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Title: EULAR RECOMMENDATIONS FOR THE USE OF IMAGING IN THE CLINICAL MANAGEMENT OF PERIPHERAL JOINT OSTEOARTHRITIS

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ABSTRACT

Objective: The increased information provided by modern imaging has led to its more extensive use. Our aim was to develop evidence based recommendations for the use of imaging in the clinical management of the commonest arthropathy, osteoarthritis (OA).

Methods: A task force (including rheumatologists, radiologists, methodologists, primary care doctors and patients) from 9 countries defined 10 questions on the role of imaging in OA to support a systematic literature review (SLR). Joints of interest were the knee, hip, hand and foot; imaging modalities included conventional radiography (CR), MRI, ultrasonography, CT and nuclear medicine. PubMed and EMBASE were searched. The evidence was presented to the task force who subsequently developed the recommendations. The strength of agreement for each recommendation was assessed.

Results: 17,011 references were identified from which 390 studies were included in the SLR. Seven recommendations were produced, covering: the lack of need for diagnostic imaging in patients with typical symptoms; the role of imaging in differential diagnosis; the lack of benefit in monitoring when no therapeutic modification is related, though consideration is required when unexpected clinical deterioration occurs; CR as the first choice imaging modality; consideration of how to correctly acquire images; and the role of imaging in guiding local injections. Recommendations for future research were also developed based on gaps in evidence, such as the use of imaging in identifying therapeutic targets, and demonstrating the added value of imaging.

Conclusions: These evidence-based recommendations and related research agenda provide the basis for sensible use of imaging in routine clinical assessment of people with OA.

INTRODUCTION

Osteoarthritis (OA) is a major cause of pain and disability worldwide. Although conventional radiography (CR) is the most commonly used technique to evaluate structural features of OA, significant advances have been made in the field of imaging over the last decade, allowing a more accurate evaluation of both bone and soft-tissue abnormalities. While newer modalities such as magnetic resonance imaging (MRI) and ultrasound have increased the understanding of the multiple pathologies contributing to the OA phenotype, it is not clear how they should be used in routine care. The role of imaging in clinical practice for OA diagnosis, management and follow-up has not been clearly defined. Despite this limitation, the increased availability of modern imaging has expanded its use, with possible excesses [1] leading to increased costs. A European League Against Rheumatism (EULAR) task force was therefore created to develop evidence-based recommendations on the use of imaging in the management of symptomatic, peripheral joint OA, for clinicians who treat OA in their clinical practice.

METHODS

A group selected from a range of expertise (rheumatologists, radiologists, primary care physicians, methodologists and patients) and representing 9 countries were included in the task force. During the first meeting, the focus of the recommendations (symptomatic OA affecting the knee, hip, hand or foot) was clarified. Clinically relevant questions on the application of imaging in OA were proposed and 9 research questions were selected by consensus to guide a detailed systematic literature review (SLR). Two questions that covered the same area were subsequently combined. The areas of diagnosis, prognosis, follow-up and treatment were covered. The questions were rephrased according to the PICO (population, intervention, comparison, outcome) (see supplementary file S1 Research Questions).

A SLR was performed by one of the authors (GS), with checking of all extractions by one of 3 other authors experienced in SLRs. The search strategies were based on both MeSh (Medical Subject Headings) terms and free text. The searches were performed separately for each joint (see supplementary file S2 Search Strategies). The titles and abstracts of the references that were retrieved were screened by the same author according to pre-defined inclusion and exclusion criteria, based on the PICO for each question, and potentially relevant articles were evaluated in their full text. Studies in English including adults (≥ 18) with symptomatic OA of the knee, hip, hand and foot were eligible for inclusion. Imaging modalities included were CR, MRI, ultrasonography (US), computed tomography (CT) and nuclear medicine techniques (scintigraphy, positron emission tomography, PET). Randomized controlled trials,

systematic reviews and meta-analyses, controlled clinical trials, case-control studies, cross-sectional studies and cohort studies were eligible for inclusion. Studies had to examine the role of imaging in the following: in making a diagnosis of OA; in detecting OA elementary lesions; for differential diagnosis; in the management of OA; in predicting outcome and therapeutic response; for follow-up of disease course; to guide treatment. The same articles could be included in more than one search. Due to the variety of joint sites and imaging and the expectation of a strong degree of heterogeneity across studies, meta-analyses were not pre-specified before study selection and extraction. The methodological quality of the included studies was not assessed by quality scores, but some aspects were considered for all studies, together with design-specific indicators. For all studies, study design, sample size, setting sampling were considered. For RCTs allocation concealment, drop-out rate as well as the presence of funding, for diagnostic studies the adequacy of the reference standard, for cohort studies the presence of adjustment for confounders were also evaluated. Each aspect was evaluated separately as leading to high, low or unclear risk of bias.

During the second meeting the results of the literature review were presented and the experts developed 'over-arching' statements (background statements to preface the recommendations) and drafted 7 recommendations through a process of discussion and consensus. The number of recommendations emerged through the discussion after the presentation of the literature, when evidence from the literature was limited the recommendations were based on the opinion of the experts. To explore the presence of additional evidence concerning two recommendations, two more research questions on 1) the different performance of various radiographic views in detecting OA features and 2) the accuracy of imaging guided compared to blind joint injections were added to the original 8, with two additional literature searches (See supplementary file S1, research questions and S2, search strategies). After evaluation of these results, the Task Force confirmed the final wording of the recommendations and scored the perceived level of agreement (LOA) for each statement using a 0-10 numeric rating scale (0=fully disagree; 10=fully agree), reflecting both literature evidence and expert opinion. Recommendations for further research were then developed based on gaps in the SLRs.

RESULTS

The searches in the electronic databases (PubMed, Embase) were performed up to the end of January 2015 for the main searches and December 2015 for the additional searches. The initial search resulted in 6858 records, (615 duplicates). Of the remaining 6243 articles, 4926 were excluded based on the title and abstracts, leaving 1317 articles for detailed review. All full text articles were retrieved, 986 articles were excluded after reviewing the full text leaving

331 articles for inclusion (supplementary file S3, online only). The hand search of the references of the included studies identified 33 additional articles, leading to a total of 364 studies finally analyzed. Articles that were relevant to more than one research question were used for each question as appropriate. The number of articles included for each site and imaging are shown in figure S4, available online only. The complete results of the SLR with references are reported in the supplementary file S5.

The additional search on the comparison of different radiographic views resulted in 4774 articles (225 duplicates). Of the remaining 4549, 4496 were excluded based on the title and abstracts, leaving 53 articles for detailed review. Twenty-three articles were excluded after reviewing the full text, leaving 30 articles for inclusion. The hand search identified 1 additional article for inclusion, leading to a total of 31 articles finally included (supplementary file S6, online only).

The additional search on the added value of imaging to guide intra-articular procedures resulted in 5379 articles, (834 duplicates). Of the remaining 4545, 4520 were excluded based on the title and abstracts, leaving 25 articles for detailed review. Nineteen articles were excluded after reviewing the full text leaving 6 articles for inclusion. The hand search identified 2 additional articles for inclusion, leading to a total of 8 articles finally included (supplementary file S7, online only). The complete results of the additional searches with references are reported in the supplementary file S8.

Recommendations

Table 1 summarizes the 7 recommendations with their corresponding level of evidence and LOA. Each recommendation is presented in detail below.

Table 1. Recommendations, levels of evidence and level of agreement (LOA)

Recommendation	Level of evidence	LOA, mean (95% CI)
1. Imaging is not required to make the diagnosis in patients with typical* presentation of OA. *typical features include: usage-related pain, short duration morning stiffness, age>40, symptoms affecting one or a few joints.	III-IV	8.7 (7.9, 9.4)
2. In atypical presentations imaging is recommended to help confirm the diagnosis of OA and/or make alternative or additional diagnoses.	IV	9.6 (9.1, 10)
3. Routine imaging in OA follow-up is not recommended. However, imaging is recommended if there is unexpected rapid progression of symptoms or change in clinical characteristics to determine if this relates to OA severity or an additional diagnosis.	III-IV	8.8 (7.9, 9.7)
4. If imaging is needed, conventional (plain) radiography should be used before other modalities. To make additional diagnoses, soft tissues are best imaged by US or MRI and bone by CT or MRI.	III-IV	8.7 (7.9, 9.6)
5. Consideration of radiographic views is important for optimizing detection of OA features; in particular for the knee, weight-bearing and patellofemoral views are recommended.	III	9.4 (8.7, 9.9)
6. According to current evidence, imaging features do not predict non-surgical treatment response and imaging cannot be recommended for this purpose.	II-III	8.7 (7.5, 9.7)
7. The accuracy of intra-articular injection depends on the joint and on the skills of the practitioner and imaging may improve accuracy. Imaging is particularly recommended for joints that are difficult to access due to factors including site (e.g. hip), degree of deformity and obesity.	III-IV	9.4 (8.9, 9.9)

Categories of evidence: **Ia**, evidence for meta-analysis of randomized controlled trials; **Ib**, evidence from at least one randomized controlled trial; **IIa**, evidence from at least one controlled study without randomization; **IIb**, evidence from at least one other type of quasi-experimental study; **III**, evidence from non-experimental descriptive studies, such as comparative studies, correlation studies and case-control studies; **IV**, evidence from expert committee reports or opinions or clinical experience of respected authorities, or both
LOA: 0-10 numerical rating scale

Overarching statements

1. These recommendations pertain only to symptomatic OA.
2. Imaging abnormalities of OA are commonly seen especially with increasing age.
3. Joint symptoms are also common and increase with age. Symptoms are not always causally related to imaging abnormalities.
4. Full history and examination is always required before considering the need for investigations, including imaging.
5. Modern imaging modalities provide the capability to detect a wide range of soft tissue, bony and cartilage pathology in OA. However, the increased information provided has not yet had any influence on clinical decision making with respect to management,

Making a diagnosis of OA

Recommendation 1: Imaging is not required to make the diagnosis in patients with typical* presentation of OA.

***typical features include: usage-related pain, short duration morning stiffness, age>40, symptoms affecting one or a few joints.** Level of evidence: III-IV. Level of agreement (95%CI): 8.7 (7.9, 9.4)

Although many studies applied imaging for diagnostic purposes, there was a lack of studies in which imaging was applied in addition to clinical findings to evaluate its additional impact on the certainty of diagnosis, which was a predefined criterion for inclusion.

A single study examined the added value of US of hand and feet over clinical findings in a cohort of patients with suspected or confirmed arthritis. When US was added to clinical findings, the diagnostic confidence in differentiating OA from inflammatory arthritis significantly increased. [2] Due to the absence of strong evidence supporting the use of different imaging modalities at different anatomical sites, the systematic use of imaging in the diagnostic process was not recommended in cases with typical clinical presentation. However, based on the joint site and clinical presentation, imaging might be considered when diagnoses other than OA are suspected. This aspect has been taken into account in recommendation 2.

Recommendation 2: In atypical presentations imaging is recommended to help confirm the diagnosis of OA and/or

make alternative or additional diagnoses. Level of evidence: IV. Level of agreement (95%CI): 9.6 (9.1, 10)

Studies were eligible for inclusion if they investigated the added value of imaging for differential diagnosis over clinical evaluation. Among studies evaluating the application of imaging for differential diagnosis, no study evaluated the impact of the addition of imaging above clinical findings. The possible application of imaging in atypical clinical scenarios was however recognized by the experts, which included this point in the recommendation.

Monitoring disease

Recommendation 3: Routine imaging in OA follow-up is not recommended. However, imaging is recommended if there is unexpected rapid progression of symptoms or change in clinical characteristics to determine if this relates to OA severity or an additional diagnosis. Level of evidence: III-IV. Level of agreement (mean, 95%CI): 8.8 (7.9, 9.7)

A specific question addressed the use of imaging for the follow-up. The 117 studies (mostly cohort studies) retrieved covered all joint sites except the foot and all imaging modalities except CT (Figure S9). Most of the 83 included studies focused on sensitivity to change. [3-86] The remaining studies investigated the trajectories of changes of elementary lesions detected by imaging when following OA natural history or described the parallel changes between different abnormalities detected by different imaging modalities. [87-105] Only a minority of studies examined the correlation between the change in imaging features and symptoms or relevant clinical outcomes (Table 2) and only 4 US studies evaluated the change of imaging after treatment (Supplementary file S10). [106-115]

Table 2. Studies correlating changes in imaging findings with symptoms, function or clinical outcome

Study	N	Site	Study design	Imaging	Outcome
Fukui 2010	68	Knee	Cohort	CR	Correlation between radiographic progression and pain and function scores Progressors had more pain and disability compared to non progressors
Eckstein 2014	189	Knee	Case-control	MRI	Cartilage loss in patients undergoing TKA vs controls OR (95%CI) for cartilage loss in patients undergoing TKA vs controls: 1.36 (1.08,1.70)
Kornaat 2007	182	Knee	Cohort	MRI	Change in BMLs/change in WOMAC pain and function No significant differences in WOMAC pain and function depending on the changes of BMLs
Phan 2006	34	Knee	Cohort	MRI	Cartilage and BMLs/WOMAC No significant correlation between cartilage loss, BMLs and WOMAC changes
Zhang Y 2011	651	Knee	Cohort	MRI	Change in pain status according to change in BMLs and effusion/synovitis score Changes in BMLs and synovitis severity (worsening or improving) significantly related to the risk of frequent knee pain (p 0.006 for worsening BMLs and p 0.045 for improving BMLs. No significant correlation with changes in effusion severity.
Haugen 2013	190	Hand	Cohort	CR	Radiographic progression/incident tenderness joints with progression had higher Odds for tenderness, joints with incident KL 3 or 4 had higher Odds for tenderness

N: number of participants; CR: conventional radiography; MRI: magnetic resonance imaging; TKA: total knee arthroplasty; OR: Odds Ratio; 95% CI: 95% confidence interval; WOMAC Western Ontario MacMaster Universities Arthritis Index; BMLs: bone marrow lesions

Moreover, there were no studies comparing clinical follow-up with imaging follow-up, or strategies adding imaging to clinical management.

The impact of imaging in the management of OA was also specifically addressed by the literature search. Three studies addressed this point. One RCT evaluating the impact of MRI in patients with knee pain assessed in a general practice setting showed that MRI led to an increase in therapeutic confidence but no significant changes in management. [116] A cross-sectional study in an orthopedic setting investigating the impact of CR over management decisions in knee OA showed that CR led to the change in the opinion in 166/400 cases. [117] A similar study evaluating the impact of CR in the assignment of priority for surgery in hip OA, showed a relative risk (95% CI) of 1.98 (1.23, 3.19) for an earlier assignment in patients with more severe radiographic scores. [118] No studies evaluated the impact of imaging for the management of hand or foot OA and no studies specifically addressed the issue of non-surgical management.

Recommendation 4: If imaging is needed, conventional (plain) radiography should be used before other modalities. To make additional diagnoses, soft tissues are best imaged by US or MRI and bone by CT or MRI. Level of evidence: III-IV. Level of agreement (95%CI): 8.7 (7.9, 9.6)

The performance of imaging in the detection of OA elementary lesions was addressed by the SLR, and highlighted heterogeneity in the use of imaging modality, lesions considered and reference standard. In fact, physical examination was frequently taken into account as reference standard, while surgery was considered in a minority of studies. Supplementary file S11 summarizes the studies with surgery as the reference standard. [119-140] As expected, the use of CR was mainly to detect bone and indirectly cartilage loss, MRI was used for bone, cartilage and soft tissues, with a single study assessing US for the evaluation of cartilage.

In general, CR was the imaging modality that was most frequently used for diagnostic, prognostic and follow-up purposes. However, no studies of the cost-effectiveness of each imaging modality or their sequence were found. In the absence of appropriate literature, the experts decided to emphasize the role of the most easily available and less costly imaging modality, proposing as second level investigations techniques that, due to their characteristics, are more suitable for the detailed assessment of soft tissues (MRI and US) or bone (CT).

Recommendation 5: Consideration of radiographic views is important for optimizing detection of OA features; in particular for the knee, weight-bearing and patellofemoral views are recommended. Level of evidence: III. Level of agreement (95%CI): 9.4 (8.7, 9.9)

This topic was addressed by an additional research question, evaluating the optimal combination of radiographic views in OA. Twenty-seven studies comparing different views for knee OA were included. In this context, all studies involving the tibiofemoral compartment considered weight-bearing views, both in extension and various degrees of flexion. [17, 127,147-159] Studies comparing fully extended and flexed views in general showed a moderate to good agreement between the two projections and similar sensitivity and specificity in detecting cartilage damage, considering arthroscopic findings as reference. [121, 145, 146, 151, 152] The flexed views demonstrated superiority in detecting joint space narrowing, a greater sensitivity to change and reproducibility compared to extended views. [17, 153,154,156, 158, 159]

Concerning the assessment of the patellofemoral compartment, skyline views had a greater inter- and intra-reader reliability and sensitivity to change compared to lateral projections. [24, 146, 158, 159] With surgery as reference standard, the skyline view had greater sensitivity and specificity to detect cartilage damage at the patellofemoral joint. [160]

There were 5 studies assessing the hip. Three studies compared weight-bearing and supine AP views of the pelvis, one of them showing greater average and maximal joint space width detected by the weight-bearing view, the remaining showing inconsistent results. [161-165] Two studies comparing pelvis, hip and oblique views projections in terms of reliability and sensitivity to change demonstrated similar reliability for views dedicated to the hip and views including all the pelvis, with comparable sensitivity to change. [166,167] No studies assessing the hand and the foot were found.

Role in prognosis

Recommendation 6: According to current evidence, imaging features do not predict non-surgical treatment

response and imaging cannot be recommended for this purpose. Level of evidence: II-III. Level of agreement (95%CI): 8.7 (7.5, 9.7)

Two specific research questions addressed the role of imaging in prognosis, referring to both the prediction of the natural history and to the prediction of non-surgical treatment outcomes. A number of studies addressed the issue of the prognostic value of imaging as predictor of the natural history of OA (Figure S12), while only a minority of studies, evaluating all joint sites, investigated the role in predicting treatment response. Due to the heterogeneity in populations, interventions, treatment and study design, a meta-analysis was not possible. In addition, progression of some imaging pathologies may have limited clinical significance. Tables 3 and 4 summarize the results of the 28

primary studies in which imaging was applied to predict treatment response. [170-193] Moreover, an existing SLR was available, without a quantitative synthesis. [194] The results on the prediction of response were mostly inconsistent across studies; for this reason the use of imaging for this purpose was not recommended.

Table 3. Summary of studies evaluating imaging in the prediction of response to treatment: systemic treatment

Study	N	Site	Study design	Imaging	Outcome
Gudbergsen 2012	192	Knee	RCT	CR MRI	mJSW, alignment and MRI scores/pain reduction in response to very low energy diet or low energy diet Among all radiographic and MRI parameters, only effusion score was significantly related to a reduction in pain
Gudbergsen 2011	30	Knee	RCT	CR MRI	KLK and MRI score/change in WOMAC pain and function during weight reduction at 32 weeks No significant association between KLK and MRI score and WOMAC
Hellio le Graverand 2013	1452	Knee	RCT	CR	KLK/structural progression in patients treated with cidunstat or placebo at 96 weeks No significant difference between KLK2 and KLK3 in terms of progression of joint space narrowing in both cidunstat and placebo group
Case 2003	82	Knee	RCT	CR	KLK and medial JSN/WOMAC response to diclofenac vs paracetamol at 12 weeks Patients with KLK 1-2 and not 3-4 and JSN grade 0-1 compared to 2 had a better response to diclofenac vs both placebo and paracetamol
Sawitzke 2008	375	Knee	RCT	CR	KLK/radiographic progression during treatment with glucosamine, chondroitin sulphate and celecoxib at 24 months OR for radiographic progression compared with the placebo group was <1 in patients with KLK 2 knees in all treatment groups, whereas it was >1 in patients with KLK 3 knees in all treatment groups
Mazuca 2010	379	Knee	RCT	CR	Alignment/radiographic progression in doxycycline vs placebo at 30 months Varus knees exhibited a greater loss of JSW than non-varus knees in patients receiving doxycycline
Knoop 2014	91	Knee	Cohort	MRI	MRI/change in WOMAC function in response to exercise program at 12 weeks The severity of the patellofemoral damage was significantly related to less improvement
Wenham 2012	65	Hand	RCT	MRI	MRI/response to prednisolone 5 mg at 12 weeks The baseline number of joints with definite synovitis or effusion did not correlate with OARSI response
Lequesne 2002	163	Hip	RCT	CR	JSW/structural progression in patients treated with avocado soybean at 2 years In patients with smaller JSW treated with avocado soybean, the reduction of JSW was half than in the placebo group; no differences in patients with more JSW
Rozendaal 2009	222	Hip	RCT	CR	KLK/WOMAC pain and function, JSN in patients taking glucosamine at 2 years Significant better WOMAC function response in patients with KLK 1 compared to KLK 2; no differences in WOMAC pain and JSN
Hoeksma 2005	103	Hip	RCT	CR	KLK/Harris Hip score and range of motion in response to manual therapy vs exercise Better response in terms of range of motion in lower compared to higher radiographic grades

N: number of participants; RCT: randomized controlled trial; MRI: magnetic resonance imaging; CR: conventional radiography; BML: bone marrow lesions; mJSW: minimal joint space width; JSN: joint space narrowing; JSW: joint space width; WOMAC: Western Ontario Mc Master Universities Osteoarthritis index; KLK: Kellgren and Lawrence grade; OARSI: osteoarthritis research society international

Table 4. Summary of studies evaluating imaging in the prediction of response to treatment: intra-articular treatment

Study	N	Site	Study design	Imaging	Outcome	
Barrett 1990	248	Knee	cohort	CR	Radiographic severity/response to intraarticular HA at 6 months	Patients with less severe radiographic grade had a better response in terms of pain at rest, at walking and at night
Gaffney 1995	84	Knee	RCT	CR	OA severity 0-3/response to intraarticular trimacinolone vs placebo at 3 weeks	No association between improvement in VAS pain and radiographic score
Toh 2002	60	Knee	cohort	CR	Alignment, sclerosis, cysts, osteophytes, JSN/WOMAC response to intraarticular HA at 12 weeks	Patients with lateral and medial JSN had less WOMAC response compared to patients without
Pendleton 2008	86	Knee	cohort	US	US/WOMAC response to intraarticular methylprednisolone	Higher baseline US scores: significant improvements in all WOMAC subscales at 1 and 6 weeks
Chao 2010	67	Knee	RCT	US	US inflammation/WOMAC response to triamcinolone at 12 weeks	statistically significant improvement in pain subscales among without inflammatory abnormalities at US patients compared to the remaining patients
Anandacoomarasamy 2008	32	Knee	Cohort	MRI	Cartilage volume/response to intraarticular HA at 6 months	no correlation between baseline MRI measures and clinical response
Drakonaki 2011	51	Foot	Cohort	CR US	Positive therapeutic response (i.a. methylprednisolone) at 12 months	No differences in terms of response in patients showing degenerative changes only on US and those showing changes in both US and CR
Han 2014	40	Foot	Cohort	CR	Response to intraarticular HA (VAS pain) at 12 months	Patients with early radiographic stage had a better response compared to those with advanced radiographic stage at 3 and 6 months, but not at 12 months
Sun 2011	46	Foot	Cohort	CR	KLG 2 and 3/AOS, AOFAS scores in response to intraarticular HA	no significant difference in the AOS, AOFAS, or clinical balance test scores between KLG 2 and 3 at any time point
Mallinson 2013	31	Hand	Cohort	CR US	CR and US/ response to intraarticular triamcinolone at 6 weeks	No significant association between treatment response and grade for osteophytes, joint-space narrowing and capsule thickness
Atchia 2011	77	Hip	RCT	US	Synovitis/response to i.a. methylprednisolone at 6 weeks	The presence of synovitis significantly predicted the response
Renneson- Rey 2008	55	Hip	Cohort	CR US	Effusion and KLG/OARSI response to HA at 6 months	Patients with KLG 1-2 had a better 1 months response compared to grades 3-4; non differences at 3 and 6 months, no differences in patients with or without effusion
Deshmukh 2011	220	Hip	Cohort	CR	KLG/pain relief after methylprednisolone injections at 2 weeks	Patients with KLG 3-4 had more frequently delayed relief compared to KLG 2
Robinson 2007	120	Hip	Cohort	CR US	US osteophytes and capsular thickening, KLG/WOMAC response to i.a. CS at 12 weeks	no baseline US or radiographic variable predictive of the outcome

N: number of participants; RCT: randomized controlled trial; MRI: magnetic resonance imaging; CR: conventional radiography; US: ultrasonography; VAS: visual analogue scale; HA: hyaluronic acid; JSN: joint space narrowing; WOMAC: Western Ontario Mc Master Universities Osteoarthritis index; KLG: Kellgren and Lawrence grade; OA: osteoarthritis; AOFAS Australian Orthopedic Foot and ankle society; OARSI: osteoarthritis research society international; CS: corticosteroids; i.a.: intra-articular

Treatment (imaging-guided procedures)

Recommendation 7: The accuracy of intra-articular injection depends on the joint and on the skills of the practitioner and imaging may improve accuracy. Imaging is particularly recommended for joints that are difficult to access due to factors including site (e.g. hip), degree of deformity and obesity. Level of evidence: III-IV. Level of agreement (95%CI): 9.4 (8.9, 9.9)

A search addressing the impact of imaging to guide intra-articular injections was run specifically for OA in the beginning. Including only studies comparing imaging-guided to blind procedures, 4 primary studies were found for the knee and one for the hand, and a qualitative systematic literature review for the knee (Table 5). The added value of US was addressed by 4 studies, while fluoroscopic guidance was tested in a single study. [195-199]

Table 5. Studies comparing imaging-guided to blind injections in OA

Study	N	Site	Study design	Imaging	Outcome
Bum Park 2012	99	Knee	RCT	US	Accuracy of HA injection vs blind injection OR (95%CI) for an accurate injection with US compared to blind: 4.68 (0.94,23.30)
Im 2006	99	Knee	RCT	US	Accuracy of HA injection vs blind injection Accurate injections: 95.5% (US-guided) vs 77.2% (blind); p=0.01
Jang 2013	126	Knee	RCT	US	Accuracy of US guided in plain injection, US guided out of plane injections and blind injection of triamcinolone exhacetonide Accuracy: US guided in plain 95.1%; US guided out of plain 97.7%; Blind 78% P<0.05 blind vs US guided injections
Sibbitt 2011	92	Knee	RCT	US	US guided vs blind triamcinolone in terms of pain relief, pain related to the injection, reinjection rate and cost Significant decrease in pain only in patients treated with US guided injection; US guided procedure was related to lower pain and reinjection rate, but higher costs
Karalezli 2007	16	Hand	Cohort	CR	Fluoroscopy-guided vs blind injections of HA in the trapezio-metacarpal joint in terms of pain related to the injection VAS pain related to the procedure: Fluoroscopic guide: 4.1 (range 3–6), anatomic guide 5.6 (range 3–7); p<0.005 No significant difference in terms of safety

N: number of participants; RCT: randomized controlled trial; US: ultrasonography; CR: conventional radiography; HA: hyaluronic acid; OR: Odds Ratio; VAS: visual analogue scale.

In order to retrieve further information on this topic, an additional search was performed (supplementary file S1 for search strategies), including studies comparing blind to guided injections in OA and also in other conditions. This search found 8 studies, of which 3 were already included in the previous results (Supplementary file S13). [200-204] Most of the studies were focused on the knee, with some studies on the hand and the foot, while no studies were found for the hip. All the additional studies investigated the impact of US. Accuracy was found to be better in imaging guided compared to blind procedures, however the results on the clinical outcomes of the injection were less consistent across studies. For this reasons the systematic use of imaging to drive injections was not recommended, leaving this tool to drive injection in specific situations, identified by the experts. Although the imaging modality is not specified in the recommendation, there is published evidence for the use of US, and imaging allows for real time evaluation of injection placement.

Future research agenda

The most important topics to drive future research were selected by the Task Force based on the (often considerable) gaps in the evidence and the needs arising from clinical practice (Table 6).

Table 6: Future Research Agenda

1	There is a need for methodologically robust studies to explore the added value of imaging (any modality) to clinical diagnosis or differential diagnosis.
2	What is the cost-effectiveness of imaging in OA clinical practice?
3	Is imaging able to help in identification of subgroups/phenotypes that may have different trajectories and enable targeted treatment based on these subgroups?
4	There is a need to understand if using imaging to measure response to therapy is of clinical benefit. This may require evaluation of novel imaging technologies that are able to sensitively detect change in relevant joint structures.
5	Quality studies are required to explore imaging (any modality) features that predict response to specific therapies.
6	There is a need for more research concerning the benefits of imaging in less commonly studied OA sites such as the foot and shoulder.
7	Specifically for hip OA, what is the added value of weight-bearing vs non weight-bearing X-rays?
8	What are the benefits of imaging-guidance in improving the efficacy of treatments?

DISCUSSION

Although a number of recommendations have been made on how to use imaging in OA clinical trials, these are the first recommendations on the use of imaging in OA in clinical practice. The development of the recommendations started from questions of clinical relevance selected by a task force of experts, with the aim to focus on topics of interest for clinical practice rather than research. The literature review identified a large number of studies, covering all the joint sites under examination. Although conventional radiography was still the most frequently applied technique, a substantial number of studies focused on modern imaging, MRI and US in particular.

However, despite the amount of data available in the literature, only a small part of this information was relevant for clinical practice. For this reason, many areas needing further investigation were identified. In particular, there was a lack of strategic studies investigating the additional value of imaging over clinical findings in making a diagnosis of OA, in the management and the follow-up of the disease, and inconsistent results dealing with the prediction of the outcome of non-pharmacological treatments. The absence of good study information in these areas did not enable the Task Force to recommend systematic imaging in all these areas. A research agenda was therefore generated in order to address these topics in the future research.

In conclusion, 7 recommendations covering different areas in the routine management of OA were developed. These are based on both available scientific evidence and expert opinion to provide a valuable and sensible guide for the use of imaging in clinical practice.

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