EXTENDED REPORT

What is the prevalence of MRI-detected inflammation and erosions in small joints in the general population? A collation and analysis of published data

Lukas Mangnus, Jan W Schoones, Annette H M van der Helm-van Mil

ABSTRACT

Introduction: MRI sensitively depicts erosions, bone marrow edema (BME) and synovitis in rheumatoid arthritis (RA). Recently developed European League Against Rheumatism (EULAR) recommendations stated that MRI is valuable to improve the certainty of a considered diagnosis and to detect structural damage at an early time point. However, these recommendations were mainly based on the data of patients with RA; prevalences of MRI features in the general population were not extensively explored. We reviewed the literature on MRI studies including symptom-free persons to assess the occurrence of MRI features.

Methods: Medical literature databases up to September 2013 were systematically reviewed for symptom-free persons. The prevalence of MRI-detected erosions, synovitis and bone marrow edema occurred frequently in symptom-free persons. Similarly, synovitis showed that erosions (RAMRIS ≥1) were present in 33–52% of symptom-free persons. Similarly, synovitis was present in 27% and BME in 0–16% of symptom-free persons. The prevalence of MRI-detected erosions increased with age.

Results: Of the 338 articles screened, 31 studies evaluated MRI findings in symptom-free persons (n=516 in total). Both the imaging techniques (≤1/≥1 T, with/without contrast enhancement) and the scoring methods (non-validated or RA MRI score (RAMRIS)) varied widely, prohibiting direct comparisons of the results of many studies. 15 studies scored data according to RAMRIS; combining data of similar joint regions showed that erosions (RAMRIS ≥1) were present in 33–52% of symptom-free persons. Similarly, synovitis was present in 27% and BME in 0–16% of symptom-free persons. The prevalence of MRI-detected erosions increased with age.

Conclusions: MRI features, erosions in particular, occur frequently in symptom-free persons. Before MRI can be implemented in the diagnostic process, larger studies should be conducted determining the degree and combination of MRI features that are disease specific.

INTRODUCTION

Early treatment initiation in rheumatoid arthritis (RA) is associated with less radiographic progression and a higher chance to achieve disease-modifying antirheumatic drug-free sustained remission, illustrating the relevance of early diagnosis. MRI detected erosions, synovitis and bone marrow edema occur frequently in symptom-free persons. Owing to the heterogeneity in the studies, RA-specific MRI criteria cannot yet be defined. Before implementing MRI in the diagnostic process of joint symptoms, further research is needed.

Key messages

- MRI detected erosions, synovitis and bone marrow edema occur frequently in symptom-free persons.
- Owing to the heterogeneity in the studies, RA-specific MRI criteria cannot yet be defined.
- Before implementing MRI in the diagnostic process of joint symptoms, further research is needed.
RA and their ability to differentiate patients with the disease from the normal situation.

Thus, to arrive at an evidence-based evaluation on the role of MRI in the diagnostic process in the early clinical and preclinical phases of RA, it is necessary to investigate the occurrence of MRI features in the general population. In case certain MRI features (to a certain degree) are also present in persons without joint symptoms, these lesions are presumably not indicative for RA. No large-scale studies have been performed to investigate the prevalence of these features in the general population. However, several MRI studies included symptom-free persons as controls. We aimed to (1) evaluate the prevalence of MRI features in symptom-free persons and (2), based on these observations, to make recommendations for future studies. To this end, we systematically reviewed the literature.

METHOD

The databases PubMed, EMBASE and Web of Science up until September 2013 were searched with the assistance of a medical librarian (JWS). Central terms in our search were MRI, healthy volunteers, wrist, metacarpal, metatarsal and RA (complete details of the search strategy can be obtained by the author). Titles and abstracts were screened on whether data on symptom-free persons and MRI of hands or feet were available. Subsequently, full-text articles were read and additional articles were identified through hand searching of reference lists. Articles were included when the studies contained (1) symptom-free persons and (2) information on MRI detected erosions, bone marrow edema (BME), synovitis or tenosynovitis of hands or feet. Since the symptom-free persons were generally used as the control group, the quality of the overall study design was not valued. Further, in order to get a comprehensive overview, we decided to include all studies fulfilling these two criteria and not to exclude studies based on the quality of the scanner, the scan protocol or scoring protocol that was used.

A standardised form was used to extract the following data: (1) study population (population size, age, recruitment method, description of study population, MRI scanner, MRI sequences, joint region scanned and scoring method), (2) MRI features (erosions, BME, synovitis and tenosynovitis) and quantitative aspects (number of patients affected, number of joints/bones affected and grading of the MRI features) and (3) relevant characteristics (location of MRI features, dominant or non-dominant hands, age and sex of symptom-free participants). MRI features were present (‘positive’) when recorded as such; studies using the RA MRI score (RAMRIS) generally considered a score of ≥1 for that feature as positive. Data were extracted and reported such as done by the authors: either by presenting the prevalence of a feature or by presenting summary measures of continuous RAMRIS. According to RAMRIS, the range per bone/joint of erosion, BME and synovitis scores are 0–10, 0–3 and 0–3, respectively; scoring of the metacarpophalangeal (MCP) region and wrist region involved evaluation of 8 and 15 bones and 4 and 3 joints (radioulnar joint, radiocarpal joint and intercarpal-carpometacarpal joint), respectively, evaluation of the 5 metatarsophalangeal (MTP) joints involved evaluation of 10 bones. In case the same joint regions were assessed using similar scan protocols (ie, either with or without use of contrast enhancement) and similar scoring methodology (RAMRIS), it was considered acceptable to combine the results of different studies. Then mean frequencies (with 95% CIs) were calculated. Since it is known that contrast enhancement increases the reliability of assessment of synovitis, studies evaluating synovitis and tenosynovitis with and without contrast enhancement were not combined but analysed separately.

RESULTS

Selection of studies

The literature search yielded 338 studies; five additional articles were found by hand searching of reference lists (figure 1). After screening, 61 articles were selected. Two studies were excluded because of a language other than English. Of the remaining articles, 33 were eligible for inclusion. One article was excluded as it concerned a population that was used in two articles. Consequently, data were extracted of 32 articles. Whereas 31 studies provided data on patient level (joint region), one study analysed the data only on individual bone/joint level; therefore, this study was only used when analysing results on bone/joint level.

Study description

The 31 included studies contained information on 3–42 (range) symptom-free persons per study; in total, 516 symptom-free persons were studied (table 1). Descriptions of the recruitment method is given in only seven studies. Most of these studies are reported to have studied hospital staff. Methods to exclude the target disease were described in 26 articles; four studies did not include this information and described their symptom-free persons as ‘healthy volunteers’ or ‘healthy controls’ and one study was described to have performed MRIs of ‘healthy volunteers’ and persons with wrist instability. The methods of excluding target disease differed. Thirteen studies described that there was no history of joint disease, arthritis or joint symptoms. Twenty studies mentioned that there were no current musculoskeletal/joint symptoms. In four studies, persons underwent clinical assessment by a rheumatologist, and in two studies laboratory investigations were done and persons were excluded in case they were rheumatoid factor positive or had increased C reactive protein levels. Of the 31 included studies, 19 used an MRI with ≥1 T, 11 with an <1 T MRI and one study used two different
scanners (one with 1 T and one with 0.6 T). Contrast enhancement was used in 17 of the 31 studies.

Sixteen studies did not use a validated scoring method; evaluations were done by experienced radiologists (in 12 studies), an experienced rheumatologist (1 study) and an ‘observer’ (2 studies), and in one study no information was provided. In 15 studies, MRIs were scored according to RAMRIS. MRI scoring was done blinded for clinical status in 18 of the 31 studies. In seven studies, scoring of patients and controls was not performed blindly, and in six studies (140 symptom-free persons) only symptom-free persons were evaluated.

Prevalence of erosions
The studies that did not use a validated scoring method reported a lower prevalence of erosions than did the studies using RAMRIS (table 2). A wrist was scanned on one or both sides and assessed using RAMRIS in 69 and 44 persons, respectively. When combining data of the wrist, a total RAMRIS erosion score ≥1 was reported in 52.2% (mean, 95% CI 40.6 to 63.5, unilateral wrist) and 40.9% (95% CI 27.7% to 55.6%, both wrists) of symptom-free persons, respectively. Unilateral MCP joints were evaluated in 97 persons and revealed erosions in 33% (95% CI 24.4% to 42.9%). No studies described the prevalence of erosions when using higher cut-offs for positivity (for instance, a total RAMRIS erosion score of ≥2).

Prevalence of BME
The recorded prevalence of BME was higher in the studies using RAMRIS than in the studies using other methods. Combining the data of the 63 persons in whom unilateral wrists were scanned yielded a mean frequency of BME (RAMRIS BME score ≥1) of 15.9% (95% CI 8.7% to 27.0%). Similarly, BME was present in 9.5% (95% CI 4.1% to 19.6%) of persons.
Table 1 Characteristics of the 31 selected studies

| First author, year of publication | N= | Recruitment method* | Age | Female/ male | MRI | Contrast | Area scanned | Uni/ bilateral | Score Method | Blinded† |
|----------------------------------|----|---------------------|-----|-------------|-----|----------|--------------|--------------|-------------|---------|
| **Scored without a validated method** | | | | | | | | | | |
| | | | | | | | | | | |
| Wrist-MCP summed | | | | | | | | | | |
| Nakahara et al, 199611 | 11 | NP | 5/5 | 1.5T | Gd+ | Wrist+MCP | NP | Described + | | |
| Lindegaard et al, 200112 | 3 | Hospital staff | 64 (34–55) | 1/2 | 0.2T | Gd+ | Wrist+MCP | Unilateral | Described + | | |
| Yoshioka et al, 200613 | 13 | NP | 34.1 (22–48) | 5/8 | 0.21T | Gd− | Wrist+MCP+PIP | Bilateral | NP | + |
| Offidani et al, 199814 | 12 | NP | 5/5 | 1.0T | Gd− | Wrist+MCP+IP | NP | Described + | | |
| **Wrist** | | | | | | | | | | |
| Beltran et al, 198715 | 6 | NP | 5/5 | 1.5T | Gd− | Wrist | NP | Described | | |
| Jorgensen et al, 199316 | 4 | NP | 30 | 2/2 | 0.5T | Gd+ | Wrist | NP | NP + | | |
| Yanagawa et al, 199317 | 10 | NP | 7/3 | 1.5T | Gd+ | Wrist | NP | Described | | |
| Østergaard et al, 199518 | 31 | NP | 28–31 | 5/5 | 0.5T | Gd+ | Wrist | NP | NP + | | |
| Tonelli-Serabian et al, 199619 | 10 | NP | 59 (46–71) | 5/5 | 1.0T | Gd− | Wrist | Bilateral | Described + | | |
| Pierre-Jerome et al, 199720 | 42 | NP | 42.1 | 42/0 | 0.5T | Gd− | Wrist | Bilateral | Described | | |
| Valeri et al, 200121 | 12 | NP | 31 | 8/4 | 1.0T | Gd− | Wrist | NP | NP + | | |
| Partik et al, 200222 | 18 | NP | 30.8 (24–34) | 9/9 | 1.0T | Gd− | Wrist | NP | NP + | | |
| Robertson et al, 200623 | 30 | Hospital staff and contacts | 31 (22–49) | 17/13 | 1.5T | Gd− | Wrist | Unilateral | Described | | |
| McGonagle et al, 199924 | 31 | Hospital staff | 48 (28–62) | 18/13 | 1.5T | Gd− | MCP | Unilateral | Described + | | |
| Klarlund et al, 199925 | 3 | NP | 31 (24–33) | NP | 1.0T | Gd− | MCP | Unilateral | Described + | | |
| Vlychou et al, 201326 | 5 | 2 volunteers and with 3 wrist instability | 41.2±3.2 | 3/2 | 3.0T | Gd+ | MCP+PIP+DIP | Unilateral | Described + | | |
| Brown et al, 200629 | 17 | NP | 38 | 12/5 | 1.5T | Gd+ | Wrist+MCP | Unilateral | RAMRIS + | | |
| Ejbjerg et al, 200430 | 28 | NP | 47 (24–67) | 20/8 | 1.0T | Gd+ | Wrist+MCP | Unilateral | RAMRIS NP | | |
| Olech et al, 201031 | 40 | Hospital staff | 36.7 (20–64) | 291 | 0.2T | Gd− | Wrist+MCP | Bilateral | RAMRIS + | | |
| Parodi et al, 200632 | 23 | Healthy relatives | 59 (25–86) | 16/7 | 0.2T | Gd− | Wrist+MCP+PIP | Bilateral | RAMRIS | | |
| Ejbjerg et al, 200533 | 9 | NP | 59 (25–86) | 16/7 | 0.2T | Gd− | Wrist+MCP+MTP | Bilateral | RAMRIS + | | |
| Duer-Jensen et al, 201134 | 24 | NP | 46 (21–71) | 17/7 | 0.6 T (12), | 1.0 T (12) | Gd− | Wrist+MCP+PIP | Unilateral | RAMRIS NP | | |
| **Wrist** | | | | | | | | | | |
| Cimmino et al, 201135 | 13 | NP | 71 (57–86) | NP | 0.2T | Gd− | Wrist | Bilateral | RAMRIS + | | |
| Palosari et al, 200936 | 31 | Hospital staff | 49 (32–64) | 18/13 | 0.23T | Gd+ (10/31) | Wrist | Bilateral | RAMRIS NP | | |
| Dehn et al, 200837 | 4 | NP | 36 (34–57) | 3/1 | 0.6T | Gd− | Wrist | Unilateral | RAMRIS + | | |
| **MCP** | | | | | | | | | | |
| Dehn et al, 200638 | 4 | NP | 35.5 (34–57) | 3/1 | 0.6T | Gd− | MCP | Unilateral | RAMRIS + | | |
| Tan et al, 200339 | 28 | NP | 40 (19–92) | 15/9 | 1.5T | Gd+ (8/28) | MCP | Unilateral | RAMRIS + | | |
| Miese et al, 201240 | 13 | NP | 51±12 (25–66) | 10/3 | 3T | Gd+ | MCP (dig 2&3) | Unilateral | RAMRIS NP | | |
| **Mean grading (Wrist+MCP)** | | | | | | | | | | |
| Xie et al, 200827 | 14 | NP | 25±5 (19–33) | 4/10 | 1.0T | Gd− | Wrist+MCP | Unilateral | RAMRIS NP | | |
| 27 | NP | 62±7 (49–74) | 22/5 | 1.0T | Gd− | Wrist+MCP | 24/27 | RAMRIS NP | | |
| Krabben et al, 201341 | 19 | NP | 46.2±11.8 | 15/4 | 1.5T | Gd− | Wrist+MCP+MTP | Unilateral | RAMRIS NP | | |
| Rastogi et al, 201342 | 10 | NP | 24–40 | 7/3 | 3T | Gd− | Wrist | Unilateral | RAMRIS NP | | |

*Description of recruitment of symptom-free persons.
†Scoring was done blind for the status (patient/symptom-free person).
*Articles that do describe their scoring method but not according to the RAMRIS method; DIP, distal interphalangeal joint; Gd, gadolinium; IP, interphalangeal joint; MCP, metacarpophalangeal joints; MTP, metatarsophalangeal; NP, Not provided; PIP, proximal interphalangeal joint; T, tesla.
| First author, year of publication | N=healthy | Uni/bilateral | Erosions (%) | BME (%) | Synovitis (%) | Tenosynovitis (%) |
|----------------------------------|-----------|---------------|--------------|---------|---------------|------------------|
| **Scored without a validated method** |
| **Wrist+MCP**                   |           |               |              |         |               |                  |
| Nakahara et al, 1996           | 10        | NP            | NP           | 0.0     | 0.0           | 0.0              |
| Lindegaard et al, 2001         | 3         | Unilateral    | 0.0          | NP      | NP            | NP               |
| Yoshioka et al, 2006           | 13 (+PIP) | Bilateral     | 0.0          | NP      | 0.0           | 0.0              |
| Offidani et al, 1998           | 12 (+IP)  | NP            | 0.0          | NP      | 0.0           | 0.0              |
| **Wrist**                      |           |               |              |         |               |                  |
| Beltran et al, 1987            | 6         | NP            | 0.0          | NP      | 0.0           | 0.0              |
| Jorgensen et al, 1993          | 4         | NP            | 0.0          | NP      | 0.0           | 0.0              |
| Yanagawa et al, 1993           | 10        | NP            | NP           | NP      | 0.0           | NP               |
| Østergaard et al, 1995         | 3         | NP            | NP           | NP      | 0.0           | NP               |
| Tonolfi-Serabian et al, 1996   | 10        | Bilateral     | 0.0          | NP      | 0.0           | NP               |
| Pierre-Jerome et al, 1997      | 42        | Bilateral     | 35.7%*       | 0.0     | 4.8           | Fl: 9.5 Ext: 7.1 |
| **MCP**                        |           |               |              |         |               |                  |
| McGonagle et al, 1999          | 31        | Unilateral    | 25.8         | 9.7     | NP            | NP               |
| Klarlund et al, 1995           | 3         | Unilateral    | 0.0          | NP      | 0.0           | NP               |
| Vlychou et al, 2013            | 5 (+PIP, DIP) | Unilateral | 0.0          | 0.0     | 0.0           | 0.0              |
| **Scored according to RAMRIS**  |
| **Wrist+MCP** (2–5)            |           |               |              |         |               |                  |
| Brown et al, 2006              | 17        | Unilateral    | NP           | 0.0     | 17.6          | 5.9              |
| Ejbjerg et al, 2004            | 28        | Unilateral    | NP           | 0.0     | 32.1          | NP               |
| Olech et al, 2010              | 40        | Bilateral     | 65.0         | 17.5    | 42.5          | NP               |
| Parodi et al, 2006             | 23 (+PIP) | Bilateral     | 26.0         | 8.7%    | NP            | Fl: 17.4 Ext: 4.3 |
| Ejbjerg et al, 2005            | 9 (+MTP)  | Bilateral     | 55.6         | NP      | NP            |                  |
| Combined data                  | 0/45      | Unilateral    | BME mean 0%  | (95% CI 0.0% to 6.8%) |
| Combined data                  | 12/45     | Unilateral    | Synovitis mean 26.7%  | (95% CI 15.8% to 41.2%) |
| **Wrist**                      |           |               |              |         |               |                  |
| Cimmino et al, 2011            | 13        | Bilateral     | 30.8         | 30.8    | 0.0           | 30.8             |
| Palosaari et al, 2009          | 31        | Bilateral     | 45.2         | NP      | 60.0%         | NP               |
| Dehn et al, 2008               | 4         | Unilateral    | 25.0         | NP      | NP            | NP               |
| Duer-Jensen et al, 2011†        | 24        | Unilateral    | 45.8         | 4.5     | 81.8          | 0.0%             |
| Xie et al, 2008‡               | 14        | Unilateral    | 0.0          | 0.0     | 0.0           | NP               |
| Age 25±5                       | 27        | Unilateral    | 88.9         | 33.3    | 3.7           | NP               |
| Combined data                  | 18/44     | Bilateral     | Erosions mean 40.9%  | (95% CI 27.7% to 55.6%) |
| Combined data                  | 36/69     | Unilateral    | Erosions mean 52.2%  | (95% CI 40.6% to 63.5%) |
| Combined data                  | 10/63§    | Unilateral    | BME mean 15.9%  | (95% CI 8.7% to 27.0%) |
| **MCP (2–5)**                  |           |               |              |         |               |                  |
| Dehn et al, 2006               | 4         | Unilateral    | 0.0          | NP      | NP            | NP               |
| Tan et al, 2003                | 28        | Unilateral    | 32.1         | NP      | NP            | NP               |
| Miese et al, 2012              | 13 MCP 2&3 | Unilateral | NP           | 0.0     | 0.0           | NP               |
| Duer-Jensen et al, 2011†        | 24        | Unilateral    | 45.8         | 4.5     | 45.5          | 0.0              |
| Xie et al, 2008‡               | 14        | Unilateral    | 0.0          | 14.3    | 0.0           | NP               |
| Age 25±5                       | 27        | Unilateral    | 44.4         | 11.1    | 14.8          | NP               |
| Combined data                  | 32/97     | Unilateral    | Erosions mean 33.0%  | (95% CI 24.4% to 42.9%) |
| Combined data                  | 6/63§     | Unilateral    | BME mean 9.5%  | (95% CI 4.1% to 19.6%) |

0% is noted when no erosions are found or an abnormality is described in the patient group and the healthy control group is only described as ‘no abnormalities’ with no further specification.

Bolt=studies in which contrast was used to score synovitis and tenosynovitis.

*Contradicting data in original article, with 35.7% erosions in the table and 14.3% erosions in the text.
†Same study.
‡Same study.
§Duer-Jensen only assessed 22 patients for BME.

DIP, distal interphalangeal joint; Ext, extensor tendons; Fl, flexor tendons; IP, interphalangeal joint; MCP, metacarpophalangeal joints; MTP, metatarsophalangeal; NP, Not provided; PIP, proximal interphalangeal joint.
in whom unilateral MCPs were evaluated. Combining studies assessing unilateral wrist and MCPs showed a mean frequency of BME of 0.0% (95% CI 0.0% to 6.8%). No studies categorised BME features with higher cut-off values.

**Prevalence of synovitis and tenosynovitis**

Synovitis was assessed without contrast enhancement in 8 studies and with contrast in 13 studies. In the studies that used no validated scoring method, synovitis was present in 0–4.8% (range) of persons when no contrast was used and 0–44.4% (range) when contrast was used. In the studies that were scanned with contrast enhancement and scored according to RAMRIS, synovitis was present (total synovitis score ≥1) in 26.7% (95% CI 15.8% to 41.2%); these studies assessed wrist and MCP joints together. Data on the studies that provided results of wrist or MCP joints separately were not combined due to differences in scanning or scoring protocols. Tenosynovitis was assessed infrequently (table 2).

### Continuous RAMRIS-scores

Three studies did not report categorised data but reported continuous RAMRIS, incorporating a semiquantitative evaluation of the severity of the features. The mean RAMRIS for erosions and BME were low (≤3.2 and 0.9, respectively, table 3). For synovitis, contrast enhancement was used in one study; this study revealed higher mean RAMRIS synovitis scores than did the two studies without contrast (mean synovitis scores ≥3 vs <1, respectively; table 3).

### Prevalence of lesions at the bone and joint level

In the aforementioned studies, total scores per joint region were evaluated. Several studies evaluated the prevalence of MRI features on the level of individual bones and/or joints, all defining a RAMRIS of ≥1 as positive. Erosions were analysed in six studies; among the 4696 bones evaluated, 161 showed erosions 3.4% (95% CI 2.9% to 4.0%). BME was analysed in only two studies; among the 1182 bones evaluated, five were positive for BME 0.4% (95% CI 0.2% to 1.0%). Three studies analysed 471 joints on synovitis and reported the prevalence of synovitis in 42 joints 8.9% (95% CI 6.6% to 11.9%).

The severity of the individual lesions was scarcely reported. Three studies contained information on the severity of erosions and reported that 80.8% (mean, 95% CI 72.8% to 86.9%) of the recorded erosions had a score of 1. None of the studies reported on the severity of BME or tenosynovitis at the local level. Two studies described the synovitis scores in more detail; 21 joints had a RAMRIS of 1 (95.5%), a RAMRIS synovitis score of 2 was seen in 1 joint (4.5%) and no joints had a RAMRIS of 3.

With regard to the location of the MRI features, erosions and synovitis were more often observed in the wrist than in the MCP joints. Most erosions were observed in the carpal bones; however, there was no clear agreement on which carpal bones showed erosions most frequently. Erosions were rarely scored on the metacarpal-l and trapezium (bones that might also be affected by osteoarthritis). Locations of BME and synovitis were not clearly reported.

### Relevant characteristics

We next evaluated to what extent differences in the scanner or differences in persons’ characteristics influenced the results. No different prevalences were observed when comparing extremity-MRI with whole-body MRI. When comparing the prevalence of MRI features in studies that used MRI scanners with <1 Tesla (T) the results were generally consistent.

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**Table 3** Mean RAMRIS score in symptom-free persons

| First author, year of publication | N=healthy | Uni/bilateral | Erosions | BME | Synovitis | Tenosynovitis |
|----------------------------------|-----------|---------------|----------|-----|-----------|------------|
| Xie et al, 2008                  | 14        | Bilateral     | 0 Pt     | Dom MCP: 1.51 | Dom MCP: 0.14 | Dom MCP: 0.29 |
|                                  | 27 Age 25±3 | 27 Age 62±7  | Dom Wr: 3.11 | MCPP/PIP: 0.1 | Dom Wr: 0.85 | Dom Wr: 0.9 |
| Krabben et al, 2013              | 19 (+MTP) | Unilateral    | T0:0.8±1.3 | T12:0.4±0.7 | T24:0.4±0.7 | T52:1.4±1.9 |
| Rastogi et al, 2013              | 10        | Unilateral    | T0:0.6±0.7 | T12:0.2±0.5 | T24:0.2±0.4 | T52:0.3±0.6 |

BME: studies in which contrast was used to score synovitis and tenosynovitis. Erosions were scored on a scale from 0–10 for each location; BME and synovitis were scored from 0–3 for each location. Erosions and BME were scored in 23 locations in the hand and 10 in the foot; synovitis was scored in 7 locations in the hand and 5 in the foot.

†Krabben summed the BME and the synovitis into an inflammation score.

*Is a longitudinal study with T0 as baseline, T12 after 12 weeks, T24 after 24 weeks, T52 after 52 weeks.

Dom, dominant hand; MCP, metacarpophalangeal joints; MTP, metatarsophalangeal; NP, Not provided; Wr, wrist.
with >1 T, a higher prevalence of erosions was detected with <1 T scanners (mean 38% vs 24%). Owing to the heterogeneity between studies, no summary results can be provided with regard to the prevalence of MRI inflammatory features in relation to the field strength of the MRI. When comparing the studies that evaluated the MRIs blindly versus those that scored the MRIs knowing that the persons were symptom-free, no differences in the prevalences of the different MRI features were observed.

The dominant and non-dominant hands were evaluated in two studies and no significant differences were observed. Differences in the frequency of features between sexes were also not detected. Four studies compared the prevalence of MRI features between age categories and showed a non-significant tendency to higher prevalence of MRI erosions in older persons. Synovitis and BME were less frequently observed in older persons only and did not use the symptom-free persons as the control group. In addition, most of the studies that did not use the RAMRIS method were done when MRI techniques were less developed.

Of all MRI features, the prevalence of synovitis varied the most between studies. This cannot be explained only by the absence or presence of contrast enhancement that may increase the sensitivity and specificity of identifying MRI-detected synovitis as both types of studies were evaluated separately. The reasons for these differences between studies are unclear to us.

The most important limitation of this review is the heterogeneity of the data collected, which is a result of the methods with which data were collected in the individual studies. For instance, in many studies the symptom-free persons were used as the control-group and information on how the symptom-free persons were recruited was missing. Some studies included symptom-free persons only and did not use the symptom-free persons as controls. A consequence of this latter approach is that the evaluators per definition were aware that they had evaluated scans of symptom-free persons. Hypothetically, awareness of the clinical status may affect the scoring with lower scores being given to symptom-free individuals. In addition, the methodology to rule out rheumatic diseases differed between the studies. A difficult issue is to what extent osteoarthritis was ruled out; joint space narrowing or other osteoarthritic features were not assessed in these studies, so no definite conclusions can be drawn as to what extent the presence of asymptomatic osteoarthritis has affected the results. Furthermore, recent studies indicated that ACPA may affect the bone in the absence of clinically apparent arthritis and that subclinical inflammation may precede clinical arthritis. In two studies, the symptom-free persons underwent laboratory testing and in three studies the symptom-free persons were even followed (for 1–5 years); none of these persons developed RA.

Another important limitation relates to the issue when it is allowed to combine the results of different studies. We combined results of studies that used similar scan protocols (same joints and uniformity in contrast enhancement) and similar scoring protocols. Still, the summary measures that we provided should be interpreted with care as the readers of the different studies were not trained together and inter-reader differences and other causes of heterogeneity most likely exist. Nevertheless, this review gives a first impression of the MRI features present in the general population.

It can be argued that more stringent quality criteria should be applied before it is acceptable to combine the results of different studies. For instance, the following quality criteria might be reasonable: (1) the recruitment
Includes a large number of symptom-free persons
Include persons of different age categories
Apply population-based recruitment methods
Describe the recruitment methodology
Apply thorough anamnesis and physical examination to exclude the presence of joint symptoms or signs of joint disorders.
Perform similar MRI scans in all persons
MRI strength of ≥ 1 Tesla
Use contrast enhancement
Score the MRIs according to RAMRIS
Also include MRIs of persons with joint diseases (eg RA) and score the MRIs blinded to the clinical status
Perform analyses stratified for age

Box 1 Recommendations for high-quality studies, formulated based on the findings of this review

method was described, (2) appropriate methodology was used to exclude persons with joint symptoms or joint disease, (3) the field strength of the MRI was ≥ 1 T and (4) scans were scored according to the RAMRIS method. None of the 32 studies included in this review fulfilled all these four criteria. This underlines that large, high quality studies on this subject are needed. Recommendations for the set-up of such studies are proposed in box 1.

Furthermore, several questions still have to be answered. More detailed studies are needed on the prevalence of MRI-detected erosions, BME, synovitis and tenosynovitis in the symptom-free persons in relation to age. Furthermore, the location and the co-occurrence of erosions and inflammation (BME, synovitis or tenosynovitis) could be important for differentiation. In none of the studies was it reported whether the erosions were accompanied by inflammatory lesions, which may also be relevant to differentiate early disease from normal variants, as disease-specific erosions might presumably more often be accompanied by measures of inflammation. Also the extent or severity of the lesions may be useful to take into account. Ultimately, comparing a large number of MRI scans of healthy persons and early RA patients will reveal which combination of features are disease specific and will allow MRI criteria specific for early disease to be defined.

In conclusion, MRI features, erosions in particular, occur frequently in symptom-free persons and are more prevalent with increasing age. Before MRI can be implemented in the diagnostic process of arthritis, further evaluation of these features in symptom-free persons is required. Preferentially, this is done in large studies, ensuring homogeneity in the scan-protocol and scoring method, by evaluating scans of symptom-free persons as well as early arthritis patients blinded to the clinical status.

Contributors

LM and AHMvdHM contributed to the conception and design of the study. All authors acquired or analysed the data. LM and AHMvdHV contributed to the interpretation of the data. All authors contributed to the final version of the manuscript.

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None.

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No additional data are available.

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