MRI and serum biomarkers correlate with radiographic features in painful hand osteoarthritis

C.H. Roux[1], V. Foltz[2], E. Maheu[3], G. Baron[4], F. Gandjbakhch[2], C. Lukas[5], D. Wendling[6], D. Loeuille[7], P. Lafforgue[8], L. Euller-Ziegler[1], P. Richette[9], X. Chevalier[10], on behalf of the French section of osteoarthritis

[1]Rheumatology Department, CHU Archet 1, LAMHESS EA6309, University of Nice Sophia Antipolis, France; [2]Rheumatology Department, University of Paris VI, CHU Pitié Salpétrière, France; [3]Rheumatology Department, Saint Antoine Hospital, AP-HP, Paris, France; [4]Epidemiology and Biostatistics Department, INSERM, U738, Bichat-Claude Bernard Hospital Group, Paris, France; [5]Rheumatology Department, Lapeyronie Hospital, Montpellier, France; [6]Rheumatology Department, CHRU Besançon, France; [7]Rheumatology Department, CHU Nancy-Brabois, Nancy, France; [8]Rheumatology Department South, CHU Sainte Marguerite, Marseille, France; [9]Rheumatology Department, Lariboisiére Hospital, Paris, France; [10]Rheumatology Department, Henri Mondor Hospital, Creteil, France.

Abstract

Objective

To explore the relationship between clinical findings, biologic biomarkers, conventional radiography and MRI in patients with painful hand OA.

Methods

The following patient baseline data from the DORA study (evaluating anti-TNF-α agents against painful hand OA) were used: clinical assessment (pain, swelling, stiffness and function: Dreiser functional hand index [FIHOA] and Cochin hand functional scale [CHFS]); measurement of biomarkers (cartilage oligomeric matrix protein (COMP), type IIA collagen N-propeptid (PIINP), hyaluronic acid (HA), ultrasensitive C-reactive protein (usCRP), tumour necrosis factor (TNF), interleukin (IL)-6, IL-1β and urinary CTXII); radiological staging (Verbruggen, Kallman, Kellgren-Lawrence); anatomical evaluation by contrast-enhanced MRI of proximal and distal interphalangeal joints of dominant hand. Associations between clinical, biomarker and imaging findings were assessed using the Spearman correlation coefficient and test.

Results

18 patients were recruited, and 144 joints studied. A correlation was found between clinical features (pain, FIHOA, CHFS) and the Verbruggen score (respectively: p=0.05, r=0.47; p=0.05, r=0.48; p=0.05, r=0.48). Serum IL-1 level was strongly associated with loss of function (FIHOA: p=0.02, r=-0.73; CHFS: p=0.01, r=-0.76) and radiological erosions (p=0.03, r=0.7) as with urinary CTX2. A significant association was found between MRI osteophytes and usCRP (p=0.0026). MRI and radiological features were significantly correlated except for synovitis and bone marrow lesions.

Conclusion

MRI synovitis was not correlated with radiological scores, clinical or biologic markers of inflammation. There was a strong correlation between other MRI features and radiological scores. Serum IL-1 level was associated with structural damage and function.

Key words

hand osteoarthritis, MRI, radiology, biologic markers

*Christian Hubert Roux, MD, PhD**
*Violaine Foltz, MD**
Emmanuel Maheu, MD
Gabriel Baron, MD
Frederique Gandjbakhch, MD
Cedric Lukas, MD, PhD
Daniel Wendling, MD, PhD
Damien Loeuille, MD, PhD
Pierre Lafforgue, MD, PhD
Liana Euller-Ziegler, MD, PhD
Pascal Richette, MD, PhD
Xavier Chevalier, MD, PhD

on behalf of the French section of osteoarthritis.

**Joint first authors who contributed equally to this work.*

Please address correspondence to:
Christian Hubert Roux,
Hôpital Pasteur,
30 voie Romaine, CS 51069,
06001 Nice cedex 1, France.
E-mail: roux.c2@chu-nice.fr

Received on December 1, 2015; accepted in revised form on March 7, 2016.

Competing interests: none declared.

Introduction

Hand osteoarthritis (OA) is the most frequent form of OA. Its prevalence in the general population over 55 years has been estimated at 56%, including 11% of symptomatic forms (Rotterdam study) (1). Despite the high frequency of hand OA, people with hand OA have received limited attention from clinicians and researchers, probably due to the lack of suitable therapeutics. Conventional radiography (CR) is the most economical, easily available and commonly used imaging modality for the assessment of structural hand OA (2). However, CR does not give any information on synovial and subchondral inflammation. These anatomical changes are very important in our understanding of the disease pathogenesis and progression. Biological markers may be regarded as surrogate markers of inflammation and bone changes in knee OA, but their validity is still a matter of debate (3).

The ability to explore all articular and periarticular structures is a major advantage of magnetic resonance imaging (MRI) (2).This is the best imaging technique for exploring bone turnover and inflammation of the synovial membrane (4). MRI is also significantly more sensitive than x-rays for the detection of erosions (5).

MRI screening of knee OA shows that while bone and synovitis are associated with pain, bone marrow lesions, meniscal damage are associated with structural changes.

Currently, only limited research on the prevalence, reliability, and validity of MRI-defined anomalies in hand OA is available (5-9). The few studies evaluating associations between CR features and clinical symptoms conclude that the association is weak to moderate (10, 11). Some studies suggest that inflammatory changes on MRI may be linked to the level of pain (12). However, studies on the diagnostic value of biological markers in hand OA are very limited (3, 13, 14).

Our objective was to explore associations between clinical findings, biologic biomarkers (BB), CR and MRI in painful hand OA unresponsive to usual analgesics and non-steroidal anti-inflammatory drugs (NSAIDs), in order to understand the hand OA pathogenesis better.

Patients and methods

The data used in this study are from the recently published DORA (digital osteoarthritis in refractory hand OA) study evaluating efficacy of anti-tumour necrosis factor (TNF) activity (15). Briefly, this is a phase 3, randomised, double-blind (patients and outcome assessors), parallel, placebo-controlled, 26-week, multicentre trial (16 sites in France) with the TNF blocker adalimumab (one subcutaneous injection at week 0 and week 2). The main inclusion criteria were patients aged between 40 and 80 with painful hand OA over 40 mm on a 100 mm visual analogue scale (VAS) meeting the classification criteria of the American College of Rheumatology for hand OA, (involving at least 3 interphalangeal joints) with at least 3 OA joints with Kellgren-Lawrence (KL) grade >2 on recent x-rays, and who did not respond to analgesics or NSAIDs. Exclusion criteria included women of child-bearing age who are not using contraception, previous therapies by TNF-α blockers, secondary hand OA (to previous inflammatory diseases). No difference was observed for the primary endpoint, which was the proportion of patients with at least a 50% improvement in their baseline pain score at week 6. For the present study, we used all the baseline clinical data (15).

Clinical and x-ray assessments (Verbruggen, (KL) and Kallman scores) (16-18) are described in the original paper (15).

Only patients from 2 centres underwent dedicated 0.2 Tesla MRI (C-Scan EsaoteBiomedica, Genoa, Italy).

The protocol and amendments were approved by the independent Ethics Committee(s) from Henri Mondor Hôpital (Comité de Protection des Personnes. Créteil, France). The study was conducted in accordance with the International Conference on Harmonisation Guideline for Good Clinical Practice and Declaration of Helsinki. This trial has been registered at ClinicalTrials.gov (n°NCT00597623).

Imaging assessment

Patients underwent postero-anterior x-ray of both hands and one reader (EM) scored the bilateral 2nd–5th distal interphalangeal (DIPs), 2nd–5th proximal interphalangeal (PIPs), thumb interphalangeal, 1st–5th metacarpophalangeal, 1st carpometacarpal and scaphotrapezial joints according to the KL scale (grade 0–4 for each joint), Verbruggen score (anatomical score: N (normal), S (stable OA without erosion or total pinching), J (phase when the joint space disappears), E 'erosion), R (remodelling) and Kallman grading scale (16-18). These scores are usually used for digital osteoarthritis scoring. As our goal is an MRI comparison for the PIPs and DIPs of the dominant hand, only these joints were analysed in the dominant hand (for KL, min–max scores were 0–32; for Verbruggen: 0–70.2; for Kallman: joint space narrowing (JSN) 0–57, osteophytes 0–57, erosions 0–9).

All MRI images were blinded for identifying data and read by two experienced rheumatologists (both members of OMERACT) independently and according to the score developed for RA (19), used by Tan *et al*. for hand OA (8). A training session was performed before. MRI scoring was performed blind (to) for radiographic scoring and clinical manifestations. The following anatomical lesions were evaluated: synovitis, tenosynovitis, erosive damage, bone cysts, osteophytes, JSN, bone marrow lesions (BML), and malalignment (Table I). Each feature was scored using a semi-quantitative scale (0 to 3) except for erosions, which were scored on a 0–10 scale, and malalignment (as well as effusion, synovitis, cartilage defects, osteophytes), scored dichotomously (absent/present).

Readers rescored 5 randomly selected MRI scans after a period of at least 1 week and the intra-reader reliability assessed by κ and intra-class correlation coefficients was calculated.

The 2nd–5th DIPs and PIPs joints of the dominant hand of each participant were selected for MR scanning. The imaging protocol comprised 3D T1 coronal and axial spin echo (SE) (repetition time 440 ms, echo time 26 ms, 1 mm slice thickness) before and after administration of 0.2 mmol/kg ml intravenous gadolinium diethylene tetrapentaacetic acid (Gd-DTPA). Imaging was completed using STIR sequences in the coronal and axial planes (repetition time 500 ms, echo time 18 ms, 2 and 3 mm slice thickness, respectively). MR scans were performed before the first injection of adalimumab.

Biologic assessment

Serum markers (cartilage oligomeric matrix protein (COMP), type IIA collagen N-propeptid (PIINP), hyaluronic acid (HA) ultrasensitive C-reactive protein (usCRP), level of cytokines TNF, interleukin (IL)-6, IL-1 and urinary level of CTX-II were measured at W0 and W6 in the Synarc laboratory in Lyon. Details of techniques have already been published (15).

Statistical analysis

All statistical analyses were performed at an independent centre (Hotel-Dieu hospital, Paris, France), using SAS software, v. 9.3 (SAS Institute Inc). Analyses were performed on the population that underwent MRI (18 patients). Only the dominant hand was analysed.

Patient characteristics for our study are described as mean and standard deviation for quantitative variables and percentages for qualitative variables. Relationships between clinical findings, CR, MRI and biologic biomarkers (BB) at baseline were assessed using the Spearman correlation coefficient and test. We also repeated the analysis for each MRI finding (synovitis, BML, erosions, JSN, osteophytes), each CR score (Kallman: osteophytes PIPs and DIPs, JSN PIPs and DIPs and erosion; Verbruggen: global score, number of OA joints and number of erosive joints; KL: PIPs and DIPs and number of joints with KL ≥2), each clinical parameter (pain [VAS, 0-100], Dreiser functional index for hand osteoarthritis [FIHOA] (20), Cochin hand functional scale [CHFS] (21), number of painful joints on pressure [0–30], number of swollen joints [0–30], number of spontaneously painful joints [0–30]) and each biologic parameter (COMP, HA, usCRP, PIIANP, IL-1β, IL-6 ,TNF-α and urinary level of CTXII).

Inter-rater agreement for PIPs and DIPson MRI was assessed using weighted (Cicchetti-Allison weights) κ coefficient (with 95% confidence interval).

Intra and inter-observer agreement (VF, FG) for MRI were calculated on PIP2 and DIP2 using a ponderated kappa coefficient estimation and a confidence interval (to) at 95%. Inter-observer agreements were evaluated for PIP2 and DIP2 and were moderate: synovitis (PID: κ=0.56 [95% CI:0.28–0.85]; PIP: κ=0.27 [95% CI:0.02–0.56]), erosions (PID: κ=0.16 [95% CI:0.01–0.32]; PIP: κ=0.28 [95% CI:0.01–0.56]), BML(PID: κ=0.55[95% CI:0.21–0.88]; PIP: κ=0.80[95% CI:0.66-0.96]), JSN (PID: κ=0.57 [95% CI:0.32–0.81]; PIP: κ=0.47 [95% CI:0.18–0.77]), osteophytes (PID: κ=0.15 [95% CI:0.10–0.39]; PIP: κ=0.32 [95% CI:0.02–0.61]). Intrareader reliability has been evaluated: synovitis (κ=0.33[95% CI:0.11–0.57]), erosions (κ=0.18 [95% CI:0.04–0.48]), BML (κ=0.66 [95% CI:0.26–0.86]), JSN (κ=0.70 [95% CI:0.34–0.89]) and osteophytes (κ=0.27 [95% CI: 0.0–0.58].

Results

Patients

Eighteen patients were recruited, for a total of 144 joints studied. Mean age was 64.4 years (SD 7.0). Participants were mainly women (77.8%). Mean pain score was 65 mm (13) (VAS, 0–100); mean number of spontaneously painful joints was 9.6 (5.4). Clinical and demographic characteristics of the patients are shown in Table II. One patient did not have any radiographic data and another did not have Kallman scoring.

Correlation between radiological and clinical manifestations of hand OA

A significant correlation was found between clinical features and radiological scoring. A relationship was found between pain and different radiological scoring systems: Verbruggen score (r=0.47, *p*=0.05), KL (r=0.6, *p*=0.008). Other relationships have been demonstrated between function (Dreiser functional hand index [FIHOA] and Cochin hand functional scale [CHFS]) and radiological scoring: Verbruggen score (r=0.5, *p*=0.05; r=0.48, *p*=0.05 re-

Table I. Scoring system, example for proximal interphalangeal (PIP).

PIP	2		3		4		5	
	lateral	medial	lateral	medial	lateral	medial	lateral	medial
Synovitis (0-3)								
Flexor tenosynovitis (0-3)								
Erosions proximal P1 (0-10								
Erosions distal P2 (0-10)								
Joint space narrowing (0-3)								
Bone marrow oedema: proximal P1 (0-3)								
Bone marrow oedema: distal P2 (0-3)								
Presence of collateral ligament (0-1)								
Thinning of collateral ligament (0-1)								
Cysts (0-1)								
Bone osteophytes: proximal P1 (0-3)								
Bone osteophytes: distal P2 (0-3)								
Luxation (coronal and sagittal)								

Table II. Demographic and clinical characteristics of patients in the DORA study.

Baseline characteristics		All patients n=18	
Age, years		64.4	(7.0)
Women, n (%)		14	(77.8%)
Weight, kg		64.1	(9.4)
Height, cm		165.5	(8.2)
Body mass index, kg/m^2		23.4	(2.8)
Duration of disease (years)		12.6	(10.7)
Dominant side affected, n (%)	Right	10	(55.6%)
	Left	4	(22.2%)
	Same	4	(22.2%)
Manual activities >4h, n (%)		13	(72.2%)
Familial history of hand OA, n (%)		17	(94.4%)
Pain score (VAS, 0-100 mm)		65.3	(13.2)
Morning stiffness (min)		33.1	(37.4)
No of painful joints (spontaneous; 0-30)		9.6	(5.4)
No of painful joints (pressure; 0-30)		13.3	(4.8)
No of swollen joints (0-30)		5.8	(4.4)
Dreiser FIHOA (range 0-30)		15.2	(6.4)
CHFS (range 0-90)		36.9	(21.5)
Physician global assessment (VAS, 0-100 mm)		63.0	(15.2)
Patient global assessment (VAS, 0-100 mm)		65.6	(16.6)
Current treatments, n (%)		15	(83.3%)
Acetaminophen		12	(66.7%)
NSAIDs		8	(44.4%)
Analgesics level 2		3	(16.7%)
Orthesis		1	(5.6%)
Anatomic Verbruggen radiological score			
Number of osteoarthritis joints (Verbruggen)		6.9	(2)
Number of erosive joints (Verbruggen)		1.9	(2)
Kellgren-Lawrence			
Score DIP/PIP (0-32)		21.5	(7)
Number of osteoarthritic joints		6.9	(2)
Kallman score			
Osteophytes score DIP/PIP (0-57)		1.1	(1)
Joint space narrowing score DIP/PIP (0-57)		0.4	(1)
MRI variables			
Synovitis (0-24)		8.7	(3.6)
Erosive (0-80)		7.9	(4.36)
Bone medullar lesion (0-24)		5.5	(4.2)
Joint space narrowing (0-24)		15.9	(5.7)
Osteophytes		4.6	2.4)

OA: osteoarthritis; FIHOA: Functional Index for Hand OA; CHFS: Cochin Hand Function Scale; VAS: visual analogue scale. Results are presented as mean (SD) or number (n) of patients (%).

spectively), KL score (r=0.6, p=0.007; r=0.6, p=0.02) and Kallman narrowing score (with FIHOA: r=0.5, p=0.03) (Table III).

Correlation between radiological and MRI features of hand OA

MRI-defined synovitis and BML were not associated with any radiological scores.

On the one hand, MRI erosions were associated with Verbruggen score (r=0.53, p=0.03,) in PIPs and DIPs as well as with erosions on the Kallman erosive score (in one hand) (r=0.6, p=0.02) and with Kallman JSN score, on the other hand (r=0.6, p=0.02). MRI JSN was strongly associated with different radiological scoring systems: Verbruggen score (r=0.6, p=0.006), KL score (r=0.5, p=0.05), number of OA joints with KL grade ≥2 (r=0.5, p=0.03), Kallman erosive score (r=0.6, p=0.008) and Kallman JSN score (r=0.8, p=0.0007). Osteophytes detected by MRI were significantly associated with all radiological scores, as shown in Table IV.

Correlation between MRI and clinical symptoms of hand OA

No correlation was found between clinical manifestations (pain and function) and any MRI features (synovitis, BMLs, erosions, JSN, osteophytes) (data not shown).

Correlation between clinical features of imaging (x-rays and MRI) and biologic biomarkers of hand OA

IL-1 serum level was significantly negatively associated with FIHOA and CHFS scores (r=-0.73, p=0.02; r=-0.76, p=0.01). No clinical symptoms were associated with any other biologic biomarkers.

Radiographic features (Kallman score and KL) were significantly positively associated with PIIANP (respectively: r=0.6, p=0.03 and r=0.5, p=0.05) as usCRP with Verbruggen score (r=0.51, p=0.04 and KL severity score (r=0,48, p=0,05). IL-1 level was strongly negatively correlated with different radiological scores: Verbruggen (r=-0.7, p=0.03), and Kallman (erosive score) (r=-0.7, p=0.03).

Table III. Correlations between radiological scores and clinical features (PIPs and DIPs).

	Radiographic scores					
	Verbruggen score	Kellgren-Lawrence score	Number of OA joints and KL≥2	Kallman score		
Clinical	r (p)	r (p)	r (p)	Osteophytes r (p)	Erosive r (p)	Narrowing r (p)
Pain intensity	**0.5 (0.05)**	**0.6 (0.008)**	**0.6 (0.02)**	NS	NS	NS
Number of painful joints	NS	NS	NS	NS	NS	NS
FIHOA	**0.5 (0.05)**	**0.6 (0.007)**	NS	NS	**0.5 (0.05)**	**0.5 (0.03)**
CHFS	**0.5 (0.05)**	**0.6 (0.02)**	**0.5 (0.07)**	NS	NS	**0.5 (0.07)**
Number of joint pains	NS	NS	NS	NS	NS	NS
Number of swollen joints	NS	NS	NS	**-0.5 (0.06)**	NS	NS

FIHOA: Dreiser Functional Index for Hand OA; CHFS: Cochin Hand Function Scale; NS: non significant; r: coefficient of correlation; p: *p*-value considered significant if less than 0.05. Numbers have been rounded off.

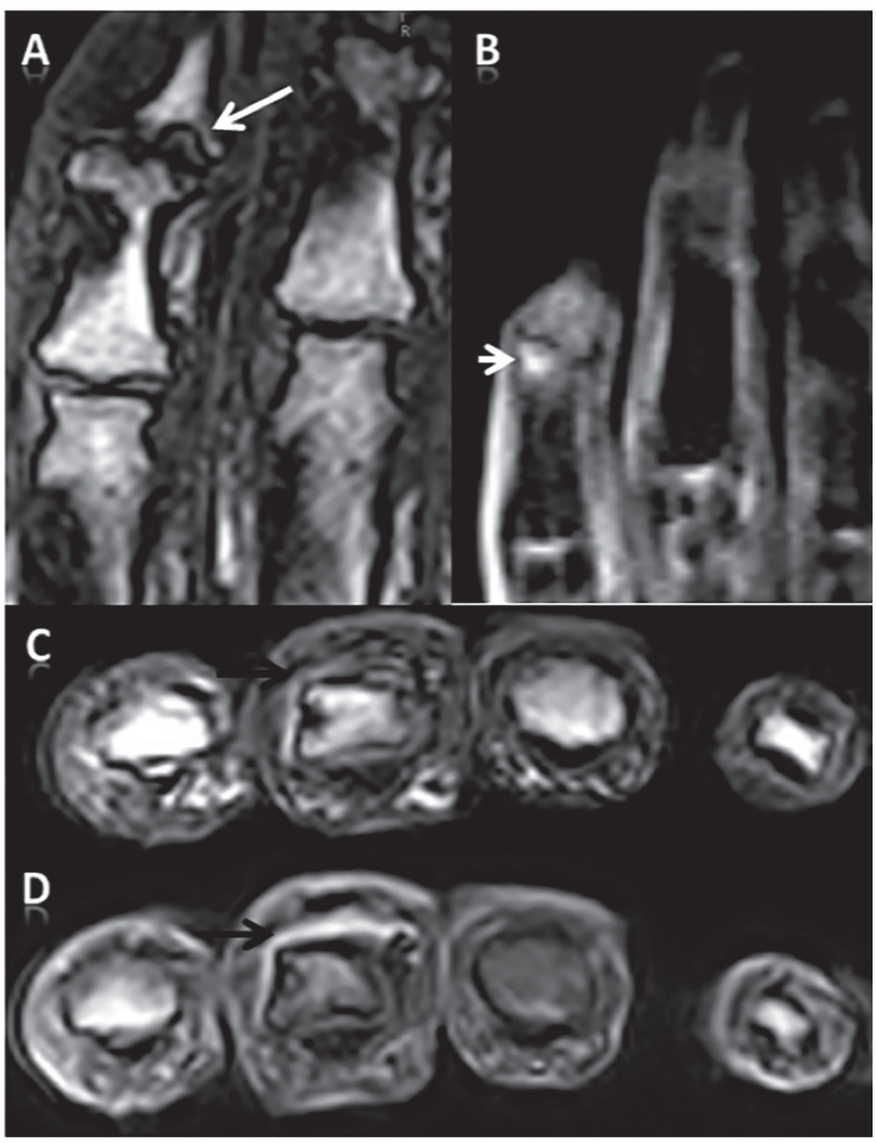

Fig. 1. Different MRI osteoarthritis features demonstrating erosion, bone marrow lesion and synovitis. **A**: Coronal T1 DIP 2 showing a marginal erosion. **B**: Coronal STIR demonstrating a bone marrow oedema in DIP 2. **C**: Axial T1 before gadolinium injection PIP 3. **D**: Axial T1 following gadolinium injection showing PIP 3 synovitis.

The only significant association found between the level of a biomarker and MRI features was between osteophytes and usCRP (r=0.7, *p*=0.0026).

Discussion

Our study found a relationship between Clinical data (function) and most radiographic severity scores but not with the different features of MRI. There is a strong correlation between some MRI features (erosions, JSN, osteophytes) and the radiological scores. However, the presence of a MRI synovitis is not associated with the severity of radiographic damage nor with a rise in biological markers. Some biologic markers, such as IL-1, were associated with structural damage and function.

Reported associations between radiographic hand OA abnormalities and hand disability are inconsistent, ranging from no to moderate association (22). A recent study using the Australian-Canadian index (AUSCAN) and the Arthritis impact Measurement Scale (AIMS 2) to assess physical function, found no relationship between functional impairment and MRI features (23). Our results confirm the lack of correlation with MRI but show an association between the severity of radiographic damage and functionality. This is in agreement with Wittoek *et al's* study showing that in 270 patients the functional handicap is associated with the number of radiologically affected IP joints (24). MRI is probably more appropriate to look for items such as subclinical synovitis and bone oedema. X rays, on the other hand; show more clearly large lesions with a higher clinical impact. The cause of pain in OA remains largely unknown even though new imaging technology is helping to define associations between pain and structural changes better. Pain and radiological scores seem to be linked in our study, with a strong correlation between pain and KL score and also with the number of OA joints with KL ≥2. In earlier CR studies, limited associations were demonstrated and the strength of the association varied according to the study (22). The use of global scores combining in a single score all the signs of several affected IP joints may

Table IV. Correlations between radiological scores and MRI features (DIP and PIP).

	Radiographic scores				
	Verbruggen	Kellgren-Lawrence	Kallman		
MRI scores	r (p)	r (p)	Osteophytes r (p)	Erosions r (p)	Narrowing r (p)
Synovitis	NS	NS	NS	NS	NS
Erosions	0.5 (0.05)	NS	NS	**0.6 (0.02)**	**0.6 (0.02)**
Bone marrow lesions	NS	**0.4 (0.09)**	**0.6 (0.008)**	NS	NS
Joint space narrowing	**0.6 (0.006)**	**0.5 (0.05)**	NS	**0.6 (0.008)**	**0.7 (0.0007)**
Osteophyte	**0.7 (0.003)**	**0.7 (0.001)**	**0.7 (0.007)**	**0.6 (0.01)**	**0.5 (0.04)**

NS: non significant; r: coefficient of correlation; p: *p*-value considered significant if less than 0.05. Numbers have been rounded

explain the variability of results (11). Kortekaas found a strong dose-dependent association between pain and the two main OA features, (which are) that is osteophytes and JSN, but this association disappeared when summated scores of structural abnormalities were used (11). This finding has not been observed in our study. Another interesting point is the absence of a link between clinical swelling of the IP joints and any CR score. Is it because the swelling is a translation only of synovitis and that the latter is independent of the observed structural lesions on CR ? This remains unclear.

Previous studies in knee OA have observed that both synovitis and BMLs are associated with pain (25, 26).The role of BML seems less clear in digital OA than for knee osteoarthritis. Haugen found a weak association between BML and pain in digital OA, a condition not found in our study (23).

The weak correlations between BMLs and radiological evaluations are consistent with the findings of Haugen and colleagues who found a low prevalence of BMLs in hand OA (5), which contrasts with the high prevalence shown in the smaller studies (28, 29). This may be due to partial volume artifacts mimicking BMLs (29). In our work, there was a good correlation between MRI and x-ray for the detection of erosions. Many studies have shown that MRI (high-resolution MRI) is more sensitive than x-rays at detecting erosions, especially marginal erosions in hand OA (5, 6, 27, 29). As the number of patients in our study is limited, erosions localisation is not (considered) taken into account.

The lack of a relationship between the different radiographic scores and MRI-detected synovitis is worth noting and has previously been observed not only in hand OA but also in knee OA (26). A parallel can be drawn with RA data, in which sub-clinical synovitis is predictive of erosive lesions (11, 30). This raises the question of synovitis signification. It should be borne in mind that our study has a cross-sectional design so it cannot look for relation between radiological progression and synovitis.

We found a good correlation between MRI and CR for osteophyte detection whatever the radiological score used. The superiority of MRI over x-rays for osteophyte detection remains controversial. Haugen (5) showed superiority of MRI while Wittoek *et al*. (27), considered MRI less optimal to visualise osteophytes and argued that this could be due to the signal void of densely packed calcium in osteophytes but with a high percentage of detection regardless of the modality.

Haugen (23) found radiographs to be superior to MRI at detecting JSN using KL scoring. Our results showed differences according to the radiological score used, with a possible superiority of Verbruggen and Kallman scores compared to the Kellgren-Laurence score: Its lack of linearity and the priority given to osteophytes are well known limitations (31).

One strength of our study was to look for relationships between clinical, radiological and also biologic markers. One surprising result was the association between IL-1 level and radiological severity specially when erosions are present. Although IL-1 plays a key role in the pathogenesis and progression of OA, such a correlation has not been observed in knee or in hip OA. The negative correlation found with IL-1 and the absence of correlation with TNF-α are surprising but may account for the lack of efficiency of biological treatment in hand osteoarthritis. The low level of IL-1α in the serum could enhance the idea that its synthesis occurs early in OA.

The negative correlation with x-rays lesions and the relationship with the function may mean that IL-1 is involved early in the structural process. The lesions of our subjects had probably been present for several years. It could (suggest) offer a window of opportunity to treat.

There are several limitations in our study. Firstly, the number of patients was limited and our results has to be reproduced in larger studies. We were able to study 144 joints but it was not enough to differenciate between erosive and non erosive subjects.

Secondly, there was a quite low inter-reader correlation in reading MRI. However, there is no real consensus on the best way to measure MRI findings. At the time our study was carried out no MRI score was known and in addition our readers were OMERACT members working on MRI hand scoring and so familiar with MRI reading. Similarly the average composite scores by each range of IP could be criticised but it is impossible to observe and make correlation between changes in one IP joint and general level of pain and disability. In addition, this study is cross-sectional.

Thirdly, as the sample we used was limited we did not go into the influence of disease duration and did not perform any adjustment on BMI, sex or age as we meant to assess/estimate non parametric correlation coefficients.

The use of dedicated low-field MRI may be regarded as an advantage for its feasibility compared to high-field MRI, but it may be less efficient in terms of BML detection and injuries of the lateral ligaments (33-35). Few studies only concern dedicated low-field MRI in rheumatology, and to our knowledge these have mainly dealt with rheumatoid arthritis, never for hand OA (34-

36). However it has been shown that high- and low-field MRI are equally efficient in detecting erosions and synovitis (when contrast is used) (36).

To conclude, our study highlights the strong correlations between MRI and x-rays for the detection of erosions, osteophytes and JSN, but not for synovitis detection. On the other hand, synovitis detected by MRI was not correlated with radiological severity signs or radiological erosions while IL-1 serum level, which may reflect some kind of inflammatory process, was correlated with radiological severity. The negative correlation is surprising but may explain the lack of efficiency of different biological therapies in hand osteoarthritis and is probably the consequence of an early intervention of IL-1 in the erosive hand OA development. This opens a possible window of opportunity for biological treatment in hand OA.

Our results warrant the conduct of further studies, particularly longitudinal studies, including biological markers for a better understanding of the pathophysiology of this disease.

Acknowledgments

We are grateful to the patients who agreed to be included in this trial, and we thank all the co-investigators: Créteil: Fevre Claire, Farrenq Valérie; Paris (Saint Antoine): Champey Julien; Lyon: Piperno Muriel; Nice: AllamYacine, Euller Ziegler Liana; Nancy: Rat Anne-Christine, Sommier Jean-Phillipe; Nantes: Maugars Yves; Tours: Mammou Saloua; Dijon: Piroth Christine; Marseille: Legré Virginie; Lille: Pouyol Francois, Flipo René-Marc: Montpellier: Gérard-Dran Delphine; Paris (Pitié-Salpêtrière): Banneville Béatrice, Inaoui Rachida; Paris (Bichat): Meyer Olivier, Ballard Magali; Poitiers: Solau-Gervais Elisabeth; Besançon: Wendling Daniel; Paris (Lariboisière): Peyr Olivier.

References

1. KWOK WY, KLOPPENBURG M, ROSENDAAL FR, VAN MEURS JB, HOFMAN A, BIERMA-ZEINSTRA SM: Erosive hand osteoarthritis: its prevalence and clinical impact in the general population and symptomatic hand osteoarthritis. *Ann Rheum Dis* 2011; 70: 1238-42.
2. WENHAM CY, GRAINGER AJ, CONAGHAN PG: The role of imaging modalities in the diagnosis, differential diagnosis and clinical assessment of peripheral joint osteoarthritis. *Osteoarthritis Cartilage* 2014; 22: 1692-702.
3. LAFEBER FP, VAN SPIL WE: Osteoarthritis year 2013 in review: biomarkers; reflecting before moving forward, one step at a time. *Osteoarthritis Cartilage* 2013; 21: 1452-64.
4. ROEMER FW, ECKSTEIN F, HAYASHI D, GUERMAZI A: The role of imaging in osteoarthritis. *Best Pract Res ClinRheumatol* 2014; 28: 31-60.
5. HAUGEN IK, BOYESEN P, SLATKOWSKY-CHRISTENSEN B *et al*.: Comparison of features by MRI and radiographs of the interphalangeal finger joints in patients with hand osteoarthritis. *Ann Rheum Dis* 2012; 71: 345-50.
6. GRAINGER AJ, FARRAT JM: MR imaging of erosions in interphalangeal joint osteoarthritis: is all osteoarthritis erosive? *Skeletal Radiol* 2007; 36: 737-45.
7. TAN AL, GRAINGER AJ, TANNER SF *et al*.: A high-resolution magnetic resonance imaging study of distal interphalangeal joint arthropathy in psoriatic arthritis and osteoarthritis: are they the same? *Arthritis Rheum* 2006; 54: 1328-33.
8. TAN AL, GRAINGERAJ,TANNER SF *et al*.: High-resolution magnetic resonance imaging for the assessment of hand osteoarthritis. *Arthritis Rheum* 2005; 52: 2355-65.
9. TAN AL, TOUMI H, BENJAMIN M *et al*.: Combined high-resolution magnetic resonance imaging and histological examination to explore the role of ligaments and tendons in the phenotypic expression of early hand osteoarthritis. *Ann Rheum Dis* 2006; 65: 1267-72.
10. DAHAGHIN S, BIERMA-ZEINSTRA SM, GINAIAZ, POLS HA, HAZES JM, KOES BW: Prevalence and pattern of radiographic hand osteoarthritis and association with pain and disability (the Rotterdam study). *Ann Rheum Dis* 2005; 64: 682-7.
11. KORTEKAAS MC, KWOK WY, REIJNIERSE M, HUIZINGA TWJ, KLOPPENBURG M: Osteophytes and joint space narrowing are independently associated with pain in finger joints in hand osteoarthritis. *Ann Rheum Dis* 2011; 70: 1835-7.
12. RAMONDA R, LORENZIN M, MODESTI V *et al*.: Serological markers of erosive hand osteoarthritis. *Eur J Intern Med* 2013; 24: 11-5.
13. PUNZI L, RAMONDA R, DEBERG M *et al*.: Coll2-1, Coll2-1NO2 and myeloperoxidase serum levels in erosive and non-erosive osteoarthritis of the hands. *Osteoarthritis Cartilage* 2012; 20: 557-61.
14. HUNTER DJ, GUERMAZI A, ROEMER F, ZHANG Y, NEOGI T: Structural correlates of pain in joints with osteoarthritis. *Osteoarthritis Cartilage* 2013; 21: 1170-8.
15. CHEVALIER X, RAVAUD P, MAHEU E *et al*.; ON BEHALF OF THE FRENCH SECTION OF OSTEOARTHRITIS: Adalimumab in patients with hand osteoarthritis refractory to analgesics and NSAIDs: a randomized, multicentre, double-blind, placebo-controlled trial. *Ann Rheum Dis* 2015; 74: 1697-705
16. VERBRUGGEN G, VEYS EM: Numerical scoring systems for the anatomic evolution of osteoarthritis of the finger joints. A*rthritis Rheum* 1996; 39: 308-20.
17. KELLGREN J, JEFFREY MR, BALL J (Eds.): The Epidemiology of Chronic Rheumatism. Volume II Atlas of Standard Radiographs of Arthritis. Oxford: Blackwell Scientific Publications, 1963.
18. KALLMAN DA, WIGLEY FM, HOCHBERG MC, TOBIN JD: New radiographic grading scales for osteoarthritis of the hand. *Arthritis Rheum* 1989; 32: 1584-91.
19. ØSTERGAARD M, PETERFY C, CONAGHAN P *et al*.: OMERACT Rheumatoid Arthritis Magnetic Resonance Imaging Studies. Core set of MRI acquisitions, joint pathology definitions, and the OMERACT RA-MRI scoring system. *J Rheumatol* 2003; 30: 1385-6.
20. DREISER RL, MAHEU E, GUILLOU GB, CASPARD H, GROUIN JM: Validation of an algofunctional index for osteoarthritis of the hand. *Rev Rhum Engl Ed* 1995; 62 (Suppl. 1): 43S-53S.
21. DURUÖZ MT, POIRAUDEAU S, FERMANIAN J *et al*.: Development and validation of a rheumatoid hand functional disability scale that assesses functional handicap. *J Rheumatol* 1996; 23: 1167-72.
22. DALAGHIN S, BIERMA-ZEINSTRA SMA, HAZES JMW, KOES BW: Clinical burden of radiographic hand osteoarthritis: a systematic appraisal. *Arthritis Rheum* 2006; 55: 636-47.
23. HAUGEN IK, BØYESEN P, SLATKOWSKY-CHRISTENSEN B, SESSENG S, VAN DER HEIJDE D, KVIEN TK: Associations between MRI-defined synovitis, bone marrow lesions and structural features and measures of pain and physical function in hand osteoarthritis. *Ann Rheum Dis* 2012; 71: 899-904.
24. WITTOEK R, CRUYSSEN BV, VERBRUGGEN G: Predictors of functional impairment and pain in erosive osteoarthritis of the interphalangeal joints: comparison with controlled inflammatory arthritis. *Arthritis Rheum* 2012; 64: 1430-6.
25. IP S, SAYRE EC, GUERMAZI A *et al*.: Frequency of bone marrow lesions and association with pain severity: results from a population-based symptomatic knee cohort. *J Rheumatol* 2011; 38: 1079-85.
26. BAKER K, GRAINGER A, NIU J *et al*.: Relation of synovitis to knee pain using contrast-enhanced MRIs. *Ann Rheum Dis* 2010; 69: 1779-83.
27. WITTOECK R, JANS L, LAMBRECHT V, CARRON P, VERSTRAETE K, VERBRUGGEN G: Reliability and construct validity of ultrasonography of soft tissue and destructive changes in erosive osteoarthritis of the interphalangeal finger joints: a comparison with MRI. *Ann Rheum Dis* 2011; 70: 278-83.
28. KWOK WY, KORTEKAAS MC, REIJNIERSEN M, VAN DER HEIJDE D, BLOEM JL, KLOPPENBURG M: MRI in hand osteoarthritis: validation of the Oslo hand osteoarthritis MRI-scoring method and association with pain. *Osteoarthritis Cartilage* 2011; 19 (Suppl. 1): iS26-S27.
29. MCQUEEN F, OSTERGAARD M, PETERFY C *et al*.: Pitfalls in scoring MR images of rheumatic arthritis wrist and metacarpophalangeal joints. *Ann Rheum Dis* 2005; 64 (Suppl. 1): i48-55.

30. GUERMAZI A, BURSTEIN D, CONAGHAN P *et al*.: Imaging in osteoarthritis. *Rheum Dis Clin North Am* 2008; 34: 654-87.
31. GOLDRING SR: Pathogenesis of bone and cartilage destruction in rheumatoid arthritis. *Rheumatology* (Oxford) 2003: 42 (Suppl. 2): Ii11-6.
32. PEARLE AD, SCANZELLO CR, GEORGE S *et al*.: Elevated high-sensitivity C-reactive protein levels are associated with local inflammatory findings in patients with osteoarthritis. *Osteoarthritis Cartilage* 2007; 15: 516-23.
33. HAUGEN IK, SLATKOWSKY-CHRISTENSEN B, BØYESEN P, SESSENG S, VAN DER HEIJDE D, KVIEN TK: MRI findings predict radiographic progression and development of erosions in hand osteoarthritis. ARD Online First, published on September 9, 2014 as 10.1136/annrheumdis-2014-205949.
34. SCHIRMER C, SCHEEL AK, ALTHOFF CE *et al*.: Diagnostic quality and scoring of synovitis, tenosynovitis and erosions in low-field MRI of patients with rheumatoid arthritis: a comparison with conventional MRI. *Ann Rheum Dis* 2007; 66: 522-9.
35. FREESTON JE, CONAGHAN PG, DASS S *et al*.: Does extremity-MRI improve erosion detection in severely damaged joints? A study of long-standing rheumatoid arthritis using three imaging modalities. *Ann Rheum Dis* 2007; 66: 1538-40.
36. DUER-JENSEN A, EJBJERG B, ALBRECHT-BESTE E *et al*.: Does low-field dedicated extremity MRI (E-MRI) reliably detect bone erosions in rheumatoid arthritis? A comparison of two different E-MRI units and conventional radiography with high-resolution CT scanning. *Ann Rheum Dis* 2009; 68: 1296-302.