represent were not found. Second, there is a significant, likely non-random loss to follow-up. This could affect the longitudinal associations we found to some extent.[36] Third, we did not have actual information on the strain or loading patients generally put on their finger joints, which could give more insight in the development of these lesions. Fourth, there might be small BMLs and collateral ligament that we were not able to detect, due to the detection limit of the MRI scanner. Our study solely investigated the right hand, which is not fully representative of both hands, as most persons have right hand dominance.[37] The selection of the cohort on having hand OA inevitably induces collider stratification bias to some extent, distorting the associations we found in unknown directions.[38] Lastly, some groups in our analyses were too small to adjust properly for potential confounders. All these limitations could bias our analyses either towards the null or away from the null.

More studies on several topics are needed. For example, data on BMLs and collateral ligament lesions in their earliest stages would help to further understand their etiology, as would more data on the duration of the presence of BMLs. Consequently, studies confirming our results using, for example, histology or more sensitive imaging techniques (such as hand MRI with > 1.5 T) are vital. Another relevant topic is the association of physical labor with BMLs and collateral ligament lesions, which could give more insight into the role of strain on the finger joints in the development of both of these lesions. In order to study this topic, the development of a grip strength meter for individual hand joints would be needed. Also, information on BMLs and collateral ligament lesions is needed in very large study groups, as even with our large study population (n=261), groups in our analyses were still sometimes small due to rare exposures and outcomes.

In conclusion, BMLs were rare and fluctuated in presence over time on joint side level, while collateral ligament lesions were more prevalent, and remained present during follow-up. There was a persistent association between both types of lesions over time. These results could provide prognostic value and more targeted treatment for hand OA patients. Future research should investigate the role of mechanical and inflammatory factors in these associations.

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Author contributions

S. Terpstra and M. Kloppenburg have contributed to the conception and design of the study, and to analysis, interpretation and collection of the data. S. Terpstra drafted the article, M. Kloppenburg obtained funding for the study, and all authors have contributed to critical revision of the article, final approval and statistical expertise.

Competing interest statement

M. Reijnierse received a International Skeletal Society (ISS) Seed Grant in 2023, M. Kloppenburg received grants from Innovative Medicines Initiative Applied Public-Private Research enabling OsteoArthritis Clinical Headway (IMI-APPROACH) and Dutch Arthritis Society, royalties or licenses from Wolters Kluwer and Springer Verlag, consultancy fees from Abbvie Kiniksa, Galapagos, CHDR, Novartis and UCB, and Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events, all paid to the institution. M Kloppenburg also was a member of the OARSI board 2017–2022, and is a member of the European League Against Rheumatism (EULAR) council and was President of the Dutch Society for Rheumatology.

Declaration of generative AI and AI-assisted technologies in the writing process

No AI tools have been used for writing this manuscript.

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Patient and public involvement statement

It was not appropriate or possible to involve patients or the public in the design, or conduct, or reporting, or dissemination plans of our research.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.joca.2025.04.009.

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