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Review

Relationships between diagnostic imaging of first carpometacarpal osteoarthritis and pain, functional status, and disease progression: A systematic review

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SUMMARY

Objective: To systematically review the association of pain, function, and progression in first carpometacarpal (CMC) osteoarthritis (OA) with imaging biomarkers and radiography-based staging.
Design: Database searches in PubMed, Embase, and the Cochrane Library, along with citation searching were conducted in accordance with published guidance. Data on the association of imaging with pain, functional status, and disease progression were extracted and synthesized, along with key information on study methodology such as sample sizes, use of control subjects, study design, number of image raters, and blinding. Methodological quality was assessed using National Heart, Lung, and Blood Institute tools.
Results: After duplicate removal, a total of 1969 records were screened. Forty-six articles are included in this review, covering a total of 28,202 study participants, 7263 with first CMC OA. Osteophytes were found to be one of the strongest biomarkers for pain across imaging modalities. Radiographic findings alone showed conflicting relationships with pain. However, Kellgren-Lawrence staging showed consistent associations with pain in various studies. Radiographic, sonographic, and MRI findings and staging showed little association to tools evaluating functional status across imaging modalities. The same imaging methods showed limited ability to predict progression of first CMC OA. A major limitation was the heterogeneity in the study base, limiting synthesis of results.
Conclusion: Imaging findings and radiography-based staging systems generally showed strong associations with pain, but not with functional status or disease progression. More research and improved imaging techniques are needed to help physicians better manage patients with first CMC OA.

Introduction

First carpometacarpal (CMC) osteoarthritis (OA) can cause disabling pain and functional limitations in performing tasks of everyday living in middle-aged and older adults,[1] and affects up to 33% of men and 39% of women at 80 years of age,[2] with the condition being more common among women of any age. As such, first CMC OA can lead to significantly diminished quality of life[3] and result in high economic and societal costs.[4–6]

The diagnosis of first CMC OA is generally established with a combination of clinical and imaging findings. Using radiography and other imaging techniques, numerous classification systems for first CMC OA have been used to stage disease and study the association with symptoms, functional status, disease progression, and need for surgery.[7,8] Radiographic staging systems include those popularized by Eaton and colleagues[9,10] and their variations (hereafter referred to

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as the Eaton classification). Other systems include those by Kellgren and Lawrence (KL),[11] Dell et al.,[12,13] Kallman et al.,[14] and Altman et al.[15,16] Despite extensive study, however, there appears to be a lack of consensus on the most useful imaging findings for evaluating first CMC OA. This may be due to discordant and sometimes contradictory findings in the literature regarding the association of imaging biomarkers with pain, functional status, and disease progression.[17–20] This has contributed to contested management approaches and likely hobbled the establishment of criteria to optimize personalized prediction of first CMC OA progression. In addition, objective evaluation of treatment outcomes based on imaging findings is problematic if imaging findings show little to no association with symptoms.

The objective of this study is therefore to systemically search and comprehensively review the medical literature to determine the associations of imaging findings and radiography-based staging with pain, functional status, and disease progression in patients with first CMC OA.

Materials and methods

Identification of studies

This systemic review was conducted in accordance with the Preferred Reporting Items for Systemic Reviews and Meta-Analyses (PRISMA) guidelines.[21] A combination of Medical Subject Headings and keywords was developed by researchers and research librarians (see Supplemental Section S.1). The search strategy was run in PubMed/MEDLINE, Embase via Ovid, and Cochrane Central Register of Controlled Trials. Records were limited to English language full text journal publications, with no starting time restrictions up to August 23, 2022 (date of the final search). To increase the number of potentially relevant records, we included "hand" in addition to "thumb base" and "CMC" OA in our search terms and included these articles if they examined thumb-base OA in addition to hand OA. Record screening at the abstract level was conducted by the lead author, and at least two additional authors conducted the full-text screening. Disagreements were resolved by consensus. Citation searching was conducted on articles that underwent full-text screening. Studies that were conducted in non-human subjects, focused on post-operative/traumatic patients, focused on inflammatory arthritis patients, or were review articles, commentaries, or meta-analyses, were excluded.

Data extraction

During full text review the following data were extracted: identification of each article; study methodology; study population characteristics including sample size, joints studied, age and sex distributions, use of control subjects, definitions of hand or first CMC OA; clinical measurement methods; imaging modalities; number of image raters; image acquisition parameters and imaging findings, staging systems or atlases used. Articles were classified based on methodology (e.g., prospective, cross-sectional) and particular focus (e.g., epidemiological, pre-operative evaluations, associational). Study results were tabulated and are summarized according to imaging modality and relations to pain, functional status, and disease progression. Progression was defined as either structural (an advance in disease as measured by imaging) or symptomatic (an increase in pain or other symptoms, or a decrease in function). Tenderness on palpation was considered a measure of pain. When comparing design characteristics across studies, a p-value < 0.05 was considered significant.

Methodological quality

Methodological quality was assessed independently by two authors according to a modified National Heart, Lung and Blood Institute (NHLBI) Quality Assessment Tool for observational cohort and cross-sectional studies, where applicable.[22] This tool assesses study objectives, population, outcome measures, and statistical methods. It provides a "good," "fair," or "poor" quality rating. Studies with different designs were assessed with other tools from NHLBI as appropriate and classified in the same manner. Disagreements were resolved by consensus of two or more additional authors.

Meta-analysis

Meta-analyses were conducted where possible. Study results had to match in terms of the specific pain or functional measures used, the specific outcome (e.g., change in pain vs. presence or absence), the imaging measures (including where possible specific grades) over which the outcome is calculated, the participant populations (for example, use of controls), and the joint assessed. The Der Simonian-Laird estimator was used to produce random effects models. Forest plots were produced, and the I^2 and τ^2 statistics were used to measure heterogeneity.

Results

Fig. 1 shows a PRISMA flow diagram summarizing the study selection process. After database and citation searching, 162 articles remained from database searches and 7 from citation searching. During full-text screening, reviewer agreement on study inclusion was 74%. After full-text screening, forty-five articles were included in this systematic review. After reporting an overview of these studies, we detail our findings of the association of imaging findings and radiography-based staging with pain, functional status, and disease progression in patients with first CMC OA.

Overview of studies

A summary of the designs, aims and imaging modalities used in the studies can be viewed in Table I. Study designs were cross-sectional and retrospective (25), longitudinal (11), treatment evaluation (2), case-control (4) and prevalence studies (3). To assess the relationship between imaging findings and symptoms, studies used: radiography (34), sonography (1), X-ray computed tomography (CT) (1), or magnetic resonance imaging (MRI) (2), while 7 studies reported multiple imaging modalities (5 studies with two modalities and 2 studies with three modalities). The forty-five articles included a total of 28,183 study participants (age: 66.1 ± 4.6 years, 66.5% female). Of these, many were without first CMC OA, as they participated in large population-based or prevalence studies, were control subjects, or suffered from generalized hand OA. In total, 7244 study participants (out of 28,183) had first CMC OA (mean age 63.6 ± 4.4, 65.0% female). Eight studies utilized control groups, for a total of 271 control subjects across the studies. Control group participants were younger and more frequently female (age: 56.7 ± 10.2 years, 82.5% female) compared to the patients with first CMC OA (t-tests, $p < 0.05$). Mean sample sizes when including population-based studies were $N = 607$ and $N = 288$ otherwise. In rating or quantifying imaging, the number of raters varied from 1 to 4. Nineteen studies reported 2 or more raters, 22 a single rater, and 6 did not report the number of raters. More details can be viewed in the Supplemental Sections S.2 and S.3, where these characteristics are detailed further, and studies are grouped into those examining pain, functional status, and progression.

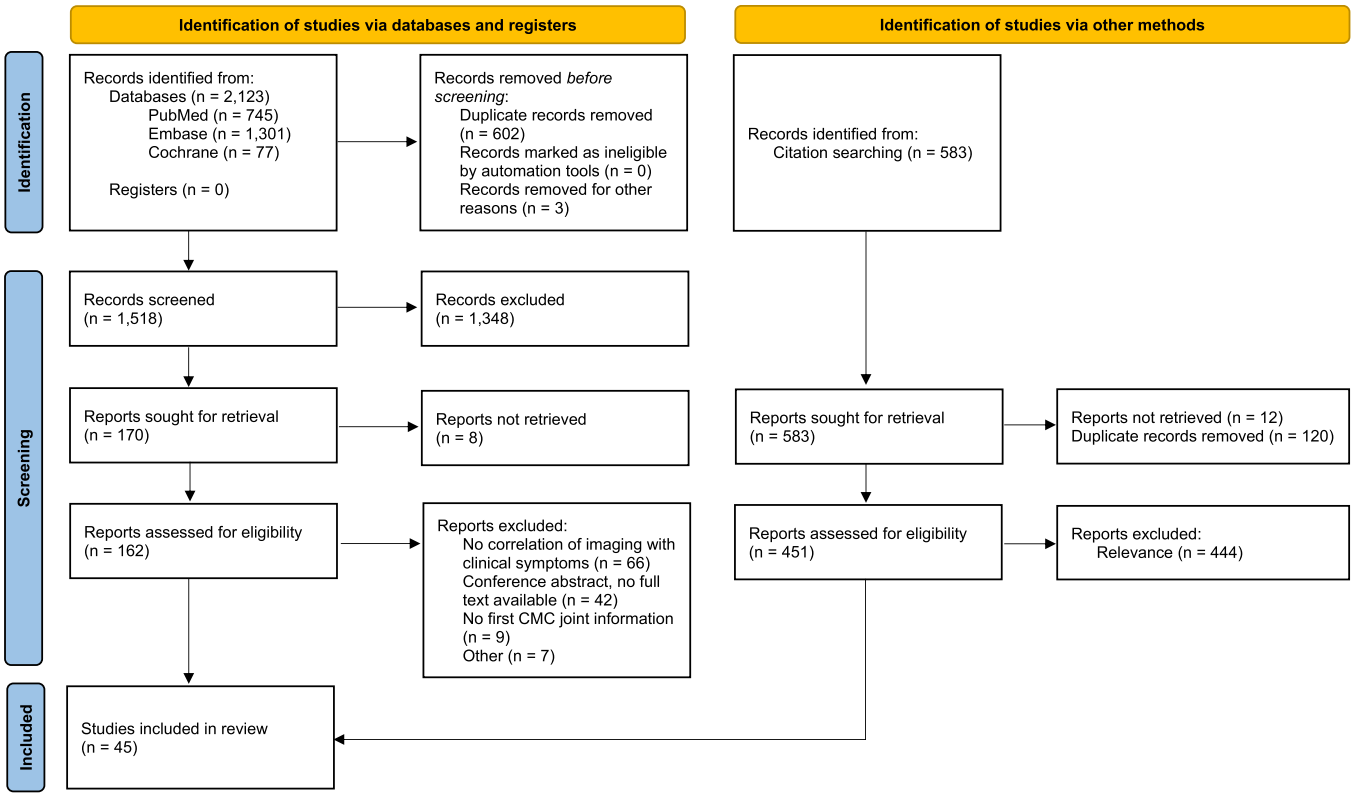

Fig. 1 Osteoarthritis and Cartilage

PRISMA flow diagram depicting the study selection process.

Pain was quantified in a variety of ways amongst the studies (including questionnaires, self-reported measures and personnel-reported measures) (Tables II–IV).[23–27] Functional measures were most commonly recorded using validated questionnaires (e.g., disabilities of the arm shoulder and hand [DASH], Australian/Canadian Osteoarthritis Hand Index [AUSCAN]).[28–30]

Imaging findings and staging also varied markedly among the studies, with the KL classification being the most common (Tables II–VI). Findings relating to single imaging markers were scored with custom scoring systems (e.g., Keen et al.[31]), with available atlases (e.g., Fjellstad et al.[26]), or subjectively in a semiquantitative manner (e.g., Naguib et al.[32]). This heterogeneity in assessment of pain, function, imaging findings and staging limited the number of studies that could be included in the meta-analyses.

Pain and imaging findings

Fifteen articles examined the relationship of radiographic imaging findings with pain or tenderness (tenderness on palpation was considered a measure of pain) (Table II). One article used CT,[18] while the others used radiography. Ten studies used radiographic staging systems, namely the KL and Eaton classifications, as well as Dell and Kallman grades.[20,24,33–40] Five studies used structural features of OA graded with the Osteoarthritis Research Society International (OARSI) atlas (joint space narrowing [JSN] and osteophytes).[19,23,25,41,42]

One article that used CT found no association between imaging findings and pain.[18] Five of the ten studies that used radiographic staging systems were positive in that they found statistically significant associations with pain. All of them used the KL classification.[20,24,35,37,39] Two of these reported odds ratios showing dose-dependent associations with presence of pain.[24,35] One study that used the Eaton classification found no association with pain.[38] Four others that used Dell, Kallman and KL classifications[33,34,36,40] also found no association of radiographic findings or staging with pain.

Overall, seven studies found an association between radiographic findings or staging and pain, whereas eight did not. When considering the total number of study results examining the relation between these findings and pain, 53.1% were positive.

Table III details the seven studies that examined the relationship between sonography markers and pain.[25,26,31,32,42–44] The most common sonographic measures were power Doppler signal (PDS), gray-scale synovitis, graded osteophytes; or quantified effusion, cartilage thinning, or JSN, amongst others (Table III). Three of seven studies found moderate to strong associations between sonographic findings (gray scale synovitis, PDS, osteophytes, cartilage thinning, and JSN) and pain (Table III).[26,32,43] In particular, the study by Fjellstad et al. found strong and dose-dependent associations between graded gray scale synovitis and power Doppler (PD) activity with three different measures of pain (Table III).[26] Associations between sonography measures and pain are conflicting (42% of study findings were positive). Exclusion of one study with a markedly different design that did not measure pain directly[44] brings this figure to 46%.

Only three studies examined the association between MRI-detected pathology and pain in thumb base OA (Table IV).[25,45,46] Measures evaluated from MRI included synovitis, bone marrow lesions (BMLs), osteophytes, and bone cysts. Overall, MRI studies show some strong associations with pain, though results are conflicting (66% of studies were positive).

Author	Study type	Design/Aim	Study population	Imaging modality
Bijsterbosch, J. 2011	Longitudinal	Disease course (radiographical)	289 patients	Radiography (JSN, osteophytes)
Botha-Scheepers, S. 2009	Longitudinal	Disease course (radiographic, functional)	189 patients	Radiography (JSN, osteophytes)
Ceceli, E. 2012	Cross-sectional	Effect of HOA on strength and function, and relation of radiography to these parameters	60 patients, 40 controls	Radiography (KL staging, graded features)
Dahaghin, S. 2005	Population-based, cross-sectional	Prevalence and pattern of radiographic OA	3906 patients	Radiography (KL staging)
Dauvissat, J. 2018	Treatment evaluation	Assess safety and predictive factors of treatment efficacy	122 patients (at baseline)	Radiography (Dell staging)
Degreef, I. 2006	Treatment evaluation	Prediction of surgical outcomes	36 patients	Radiography (EL staging)
Deveza, L. 2020	Cross-sectional, first CMC focused	Impact of interphalangeal OA on first CMC OA	204 patients	Radiography (KL staging)
Dominick, K. L. 2005	Cross-sectional, associational	Hand OA and grip strength	700 patients	Radiography (KL staging, individual joints, rows, rays)
Fjellstad, C. M. 2020	Cross-sectional, associational	Association of imaging with pain and function	290 patients	Sonography (gray-scale synovitis, PDS)
Gil, J. A. 2022	Longitudinal, first CMC focused	Radiographic OA relation to symptoms	91 patients	Radiography (EL staging)
Haara, M. M. 2005	Population-based, Longitudinal, first CMC focused	Prevalence, follow-up for mortality and work disability	7200 patients, 3595 hand radiographs	Radiography (KL staging)
Hart, D. 1994	Cross-sectional, associational	Comparison of clinical and radiological examination for HOA	976 participants	Radiography (KL staging)
Haugen, I.K. 2013	Longitudinal	Radiographic OA relation to symptoms	190 patients	Radiography (KL staging, Altman atlas)
Hoffler, C. E. 2015	Cross-sectional, first CMC focused	Radiographic OA relation to symptoms	62 patients	Radiography (EL staging)
Hoogendam, L. 2021	Cross-sectional, first CMC focused	Radiographic OA relation to symptoms	255 patients	Radiography (EL staging)
Jones, G. 2001	Cross-sectional	Radiographic OA relation to symptoms and function	522 patients	Radiography (JSN and osteophytes, assessed with Altman atlas)
Jónsson, H. 2009	Case-control	Radiographic OA relation to joint hypermobility	384 patients	Radiography (KL staging)
Jónsson, H. 1996	Case-control	Radiographic OA relation to joint hypermobility	50 patients and 94 matched controls	Radiography (KL staging)
Keen, H. 2008	Case-control	Relation of ultrasound-detected pathology with symptoms	36 patients and 19 controls	Ultrasound detected pathology (JSN, osteophytes, power Doppler, gray-scale synovitis)
Kim, S.-K. 2021	Cross-sectional	Association of FIHOA functional questionnaire with symptoms and radiography	95 patients	Radiography (KL staging)
Kodama, R. 2016	Population-based, Prevalence & associational	Prevalence of hand osteoarthritis and radiographic relation to grip strength and pain	1535 participants	Radiography (KL staging)
Komatsu, M. 2017	Cross-sectional	Association of joint pain and bony alterations detected by MRI	20 patients (37 thumbs)	MRI and radiography
Kraus, V.B. 2004	Cross-sectional	Association of hypermobility with OA in hand joints	1043 patients	Radiography (KL staging)
Kroon, F. P. B. 2018	Cross-sectional, first CMC focused	Association of inflammatory features with pain	289 patients	MRI, sonography and radiography
Kwok, Y.W. 2011	Population-based, prevalence & associational	Relation of erosive OA to hand OA, pain and disability	3430 participants	Radiography (EL staging, Verbruggen-Veys scoring)
Lai, C. 2021	Case-control	Relation of muscle thickness and grip strength to early OA	23 patients (32 thumbs)	Sonography
Larsen, S. 2015	Longitudinal	Relation of subluxation to symptoms and treatment	137 patients (172 hands)	Computed tomography (EG staging)
Lee, H.J. 2012	Cross-sectional	Impact of radiographic OA on hand function	378 patients	Radiography (EL staging)
Mallinson, P.I. 2013	Treatment evaluation	Relation of ultrasound grading of OA to disability and treatment response	31 patients, 37 controls	Sonography (JSN, osteophytes and capsule size)
Marshall, M. 2011	Cross-sectional	Association of clinical signs and presence of ROA	592 participants	Radiography (KL staging)
Mathiessen, A. 2015	Longitudinal	Can ultrasound predict radiographic progression of HOA?	78 patients	Sonography (gray-scale synovitis and PDS) and radiography (KL staging)
Mathiessen, A. 2013	Cross-sectional	Investigate concordance of ultrasound detected osteophytes with other imaging and clinical examination	127 patients	Sonography, MRI, and radiography
Naguib, A. 2011	Cross-sectional	Study relationship between sonographic findings and symptoms	30 patients and 15 controls	Sonography (JST, osteophytes and cartilage thinning) and radiography (KL staging)
Oo, W. M. 2019	Cross-sectional, first CMC focused	Association between ultrasound pathologies and pain, function, and radiographic scores	93 patients	Sonography (synovitis, osteophytes, and power doppler) and radiography (KL staging)
Ozkan, B. 2007	Cross-sectional	Examine the effect of OA on hand function	100 patients	Radiography (KL staging)
Reissner, L. 2016	Longitudinal, first CMC focused	Relation of pre- and post-operative first CMC position to clinical outcomes	105 patients	Radiography (subluxation and thumb metacarpal migration)
Riordan, E. 2018	Cross-sectional, first CMC focused	Relationship between joint laxity and OA severity	100 patients	Radiography (KL and EL grades, subluxation ratios)
Riordan, E. 2022	Cross-sectional, first CMC focused	Investigate association between markers of radiographic disease, pain and function	100 patients	Radiography (KL staging)

(*continued on next page*)

Table I (*continued*)

Author	Study type	Design/Aim	Study population	Imaging modality
Shi, Y. 2022	Longitudinal, first CMC focused	Investigate associations between radiographic and sonography features with pain and function	166 patients	Radiography (JSN, osteophytes, subchondral bone sclerosis) and sonography (synovitis, PDS and osteophytes)
Sonne-Holm, S. 2006	Population-based, prevalence and associational, first CMC focused	Prevalence of first CMC OA and association of radiology with pain	3355 participants	Radiography (KL staging)
Spacek, E. 2004	Cross-sectional	Evaluate and compare disability in patients with more symptoms in first CMC OA or IP OA	116 patients	Radiography (Kallman staging)
Tenti, E. 2020	Observational retrospective	Compare impact of first CMC OA on pain, function, and quality of life in erosive and non-erosive OA.	232 patients	Radiography (Kallman staging)
van Beest, S. 2021	Longitudinal, first CMC focused	Changes in pain and OA features over two years	165 patients	MRI (OMERACT TOMS)
Weinstock-Zlotnick, G. 2019	Cross-sectional, first CMC focused	Relation between hand function and radiographic OA	5 patients, 9 controls	Radiography (EL staging)
Wilkens, S. 2019	Cross-sectional, first CMC focused	To study factors associated with radiographic first CMC OA	59 patients	Radiography (EL staging)

EL, Eaton and Littler; EG, Eaton and Glickel; HOA, hand osteoarthritis; IP, interphalangeal joint; OMERACT TOMS, Outcome Measures in Rheumatology Clinical Trials thumb base osteoarthritis scoring system; ROA, radiographic osteoarthritis.

Table I
Summary of included studies.

Osteoarthritis and Cartilage

Finally, we found that osteophytes stand out as biomarkers for pain across all three imaging modalities, with most study findings showing significant associations.[19,23,25,31,32,41,42] In particular, Haugen et al.[24] found an increase in the odds of pain being present when osteophytes either progressed or were incident over follow-up.

Functional status and imaging findings

The relationship between radiographic thumb OA and measures of hand function are provided in Table V. The twenty-two studies were highly heterogeneous in their choice of imaging findings and measures of functional status. The most commonly used tools in the studies were the DASH (7), AUSCAN (5) and Functional Index of Hand Osteoarthritis (FIHOA) (4). Other outcome questionnaires utilized included the Stanford Health Assessment Questionnaire (HAQ),[47] the Michigan Hand Questionnaire (MHQ),[48] and several others (Table V). The most common radiographic imaging markers used were the Eaton and KL classifications, or variations of these systems.

Overall, the majority of study findings (40/55, 73%) relating imaging findings to functional status were negative, showing no association. This did not differ much among studies utilizing radiography (69%) or sonography (73%). However, use of KL staging (or measures based on them) was associated with a higher chance of reporting significant associations (7/10), compared with results from studies that used the Eaton-based staging systems (1/12), and compared to all other imaging findings or markers used (including Eaton) (3/17). Although not clearly reported, two studies using the DASH suggest that minimal clinically important differences (MCID)[49] between participants with differing radiological scores of first CMC OA exist.[33,50] Similarly, Jones et al.[19] found their radiological score associates with MCIDs in AUSCAN scores (4 points),[51] particularly in women. The MCID for the FIHOA is unknown,[52] however four studies strongly suggest differences of several points in the FIHOA between KL grades as well with graded osteophytes, JSN, and bone sclerosis.[39,42,53,54]

Six studies examined the association of sonography-detected pathology and functional status (Table VI).[26,31,32,42,43,55] Only 20% of results showed significant associations. Overall, studies show limited associations between sonography-detected pathology and functional status. Results that were significant utilized osteophyte grading, JSN, and PD activity relating to the DASH and the AUSCAN. It seems likely that these measures can detect MCIDs.[26,32,55]

Progression of OA and imaging findings

Eight studies had longitudinal findings examining predictors of structural[56] or symptomatic[23,24,27,41,55,57,58] progression of first CMC OA (Table VII).[23,24,27,41,55–58] Thirty-seven percent of results relating to progression were positive. Results from Mathiessen et al. showed that sonography findings can predict radiographic worsening.[56] Other significant results include an increase in pain in those with increased Eaton or KL grades,[24,57] an increase in pain on palpation with increases in MRI-assessed synovitis and BML severity,[27] and an increased mortality rate for those with KL grades 3-4 at baseline (adjusted for age).[58]

Methodological quality and risk of bias

The results of the methodological quality assessment for observational cohort and cross-sectional studies are presented in Supplemental Section S.4. Results for case-control and treatment evaluation studies are in Supplemental Section S.5. Overall, methodological quality was sound. The most common limitations were those relating to power calculations and measurements of exposures

Author	Pain measure	Imaging scoring	Joint/Joint group	Comparison	Outcome	Measure	Result
Bijsterbosch 2011	AUSCAN Pain	OARSI JSN and Osteophytes	Whole hand	Poor pain outcomes after 6 years	Association with osteophytes and JSN	Risk Ratio Osteophytes JSN	1.22 (0.77, 1.73) 1.02 (0.64, 1.46)
Botha-Scheepers 2009	AUSCAN Pain (baseline)	OARSI JSN and Osteophytes	Whole hand	Pain at baseline	Association with change in osteophytes and JSN	Mean Difference	JSN, AUSCAN 1.8 (0.2, 3.4) Osteophytes Authors stated no association
	AUSCAN Pain (change)	OARSI JSN and Osteophytes	Whole hand	Pain change over 2 years	Association with change in osteophytes and JSN	Not reported	Authors stated no association
Ceceli 2012	VAS Pain	Kallman radiological scores	Whole hand (sum of scores at each joint)	Within-group	Correlation of VAS with Kallman scores	Correlation coefficient (p-value)	r = 0.171 (right hand), 0.178 (left hand). P > 0.05
Dahaghin 2005	Present/Absent	KL grades	First CMC/TS	KL grade ≥2 vs KL < 2	Odds of pain present	Odds ratio (95% C.I.)	**1.7 (1.4, 2.2)**
Dauvissat 2018	NRS Pain	Dell grades	First CMC	Difference between groups	Difference in mean pain	t-test Dell 4 vs. 3 Dell 3,4 vs. 1,2	p = 0.33 p = 0.21
Haugen 2013 (cross-sectional)	Pain on palpation	KL grades	PIP, DIP and first CMC joints	Increasing KL grades (0-IV)	Odds of pain present (compared to grade 0)	Odds ratios (95% C.I.)	**1.4 (1.2, 1.7), 3.0 (2.4, 3.7), 6.8 (4.5, 10), 5.3 (3.3, 8.6)**
Haugen 2013 (longitudinal)	Incident pain on palpation	KL grades	PIP, DIP and first CMC joints	Increasing KL grades (0-IV)	Odds of pain present (compared to grade 0)	Odds ratios (95% C.I.)	1.2 (0.7, 2.0), 1.5 (0.9, 2.4), **5.7 (3.0, 11),11 (4.0, 33)**
Jones 2001	AUSCAN Pain Subscale	OARSI JSN and Osteophytes	First CMC	Presence of OA (based on radiographic score) vs. pain	Correlation	Regression Coefficient (p-value) Kappa coefficient (95% C.I.)	**+0.14 (0.024)** **0.21 (0.13, 0.29)**
Kodama 2016	Present/Absent	KL grades	Whole hand (present/absent)	KL ≥ 3, KL = 2 vs. KL ≤ 1 (in at least one joint)	Odds of pain present	Odds ratios (95% C.I.)	**4.82 (1.67, 17.69)**, 2.30 (0.85, 8.14), 1.0
	Present/Absent	KL grades	Whole hand (present/absent)	Pain vs No Pain	Odds of KL ≥ 3 (Severe HOA)	Odds ratio (95% C.I.)	**2.23 (1.45, 3.45)**
	Present/Absent	KL grades	First CMC	Pain vs No Pain	Odds of KL ≥ 3	Odds ratio (95% C.I.)	**2.31 (1.30, 3.92)**
Kroon 2018	Tenderness on Palpation	OARSI JSN and Osteophytes	First CMC or STT	Osteophytes present vs. absent	Odds of pain present	Odds ratio (95% C.I.)	**5.1 (2.7, 9.8)**
	Tenderness on Palpation	OARSI JSN and Osteophytes	First CMC	Osteophytes graded as absent, 1, 2, 3	Odds of pain present	Odds ratio (95% C.I.)	1.0, 1.2 (0.5, 2.6), 1.5 (0.5, 4.5), **5.3 (1.1, 23.2)**
Marshall 2009	AUSCAN Pain Subscale	KL grades	Whole Thumb	Pain scores of thumbs only OA (K-L ≥ 2) vs. no OA	Difference between means	t-test	p = 0.077
Riordan 2022	VAS Pain	KL grades	First CMC	KL grades association with VAS Pain	Results of Multivariate Regression	Beta coefficient, p-value	3.7 (0.05)
Shi 2022	VAS Pain	Radiographic: JSN Osteophytes Sclerosis	First CMC	Association of VAS pain with radiographic features	Results of Multivariate Regression	Beta coefficients, p-values	1.44 (0.17) −1.22 (0.31) −2.62 (0.25)
Sonne-Holm 2006	Present/Absent	KL grades	First CMC	Prevalence of pain among KL grades	Proportion of participants with pain for K-L grade 3 vs. 0 Proportion of participants with pain across K-L grades	Difference between groups Rising trend across groups	**p < 0.001** **p < 0.001**
Tenti 2020	VAS Pain	Kallman grading	First CMC	Association of VAS Pain with THOA (presence or absence)	Results of Multivariate Regression	Beta coefficient, p-value	6.4 (0.054)
Weinstock-Zlotnick	PRWHE Pain	EL grades	First CMC	PWHRE Pain association with EL grades	Correlation	Correlation coefficient (95% C.I.)	−0.14 (−0.78, 0.8)

CI, confidence interval; DIP, distal interphalangeal joint; EL, Eaton and Littler; NRS, numerical rating scale; PIP, proximal interphalangeal joint; PWHRE, Patient-Rated Wrist/Hand Evaluation; THOA, thumb base osteoarthritis; TS, trapezioscaphoid joint. Statistically significant results shown in bold. Tenderness on palpation was considered a measure of pain.

Table II

Association of radiographic measures with pain.

Author	Pain measure	Imaging scoring	Joint/Joint group	Comparison	Outcome	Measure	Result
Fjellstad 2019	Tenderness on palpation	Gray-scale synovitis	First CMC	Grades 2-3 vs. Grade 0 Grade 1 vs. Grade 0	Odds of pain in the joint	Odds Ratios (95% CI)	**4.40 (2.10, 9.24) 2.76 (1.36, 5.63)**
	Tenderness on palpation	PDS (grade 2-3) PDS (grade 1)	First CMC	Grades 2-3 vs. Grade 0 Grade 1 vs. Grade 0	Odds of pain in the joint	Odds Ratios (95% CI)	**5.36 (1.16, 14.31) 3.24 (1.73, 6.04)**
	Pain in previous 24 hours	Gray-scale synovitis (grade 2-3), Gray-scale synovitis (grade 1)	First CMC	Grades 2-3 vs. Grade 0 Grade 1 vs. Grade 0	Odds of pain in the joint	Odds Ratios (95% CI)	**1.88 (1.06, 3.31) 2.16 (1.25, 3.74)**
	Pain in previous 24 hours	Power activity (grade 2-3) Power activity (grade 1)	First CMC	Grades 2-3 vs. Grade 0 Grade 1 vs. Grade 0	Odds of pain in the joint	Odds Ratios (95% CI)	**2.28 (0.88, 5.90) 1.42 (0.85, 2.39)**
	Pain in previous 6 weeks	Gray-scale synovitis (grade 2-3), Gray-scale synovitis (grade 1)	First CMC	Grades 2-3 vs. Grade 0 Grade 1 vs. Grade 0	Odds of pain in the joint	Odds Ratios (95% CI)	**2.62 (1.60, 4.30) 1.86 (1.02, 3.39)**
	Pain in previous 6 weeks	Power activity (grade 2-3) Power activity (grade 1)	First CMC	Grades 2-3 vs. Grade 0 Grade 1 vs. Grade 0	Odds of pain in the joint	Odds Ratios (95% CI)	**5.79 (2.46, 13.61) 2.07 (1.35, 3.20)**
Kroon 2018	Tenderness on palpation	Synovial thickening	First CMC	Grades 2-3, grade 1 vs. Absent	Odds of pain present	Odds Ratios (95% CI)	1.2 (0.3, 4.6) 1.1 (0.5, 2.6)
	Tenderness on palpation	Effusion PDS	First CMC	Grades 2-3, grade 1 vs. Absent	Odds of pain present	Odds Ratios (95% CI) Odds Ratios (95% CI)	1.0 (0.3, 3.1) 0.9 (0.4, 2.2) 1.5 (0.6, 3.9) 0.9 (0.4, 2.7)
Lai 2021	Presence of early OA (clinical)	Thickness of APB, OPP and FDI muscles	First CMC	Association with clinical OA	Odds of increased pain	Odds Ratios (95% CI)	APB 0.96 (0.88, 1.03) OPP 0.85 (0.71-0.97) FDI 0.95 (0.87, 1.003)
Naguib 2011	VAS Pain	Osteophytes, cartilage thinning, and JSN	Various hand joints	Association with pain	Correlation	Coefficients JSN, OST, Cartilage thinning	**Not given, p = 0.001Not given, p = 0.002r = −0.579, p = 0.001**
Oo 2019	VAS Pain	PDS	First CMC	Association with pain	Association	Regression coefficient, p-value	**Beta = 11.29p-value = 0.02**
Keen 2008	Global VAS, AUSCAN Pain	Summated gray-scale and power Doppler synovitis, osteophytes, JSN	Whole hand	Association with pain	Association	Correlation Coefficients	All p > 0.05
	Global VAS, AUSCAN Pain	Number of joints with gray-scale and power Doppler synovitis, osteophytes, JSN	Whole hand	Association with pain	Association	Correlation Coefficients	All p > 0.05
Shi 2021	VAS Pain	Synovitis PDS Osteophytes	First CMC	Association of VAS pain with sonography metrics	Results of Multivariate Regression	Beta coefficients, p-values	0.42 (0.78) −5.16 (0.08) 0.23 (0.90)

APB, abductor pollicis brevis; CI, confidence interval; FDI, first dorsal interosseous; OPP, opponens pollicis. Statistically significant results shown in bold. Tenderness on palpation was considered a measure of pain.

Table III

Association of sonographic measures with pain.

Author	Pain measure	Imaging scoring	Joint/Joint group	Comparison	Outcome	Measure	Result
Komatsu 2017	Denis Scale	MRI-detected bone signal changes, bone cysts and EL grades	First CMC	Group with moderate or severe pain	Frequency of bone signal changes in patients with pain	Percentage	85%
			First CMC	Group with moderate or severe pain	Incidence of bone signal changes by EL grade	Percentages: EL 1 EL 2 EL 3-4	20%, 77.8%, 100%
			First CMC	Bilateral pain group	Bone signal changes	Presence	Only on more painful side
			First CMC	Non-painful contralateral thumbs	Bone signal changes	Number present	None, even in advanced ROA
			First CMC	Group with moderate or severe pain	Frequency of bone cysts by EL grade	Percentages: EL 1 EL 2 EL 3-4	40%, 77.8%, 100%
Kroon 2018	Tenderness on palpation	Synovitis	First CMC and STT joints	Grades 2-3 vs. grade 1 Same OR adjusted for osteophyte presence	Odds of pain present	Raw and adjusted Odds Ratios (95% CI)	**3.6 (1.7, 7.6)**2.1 (0.9, 4.7)
		BMLs	First CMC and STT joints	Grades 2-3 vs. grade 1 Same OR adjusted for osteophyte presence	Odds of pain present	Raw and adjusted Odds Ratios (95% CI)	**3.0 (1.6, 5.5)**1.3 (0.6, 2.7)
		Osteophytes present at First CMC or STT	First CMC and STT joints	Synovitis Absent Synovitis Present	OR magnitude comparison	Odds Ratios (95% CI)	2.7 (0.7, 10.1),**9.1 (3.6, 23.0)**
		Osteophytes present at First CMC or STT	First CMC and STT joints	BMLs Absent BMLs Present	OR magnitude comparison	Odds Ratios (95% CI)	1.4 (0.5, 4.1),**6.6 (3.1, 14.0)**
van Beest 2021	Pain on palpation	Synovitis	First CMC	Increasing pain scores	Odds of increased pain (raw, adjusted for osteophytes)	Odds Ratios (95% CI)	**3.05 (1.35, 6.9)**, 1.63 (0.66, 4.0)
	Pain on palpation	BMLs	First CMC	Increasing pain scores	Odds of increased pain (raw, adjusted for osteophytes)	Odds Ratio (95% CI)	**2.50 (1.28, 4.9)**, 1.10 (0.49, 2.46)
	Change in pain on palpation (2 years)	Increase in Synovitis	First CMC	Increasing pain scores	Odds of increased pain	Odds Ratio (95% CI)	**3.44 (1.28, 9.3)**
	Change in pain on palpation (2 years)	Increase in BMLs	First CMC	Increasing pain scores	Odds of increased pain	Odds Ratio (95% CI)	5**.1 (2.10, 12.6)**
	Change in pain on palpation (2 years)	Decrease in BMLs	First CMC	Increasing pain scores	Odds of increased pain	Odds Ratio (95% CI)	2.67 (0.80, 8.9)

CI, confidence interval; EL, Eaton and Littler staging; ROA, radiographic osteoarthritis; OR, odds ratio; STT, scaphotrapeziotrapezoidal. Statistically significant results shown in bold. Tenderness on palpation was considered a measure of pain.

Table IV

Association of MRI measures with pain.

Osteoarthritis and Cartilage

Author	Functional measure	Imaging scoring	Joint/Joint group	Comparison	Outcome	Measure	Result
Bijsterbosch 2011	AUSCAN baseline scores (functional)	Radiographic score (osteophytes + JSN)	Various hand joints	Highest vs lowest tertile of baseline function scores	Risk of radiographic progression at follow-up	Risk Ratio (95% CI)	1.33 (0.95, 1.73)
Botha-Scheepers 2009	Change in function over two years (AUSCAN)	OARSI JSN and Osteophytes	Various hand joints	Within patient group	Association with change in osteophytes and JSN	Not reported	Authors stated no association
Ceceli 2012	DASH	Kallman scores	Various hand joints	Within group association (patient group)	Correlation	Correlation coefficient (p-value)	**Right Hand r = 0.289 (p = 0.024) Left Hand r = 0.300 (p = 0.017)**
Degreef 2006	DASH Score (postoperative)	EL grading	First CMC	Within patient group	Results of Multivariate Regression	Parameter estimate, p-value	−0.30, 1.0
Deveza 2020	FIHOA	KL grading	First CMC + IP joints	Within group association	Association	Regression coefficient (p-value)	**1.82 (0.015)**
Haara 2005	Inability to perform daily tasks	KL grading	First CMC	KL ≥ 2 vs KL < 2	Odds of being unable to perform daily activities	Odds Ratio	0.8 (0.63, 1.01)
	Physical status in right and left hands (clinical findings)	KL grading	First CMC	KL ≥ 2 vs KL < 2	Odds of OA present	Odds Ratios	**Right hand 3.29 (2.03, 5.33) Left Hand 2.16 (1.34, 3.51)**
	Work disability	KL grading	First CMC	KL ≥ 2 and KL 3&4 compared to KL < 2	Incidence of work disability	Risk Ratio (95% CI)	0.91 (0.61, 1.38), 1.47 (0.65, 3.31)
Haugen 2013	AUSCAN Physical function	Summed KL grades	First CMC	Within group association	Association	Regression coefficient (95% CI)	0.19 (−0.40, 0.79)
Hoffler 2015	QuickDASH	EL grading	First CMC	Association of EL stage with QuickDash	Correlation	Spearman's Rho (p-value)	−0.014 (0.91)
	PCS-12	EL grading	First CMC	Association of EL stage with PCS-12	Correlation	Spearman's Rho (p-value)	0.145 (0.26)
	MCS-12	EL grading	First CMC	Association of EL stage with MCS-12	Correlation	Spearman's Rho (p-value)	0.019 (0.89)
Hoogendam 2019	MHQ total score	EG staging	First CMC	Within group associations	Association of EL Stage with MHQ (regression analysis)	Adjusted Beta coefficient (p-value)	0.18 (p > 0.05)
Jones 2001	AUSCAN (function)	Presence of OA (Altman Atlas)	First CMC	OA vs. no OA	Association with dysfunction (binary classifier)	Kappa coefficient (95% CI)	**0.36 (0.28, 0.44)**
Kim 2021	FIHOA	Summed KL grades (radiographic severity score)	Various hand joints	Association with FIHOA scores	Odds of higher FIHOA scores	Odds Ratio	0.97 (0.96–1.03)
Kwok 2011	Stanford HAQ	Presence of erosions (OARSI)	Various hand joints	Presence of 1 or more erosions in those with K-L ≥ 2	Odds of HAQ > 0.5	Odds Ratio (95% CI)	**≥2 Erosions 3.57 (1.20, 10.61)**
Lee 2012	DASH	Summed KL grades	First CMC and IP	Summed thumb KL grades in participants	Association of these scores with DASH scores	Regression coefficient (p-value)	**1.53 (0.045)**
Marshall 2011	Inability to achieve position 10 of Kapandji test	KL staging	First CMC	KL ≥ 2 vs. KL < 2	Odds of OA present (KL ≥ 2)	Odds Ratio (95% CI)	1.0 (0.7, 1.4)
	Thumb extension < 40 degrees	KL staging	First CMC	KL ≥ 2 vs. KL < 2	Odds of OA present (KL ≥ 2)	Odds Ratio (95% CI)	1.3 (0.9, 1.8)
Reissner 2016	MHQ	Radial subluxation	First CMC	Association between radial subluxation and three components of the MHQ	Correlation	Correlation coefficients	All r < 0.1, p > 0.3
Riordan 2022	FIHOA	KL grades	First CMC	FIHOA grades association with KL grades	Results of Multivariate Regression	Beta coefficient, p-value	**1.0, (0.021)**
Shi 2021	FIHOA	Radiographic: JSN Osteophytes Bone Sclerosis	First CMC	Association of FIHOA with radiographic measures	Results of Multivariate Regression	Beta coefficients, p-values	**0.90 (0.02)** 0.45 (0.17) **1.89 (0.03)**

(*continued on next page*)

Table V (*continued*)

Author	Functional measure	Imaging scoring	Joint/Joint group	Comparison	Outcome	Measure	Result
Spacek 2004	Cochin Hand Functional Scale (CHFS)	Kallman scores	First CMC	Within group association	Correlation	Correlation coefficients	0.199 (statistical significance not reported). Authors stated no association.
Wilkens 2019	TASD	EL Staging	First CMC	Within group association	Correlation	Kruskal Wallis test	p = 0.37
Weinstock-Zlotnick 2019	DASH	Modified EL grades	First CMC	Within group association	Correlation	Spearman's Rho (95% C.I.)	−0.15 (−0.94, 0.87)
	DASH work	Modified EL grades	First CMC	Within group association	Correlation	Spearman's Rho (95% C.I.)	**0.68 (0.4, 0.94)**
	DASH sport	Modified EL grades	First CMC	Within group association	Correlation	Spearman's Rho (95% C.I.)	−0.4 (−0.98, 0.87)
	M-SACRAH (various)	Modified EL grades	First CMC	Within group association	Correlation	Spearman's Rho (95% C.I.)	All non-significant
	PRWHE (various)	Modified EL grades	First CMC	Within group association	Correlation	Spearman's Rho (95% C.I.)	All non-significant
	PSFS	Modified EL grades	First CMC	Within group association	Correlation	Spearman's Rho (95% C.I.)	0.57 (−0.24, 0.99)
	AHFT (various)	Modified EL grades	First CMC	Within group association	Correlation	Spearman's Rho (95% C.I.)	All non-significant
Ozkan 2007	Dreiser's Functional Index (FIHOA)	Modified KL grades	Various hand joints	Grades 3&4 OA vs. control (grades 0&1)	Difference in FIHOA scores	Difference in mean FIHOA scores, p-value	**6.52 points, p = 0.004**
	Stanford HAQ	Modified KL grades	Various hand joints	Grades 3&4 OA vs. control (grades 0&1)	Difference in HAQ scores	Difference in mean HAQ scores, p-value	**2.45 points, p = 0.025**

AHFT, Arthritis Hand Function Test; EG, Eaton and Glickel; EL, Eaton and Littler; IP, interphalangeal joint (thumb); M-SACRAH, modified Score for the Assessment and quantification of Chronic Rheumatoid Affections of the Hand; MSC-12, Mental Component Score; PCS-12, Physical Component Score; PRWHE, Patient Rated Wrist/Hand Evaluation; PSFS, Patient-Specific Functional Scale; TASD, Trapeziometacarpal joint Arthrosis Symptoms and Disability questionnaire. Statistically significant results shown in bold.

Table V

Osteoarthritis and Cartilage

Association of radiographic measures with function.

and outcomes; however, these are mostly reflections of study design, not poor methodology. Besides heterogeneity concerns, we found that the evidence base is generally of a high quality, with a notable limitation being the sample size of some studies.[32,38,44,45,59] We estimate a low risk of bias due to study designs and methodology.

Meta-analysis

Due to heterogeneity in outcomes, imaging, and specific pain and functional measures utilized, no more than two studies could be combined in a single meta-analysis. Analyses were conducted and forest plots produced for ultrasound PDS and tenderness on palpation odd ratios (ORs)[25,26]; ultrasound PDS and visual analog scale (VAS) pain beta coefficients[42,43]; MRI synovitis and pain on palpation ORs[25,27]; and MRI BMLs and pain on palpation ORs.[25,27] The forest plots and heterogeneity statistics can be viewed in Supplemental Section S.6.

Discussion

Given that there is controversy regarding the relationship between clinical and imaging findings, this systematic review examined the medical literature to determine if an association could be established between imaging findings and radiography-based staging with pain, dysfunction, and longitudinal progression of first CMC OA.

Pain and imaging findings

As noted above, with respect to pain/tenderness, we found that osteophytes stand out as a biomarker of first CMC OA. Three studies showed a strong, dose-dependent, and possibly independent association with pain/tenderness.[19,25,32] In a study of 289 patients using radiography and MRI, Kroon et al.[25] found strong and dose-dependent associations of radiographically-graded osteophytes with tenderness on palpation. Furthermore, with MRI, they found that associations of pain with synovitis or BMLs were attenuated to non-significance by adjusting for the presence of osteophytosis.[25] Two other studies in a total of 552 patients,[19,32] both utilizing radiography and sonography, also found that osteophytes are associated with pain severity in first CMC OA. To our knowledge, only one study has tested the prognostic value of baseline osteophytes in a longitudinal setting.[27] There is potential here for more research.

The relationship between pain and radiographic OA findings is conflicting with only 53.1% of all study results being positive. However, there is strong evidence from three studies (in 2014 patients) that showed positive dose-dependent associations,[24,25,35] and contradict the view[17–20] that patients' radiographic findings and symptoms are unrelated. Positive and negative studies (those reporting significant associations and vice versa) did not differ in mean sample size, number of raters, or age and sex distributions. This adds some reliability and credibility to summary statistics about the highly heterogeneous evidence base. However, evaluation of the association between pain and radiographic findings of OA may still be limited by the heterogeneous methods utilized for quantification of pain and imaging findings in the available evidence.

Author	Pain measure	Imaging	Joint/Joint group	Comparison	Outcome	Measure	Result
Fjellstad 2019	AUSCAN physical function	Gray Scale Synovitis	First CMC	Within patient group. Logistic regression, grades 2-3	Association	Beta coefficient (95% CI)	2.28 (−0.17, 4.72)
	AUSCAN physical function	Power activity	First CMC	Within patient group. Logistic regression, grades 2-3	Association	Beta coefficient (95% CI)	**4.57 (1.23, 7.91)**
Mallinson 2013	DASH	Osteophytes grades (1-4)	First CMC	Within patient group (ANOVA)	Association	F-score, p-value	**F-score not reported, p = 0.017**
	DASH	JSN grade (1-4)	First CMC	Within patient group (ANOVA)	Association	F-score, p-value	F-score not reported, p = 0.427
	DASH	Capsular thickness grade (1-4)	First CMC	Within patient group (ANOVA)	Association	F-score, p-value	F-score not reported, p = 0.735
	DASH	Capsular size (mm)	First CMC	Within patient group (logistic regression)	Association	Beta-coefficient, p-value	Beta not reported, p = 0.121
Naguib 2011	AUSCAN total score	Cartilage thinning	First CMC	Within patient group (correlations)	Correlation	Coefficient, p-value	Not reported, p = 0.08
		Osteophytes	First CMC	Within patient group (correlations)	Correlation	Coefficient, p-value	**Not reported, p = 0.01**
		JSN	First CMC	Within patient group (correlations)	Correlation	Coefficient, p-value	**Not reported, p = 0.001**
Oo 2019	FIHOA	Synovitis	First CMC	Within patient group (logistic regression)	Association	Beta coefficient (95% CI)	−0.35 (−1.47, 0.78)
		PD	First CMC	Within patient group (logistic regression)	Association	Beta coefficient (95% CI)	0.40 (−1.93, 2.72)
		Osteophytes	First CMC	Within patient group (logistic regression)	Association	Beta coefficient (95% CI)	0.21 (−1.52, 1.94)
		Erosions	First CMC	Within patient group (logistic regression)	Association	Beta coefficient (95% CI)	−2.84 (−8.53, 2.86)
Keen 2008	AUSCAN stiffness	No. of joints with synovitis (GS), synovitis (PD), osteophytes and JSN	Various hand joints*	Joint level analysis	Correlation	Spearman's rho (p-value)	0.213 (0.212), 0.098 (0.568), 0.181 (0.292), 0.217 (0.204)
	AUSCAN function	No. of joints with synovitis (GS), synovitis (PD), osteophytes and JSN	Various hand joints*	Joint level analysis	Correlation	Spearman's rho (p-value)	0.051 (0.766), -0.043 (0.805), 0.067 (0.700), 0.113 (0.510)
Shi 2021	FIHOA	Synovitis PD Osteophytes	First CMC	Association of FIHOA with sonography measures	Results of multivariate regression	Beta coefficients, p-values	0.58 (0.17) −0.79 (0.34) 0.82 (0.09)

ANOVA, Analysis of Variance; GS, gray scale. Statistically significant results shown in bold. *Including first CMC joint.

Table VI

Association of sonographic measures with function.

Osteoarthritis and Cartilage

Author	Progression outcome	Imaging	Joint/Joint group	Comparison	Evaluation	Measure	Result
Bijsterbosch 2011	Change in self-reported pain scores (AUSCAN)	Sum of radiographic osteophyte scores	Whole hand	Participants with and without radiographic progression	Change over 6 years	Adjusted mean difference	−0.14 (−1.21, 0.92)
	Change in AUSCAN function scores	Sum of radiographic JSN scores	Whole hand	Participants with and without radiographic progression	Change over 6 years	Change in mean scores	−0.57 (−2.36, 1.22)
Botha-Scheepers 2009	Change in AUSCAN pain and function scores	Progression of Radiographic Osteophytes and JSN (OARSI)	Whole hand	Follow-up compared to baseline (2 years)	Association	Results from linear mixed models	Not reported, authors stated no association
	Progression of JSN over 2 years	Radiographic JSN (OARSI)	Whole hand	Baseline pain in those with and without JSN progression	Difference between groups	Mean difference	1.8 (0.2, 3.4)
	Progression of osteophytes over 2 years	Radiographic Osteophytes (OARSI)	Whole hand	Baseline pain in those with and without osteophyte progression	Difference between groups	Mean difference	No difference
Gil 2022	18-month changes in PRWHE	EL grades	First CMC	Subjects with and without radiographic progression	Odds of increased: PRWHE Pain PRWHE Function (specific) PRWHE Function (usual) PRWHE total	Odds ratios (95% C.I.)	1.01 (0.97, 1.06) 1.02 (0.99, 1.06) 1.05 (0.98, 1.13) 1.01 (0.99, 1.04)
	36-month changes in PRWHE	EL grades	First CMC	Subjects with and without radiographic progression	Odds of increased: PRWHE Pain PRWHE Function (specific) PRWHE Function (usual) PRWHE total	Odds ratios (95% C.I.)	**1.05 (1.01, 1.11)** 1.03 (0.99, 1.07) 1.01 (0.96, 1.07) 1.02 (1.00, 1.05)
	18-month changes in AUSCAN	EL grades	First CMC	Subjects with and without radiographic progression	Odds of increased: AUSCAN Pain AUSCAN Function AUSCAN Stiffness AUSCAN Total	Odds ratios (95% C.I.)	1.07 (0.95, 1.20) 0.92 (0.55, 1.56) 1.03 (0.96, 1.11) 1.02 (0.98, 1.07)
	36-month changes in AUSCAN	EL grades	First CMC	Subjects with and without radiographic progression	Odds of increased: AUSCAN Pain AUSCAN Function AUSCAN Stiffness AUSCAN Total	Odds ratios (95% C.I.)	0.97 (0.86, 1.10) 1.33 (0.78, 2.26) 1.02 (0.95, 1.09) 1.01 (0.96, 1.05)
Haara 2004	Mortality in men	KL grades	First CMC	Advanced radiographic OA (KL 3-4)	Follow-up of up to 17 years	Risk Ratio	**1.32 (1.03, 1.69)**
	Incidence of work disability	KL grades	First CMC	KL grade ≥2	Follow-up of up to 17 years	Risk Ratio	0.91 (0.61, 1.38)
	Incidence of work disability	KL grades	First CMC	KL grades (3-4)	Follow-up of up to 17 years	Risk Ratio	1.47 (0.65, 3.31)
Haugen 2013	Incident pain on palpation	KL grades	PIP, DIP and First CMC joints	Incident increase in KL grades (1-4) vs. no change	Odds of pain present	Odds ratios (95% C.I.)	1.2 (0.7-2.0) 1.5 (0.9-2.4) **5.7 (3.0-11)** **11 (4.0-33)**
	Incident pain on palpation	Radiographic Osteophytes	PIP, DIP and First CMC joints	Incident increase in feature vs. no change	Odds of pain present	Odds ratio (95% C.I.)	1.6 (1.0, 2.4)
		Radiographic JSN	PIP, DIP and First CMC joints	Incident increase in feature vs. no change	Odds of pain present	Odds ratio (95% C.I.)	**2.1 (1.2, 3.7)**
		Malalignment	PIP, DIP and First CMC joints	Incident increase in feature vs. no change	Odds of pain present	Odds ratio (95% C.I.)	**6.2 (3.2, 12)**
		Cysts	PIP, DIP and First CMC joints	Incident increase in feature vs. no change	Odds of pain present	Odds ratio (95% C.I.)	2.2 (0.9, 5.0)
		Sclerosis	PIP, DIP and First CMC joints	Incident increase in feature vs. no change	Odds of pain present	Odds ratio (95% C.I.)	2.4 (0.8, 8.0)

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Table VII (*continued*)

Author	Progression outcome	Imaging	Joint/Joint group	Comparison	Evaluation	Measure	Result
Mallinson 2013	Change in DASH score post injection	Sonography-evaluated osteophytes & JSN grades, capsular thickness	First CMC	Within group association	Association (ANOVA) between baseline sonography metrics and change in DASH	F-scores, p-values	F-scores not reported Osteophytes ($p = 0.568$), JSN ($p = 0.627$), capsular thickness ($p = 0.218$)
Mathiessen 2015	Progression in KL grades after 5 years	Sonography-graded gray scale synovitis	Whole hand	Increasing grades of gray-scale synovitis (grades 0-3)	Baseline synovitis as a predictor of progression	Odds Ratios (95% CI)	1.0 (reference) **2.8 (1.8, 4.2)** **3.6 (2.2, 5.8)** **15.2 (6.9, 33.6)**
		US-graded power doppler activity	Whole hand	Increasing grades of power doppler activity (grades 0, 1, 2-3)	Baseline power doppler activity as a predictor of progression	Odds Ratios (95% CI)	1.0 (reference) **2.9 (1.2, 6.8)** **12.0 (3.5, 41.0)**
van Beest 2021	Increase in pain on palpation (2 years)	Increase in synovitis (MRI)	First CMC	Increase in synovitis vs. stable/ decrease	Odds of pain increased	Odds Ratio (95% CI)	**3.44 (1.28-9.3)**
	Increase in pain on palpation (2 years)	Increase in BMLs (MRI)	First CMC	Increase in BMLs vs. stable/ decrease	Odds of pain increased	Odds Ratio (95% CI)	**5.1 (2.10-12.6)**
	Increase in pain on palpation (2 years)	Baseline radiographic osteophytes	First CMC	Present vs. absent	Odds of pain increased	Odds Ratio (95% CI)	1.73 (0.73, 4.1)
	Decrease in pain on palpation (2 years)	Decrease in BMLs (MRI)	First CMC	Decrease in BMLs vs. stable/ increase	Odds of pain decreased	Odds Ratio (95% CI)	2.67 (0.80-8.9)
	Decrease in pain on palpation (2 years)	Baseline radiographic osteophytes	First CMC	Present vs. absent	Odds of pain decreased	Odds Ratio (95% CI)	0.78 (0.26, 2.28)

DIP, distal interphalangeal joint; EL, Eaton and littler grading; PIP, proximal interphalangeal joint. Statistically significant results shown in bold.

Table VII

Longitudinal findings on first CMC OA progression.

Osteoarthritis and Cartilage

With regard to staging systems, results from this review suggest that the KL classification may show a stronger association with pain compared to Eaton and other systems. The reason for this is possibly related to differences in study design (e.g., studies using KL generally evaluated large populations of non-operative patients, whereas Eaton staging was generally used in studies on orthopedic surgery patients, which had smaller sample sizes and likely a narrower range of radiographic stages and pain). It may be, however, that the KL system does have a stronger association with pain than other staging systems or individual metrics. The KL group of studies did not differ from other radiographic studies in mean sample size (population-based studies excluded), raters, or age and sex distributions ($p > 0.05$). Furthermore, after excluding population-based studies, all studies (3/3) that used KL reported positive results, compared to 3 of 9 that used other staging or metrics, including Eaton. This could also be due to differences between the two systems such as their definition of late-stage disease (stage 4 in each). The Eaton system includes progression to the scaphotrapeziotrapezoidal joint (STT), as well as subluxation in stage 4, whereas KL classifies it as a simple progression from stage 3. The latter system may be more predictive of CMC joint osteoarthritic progression, and this could make it more sensitive to pain.

Among the associations of sonography- and MRI-derived biomarkers with pain there are also strong results, namely, for sonography, those using gray scale synovitis, PDS and osteophytes[26,32,43] (Table III), and for MRI, those using synovitis and BMLs[25,27] (Table IV). In the sonography group, positive and negative studies did not differ in mean sample sizes, raters, age, or proportion of female participants. MRI studies differed only in that they had a higher proportion of female participants compared to the average across all studies, which could have influenced their findings given a reported higher sensitivity to pain reported among females.[60]

Functional status and imaging findings

With respect to physical dysfunction, we found that there was no compelling association across imaging modalities (73% of results were negative). In four of eight studies that used radiography, KL staging was positively associated with physical dysfunction.[50,53,54,58] In two sonography studies, graded osteophytes were associated with physical dysfunction measured with the AUSCAN and DASH questionnaires.[32,55] However, most studies show negative results. Positive and negative studies did not differ in number of raters, sample size, or in their age and sex distributions. Therefore, we estimate little influence of these parameters on the overall lack of association between imaging and functional status. However, there were several studies that strongly suggest that radiography and sonography are able to detect clinically important differences in function. We suggest that future research incorporate MCIDs and present their results in a manner in which this can be easily assessed.[19]

No studies examined the association of CT or MRI findings with physical function. This could be an area for future research.

Progression of OA and imaging findings

Regarding the association of imaging findings with the longitudinal progression of first CMC OA, we found only 8 studies.[23,24,27,41,55–58] Limited associations of imaging findings with progression of first CMC OA were found, but future research is needed.

Meta-analysis

As discussed, due to heterogeneity in outcomes, imaging, and utilized measures, only a maximum of two studies could be combined for a given outcome. This limits the insight that can be drawn but does provide a framework for future research to add to. From our analyses, MRI-detected synovitis and BMLs show promise as markers of pain (Sections S.6.4, S.6.5). However, some of the meta-analyses show high heterogeneity statistics. We therefore suggest caution in interpreting the results of these small meta-analyses.

Limitations

There are limitations to consider when interpreting the findings of this review. Most importantly, the heterogeneity of measurements of clinical and imaging variables and scoring systems limits comparison of results between studies. Secondly, the study populations were also of significant heterogeneity. The most common limitation in this evidence base is a lack of prospective cohort or observational studies.

Future research should aim to use more consistent definitions of clinical and imaging measures and grading systems to increase cross-study interpretability and results synthesis. This could enable meta-analysis of other outcomes or the addition of studies to ours, so as to reach more firm conclusions. There is the possibility for creating new scoring systems based on weighting of imaging markers (e.g., osteophytes or synovitis) or even including multiple domains (e.g., imaging markers, clinical symptoms, functional performance, and laboratory data on inflammatory markers). Newer methods to assess joints of the hand in real-time using CT and MRI during motion have become available,[61,62] and they could provide additional biomarkers based on first CMC joint mechanics.[62,63] Lastly, molecular imaging modalities such as single photon emission computed tomography and positron emission tomography have shown initial promise in assessing measures of bone turnover, local blood flow and glucose metabolism.[64–66] These could possibly better reflect the symptomatology of first CMC OA, which could in turn contribute to improved clinical decision making, patient stratification, and objective treatment evaluation.

Conclusion

This review demonstrates that imaging measures and radiography-based scoring systems generally show moderate and sometimes strong correlations with clinical pain assessments. However, these same measures do not appear able to consistently predict functional status or disease progression. This review therefore calls for improved imaging techniques to help physicians manage patients with first CMC OA.

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Competing interest statement

None of the authors have competing interests. We derive no financial benefits from this work.

Author contributions

Dr. Robert D. Boutin and Abhijit J. Chaudhari take overall responsibility for the integrity of this work. Conception and design: DFM, RMS, AJC, RDB. Collection and assembly of data: DFM, PSB, AA, RDB. Analysis and interpretation of the data: DFM, COB, RMS, AJC, RDB. Drafting of the article: DFM, PSB, AA, AJC, RDB. Critical revision of the article for important intellectual content: DFM, COB, RMS, AJC, RDB. Final approval of the article: DFM, PSB, AA, COB, RMS, AJC, RDB. Provision of study materials or patients: RMS, AJC, RDB. Statistical expertise: DFM, AJC. Obtaining of funding: AJC, RDB.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.joca.2023.11.023.

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