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Inflammation as a target for treatment in hand osteoarthritis

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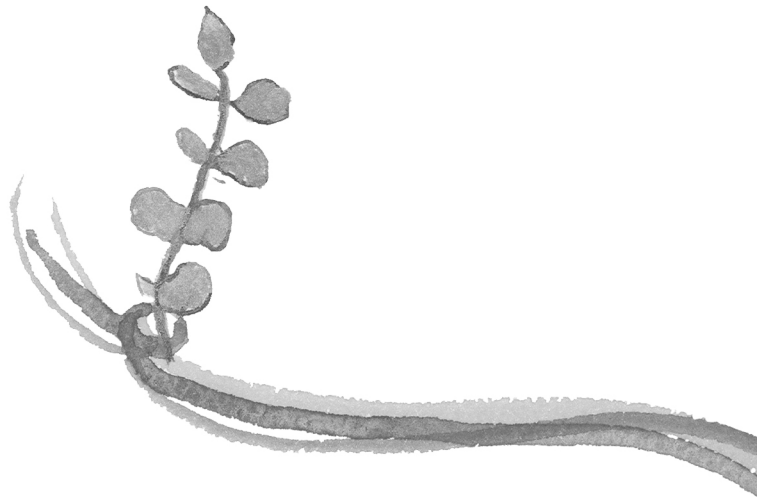


CHAPTER 4

2018 update of the EULAR recommendations for the management of hand osteoarthritis

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ABSTRACT

Since publication of the European League Against Rheumatism (EULAR) recommendations for management of hand osteoarthritis (OA) in 2007 new evidence has emerged. The aim was to update these recommendations. EULAR standardised operating procedures were followed. A systematic literature review was performed, collecting the evidence regarding all non-pharmacological, pharmacological and surgical treatment options for hand OA published to date. Based on the evidence and expert opinion from an international task force of 19 physicians, healthcare professionals and patients from 10 European countries overarching principles and recommendations were formulated. Level of evidence, grade of recommendation and level of agreement were allocated to each statement. Five overarching principles and 10 recommendations were agreed on. The overarching principles cover treatment goals, information provision, individualisation of treatment, shared decision-making and the need to consider multidisciplinary and multimodal (non-pharmacological, pharmacological, surgical) treatment approaches. Recommendations 1-3 cover different non-pharmacological treatment options (education, assistive devices, exercises and orthoses). Recommendations 4-8 describe the role of different pharmacological treatments, including topical treatments (preferred over systemic treatments, topical non-steroidal anti-inflammatory drugs (NSAIDs) being first-line choice), oral analgesics (particularly NSAIDs to be considered for symptom relief for a limited duration), chondroitin sulfate (for symptom relief), intra-articular glucocorticoids (generally not recommended, consider for painful interphalangeal OA) and conventional/biological disease-modifying antirheumatic drugs (discouraged). Considerations for surgery are described in recommendation 9. The last recommendation relates to follow-up. The presented EULAR recommendations provide up-to-date guidance on the management of hand OA, based on expert opinion and research evidence.

INTRODUCTION

Hand osteoarthritis (OA) is a common musculoskeletal disease, with prevalence rising steeply with increasing age.¹⁻³ The disease is associated with hand pain, stiffness, functional limitation, decreased grip strength and reduced quality of life.⁴⁻⁶ Clinical hallmarks of the disease include bony enlargement and deformities of the hand joints, at times accompanied by soft tissue swelling.⁷ Hand OA has a variable disease course.⁸ The first European League Against Rheumatism (EULAR) recommendations for the management of hand OA were published in 2007.⁹ The American College of Rheumatology (ACR) published management recommendations for hand, hip and knee OA in 2012, including evidence available to the end of 2010, and other societies, including an expert group of occupational therapists and the Italian Society for Rheumatology, formulated treatment recommendations in 2011 and 2013, respectively.¹⁰⁻¹²

For a long time, hand OA was a “forgotten disease”, resulting in a paucity of clinical trials to guide recommendations, and therefore many of the propositions of previous recommendations were based mainly on expert opinion.¹³ However, in recent years, hand OA has attracted more attention, and new data have become available on several pharmacological and non-pharmacological treatments, including but not limited to: self-management, application of thumb base orthoses, topical non-steroidal anti-inflammatory drugs (NSAIDs), oral corticosteroids, various intra-articular therapies and treatment with conventional synthetic and biological disease-modifying antirheumatic drugs (cs/bDMARDs), for example, hydroxychloroquine and tumour necrosis factor (TNF) inhibitors.

These more recent data have given new insights into treatment options. It was therefore timely to update the 2007 management recommendations. In this paper, we present the 2018 update of the EULAR recommendations for the management of hand OA.

METHODS

The development of the update was performed according to the 2014 EULAR Standard Operating Procedure (SOP).¹⁴ As prescribed by the SOP, the process set out in Appraisal of Guidelines for Research & Evaluation II (AGREE II) was followed.¹⁵ The convenor (MK), methodologist (LC) and fellow (FK) defined research questions for the systematic literature review (SLR) and prepared a 1-day task force meeting. The task force further comprised 10 rheumatologists, 1 plastic surgeon (MR), 3 healthcare professionals in the field of physiotherapy and occupational therapy (KD, IK, TS) and 2 patient research partners (EG, WS). Two task force members were Emerging Eular NETwork members (IKH, FK). The task force represented 10 countries across Europe.

Under guidance of the methodologist, the fellow performed an SLR on the efficacy and safety of all non-pharmacological, pharmacological and surgical therapies available for hand OA. Although published separately, the SLR¹⁶ and the current updated management recommendations are complementary and should be considered together.

To explore current clinical practice in hand OA treatment and which topics healthcare professionals and patients felt should be covered in the update of the recommendations, members of the task force completed an online survey prior to the 1-day meeting.

Using the previous recommendations as a basis, together with the data obtained from the survey and the SLR, the convenor, methodologist and fellow prepared a proposal for wording for the update of the recommendations.

The results of the survey and the SLR were sent to the task force members in advance of a 1-day meeting where they were again presented. Through group discussion, overarching principles were formulated and the recommendations were updated. For every proposed overarching principle and recommendation, the results from the survey, evidence from the SLR and a proposed formulation were presented. Following discussion and rewording of the statement, voting was undertaken. A 75% majority was required to approve the statement. In case of disagreement, discussion was resumed and changes to the statement were made. The second voting round required a 67% majority, and if the formulation remained unagreed, an additional round of discussion followed. The third voting round required only 50% support for approval of the statement. The wording of the statements was considered final after the 1-day meeting.

After the meeting, the level of evidence (LoE) and grade of recommendation (GoR) were added to each recommendation, derived from the evidence from the SLR and according to the Oxford Centre for Evidence-Based Medicine standards.¹⁷ Finally, the overarching principles and recommendations (including LoE and GoR, and rationale for each statement based on the survey data, evidence from the SLR and discussion during the 1-day meeting) were sent to all task force members, who were asked to add their level of agreement (LoA) to each of the statements. The vote for the LoA was carried out anonymously on a numerical rating scale of 0-10 (0: do not agree at all, 10: fully agree). The mean and SD were calculated.

The final manuscript was reviewed, revised and approved by all task force members, followed by a final review by the EULAR Executive Committee.

RESULTS

Overarching principles

Overarching principles were not stated in the 2007 recommendations and were a new inclusion in the 2018 update. Overarching principles are generic statements, serving as the basis for management of patients with hand OA. Some of the 2007 recommendations were included in the 2018 update in the form of an overarching principle. The LoA of each overarching principle is presented in table 1.

Table 1. 2018 Update of the EULAR recommendations for the management of hand OA

Overarching principles		LoE*	GoR†	LoA (0-10)
A.	The primary goal of managing hand OA is to control symptoms, such as pain and stiffness, and to optimise hand function, in order to maximise activity, participation and quality of life			9.7 (0.7)
B.	All patients should be offered information on the nature and course of the disease, as well as education on self-management principles and treatment options			9.8 (0.8)
C.	Management of hand OA should be individualised taking into account its localisation and severity, as well as comorbidities			9.9 (0.2)
D.	Management of hand OA should be based on a shared decision between the patient and the health professional			9.6 (1.1)
E.	Optimal management of hand OA usually requires a multidisciplinary approach. In addition to non-pharmacological modalities, pharmacological options and surgery should be considered			9.3 (1.2)
Recommendations				
1.	Education and training in ergonomic principles, pacing of activity, and use of assistive devices, should be offered to every patient	1b	A	9.3 (1.1)
2.	Exercises to improve function and muscle strength, as well as to reduce pain, should be considered for every patient	1a	A	9.1 (1.6)
3.	Orthoses should be considered for symptom relief in patients with thumb base OA. Long term use is advocated	1b	A	9.3 (1.0)
4.	Topical treatments are preferred over systemic treatments because of safety reasons. Topical NSAIDs are the first pharmacological topical treatment of choice	1b	A	8.6 (1.8)
5.	Oral analgesics, particularly NSAIDs, should be considered for a limited duration for relief of symptoms	1a	A	9.4 (0.9)
6.	Chondroitin sulfate may be used in patients with hand OA for pain relief and improvement in functioning	1b	A	7.3 (2.7)
7.	Intra-articular injections of glucocorticoids should not generally be used in patients with hand OA*, but may be considered in patients with painful interphalangeal joints**	*1a- **1b	A	7.9 (2.4)
8.	Patients with hand OA should not be treated with conventional or biological disease modifying antirheumatic drugs	1a	A	8.8 (1.8)
9.	Surgery should be considered for patients with structural abnormalities when other treatment modalities have not been sufficiently effective in relieving pain. Trapeziectomy should be considered in patients with thumb base OA and arthrodesis or arthroplasty in patients with interphalangeal OA	5	D	9.4 (1.4)
10.	Long-term follow-up of patients with hand OA should be adapted to the patient's individual needs	5	D	9.5 (1.7)

*1a: Systematic review of RCTs; 1b: individual RCT; 2a: systematic review of cohort studies; 2b: individual cohort study (including low-quality RCT; eg, <80% follow-up); 3a: systematic review of case-control studies; 3b: individual case-control study; 4: case-series (and poor quality cohort and case-control studies); 5: expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles".¹⁷ †A: Based on consistent level 1 evidence; B: Based on consistent level 2 or 3 evidence or extrapolations from level 1 evidence; C: Based on level 4 evidence or extrapolations from level 2 or 3 evidence; D: Based on level 5 evidence or on troublingly inconsistent or inconclusive studies of any level.¹⁷ EULAR, European League Against Rheumatism; GoR, grade of recommendation; LoA, level of agreement; LoE, level of evidence; NSAIDs, non-steroidal anti-inflammatory drugs; OA, osteoarthritis; RCT, randomised clinical trial.

The primary goal of managing hand OA is to control symptoms, such as pain and stiffness, and to optimise hand function, in order to maximise activity, participation and quality of life

Management should aim to achieve the best possible activity performance, participation and quality of life. Studies have shown that patients with hand OA have a decreased health-related quality of life.¹⁸ Symptoms such as pain, stiffness and decreased hand function are hallmarks of the disease, and contribute to altered quality of life.^{6,19} This overarching principle was based on the International Classification of Functioning, Disability and Health framework.²⁰ The wording 'optimise' and 'maximise' were chosen to reflect that management of hand OA should be more ambitious than merely aiming for a patient-acceptable symptom state.

All patients should be offered information on the nature and course of the disease, as well as education on self-management principles and treatment options

Education is considered a core treatment in the management of patients with hand OA, and should be offered to all patients. This overarching principle is an additional, more generic statement on education, besides the first recommendation concerning specific education and training. In patients with chronic complaints returning for follow-up, information and education provision should be an ongoing process involving reinforcement and expansion. Explicit evidence supporting the efficacy and content of provision of information and education in hand OA is lacking. Trained health professionals other than the physician can play an important role in the provision of information and education.

Management of hand OA should be individualised taking into account its localisation and severity, as well as comorbidities

This overarching principle was modified from the 2007 recommendation about individualisation of treatment. In the premeeting survey, >75% of health professionals indicated that patient characteristics that are considered important include: age, type of complaint (eg, pain or disability), mechanical factors, patient's wishes and expectations, presence of inflammation, severity of structural damage and presence of erosions. In the survey, most health professionals also supported different treatment approaches according to disease location (especially thumb base OA) or OA subset (especially erosive or "inflammatory" OA). The 2007 recommendation included consideration of many of these individual factors. Yet although many of these factors are known to be determinants of worse outcome (eg, presence of inflammation is known to be associated with disease progression²¹⁻²³), evidence of effect modification is lacking for most of these factors.²⁴ Moreover, it is unknown whether treatment of modifiable factors will in turn change disease outcomes (eg, there is no evidence that treatment of inflammation reduces disease progression). OA localisation (most importantly finger vs thumb base OA), OA severity and presence of comorbidities were thought to be the only aspects that may currently influence treatment decisions. This is also reflected in the recommendations. 'Severity' can encompass several features, including a high number of hand joints with OA, one or two severely affected joints or acute joint inflammation due to OA. The patient's wishes and expectations were not mentioned separately in this overarching principle, since this concept is incorporated in the overarching principle concerning shared decision-making.

Management of hand OA should be based on a shared decision between the patient and the health professional

Shared decision-making, an approach to healthcare in which health professionals and patients mutually share information to reach consensus about the preferred management strategy, should be the basis of management in hand OA.²⁵ This overarching principle implies that not only the best available evidence, but also the patients' wishes and expectations are important to be considered when making decisions on managing the disease. Achieving shared decision-making depends on building and maintaining a good relationship between patient and health professional, and sharing the best evidence, in order to be able to make an informed decision. It pertains to all stages of management, including, for example, setting a treatment goal, choosing the best strategy to achieve it or considering other strategies when the treatment goal is not reached.

Optimal management of hand OA usually requires a multidisciplinary approach. In addition to non-pharmacological modalities, pharmacological options and surgery should be considered

Hand OA is both a heterogeneous disease, leading to a variety of signs and symptoms, and a chronic disease. Over the course of the disease, patients with hand OA therefore often require multidisciplinary care. Health professionals involved in care for patients with hand OA, may include, for example, the general practitioner, rheumatologist, occupational or physical therapist, orthopaedic or plastic surgeon and the rehabilitation specialist. Which care is delivered by each health professional differs by country, depending for example on local preferences or customs and social security systems. In some clinics, structured multidisciplinary care programmes or integrated care pathways are provided. However, it is unclear whether such programmes providing a structured combination of different non-pharmacological therapies are efficacious. For example, no consistent beneficial effect of combination programmes including education, joint protection and exercises over education alone has been determined.²⁶⁻²⁸

The second part of this overarching principle, that different treatment modalities should be considered, was modified from the first 2007 recommendation, and initially discussed as a separate overarching principle (LoA: 100%). Later, the concept 'multidisciplinary care' was added, since it was recognised that different modalities may be provided by different health professionals. By modifying the 2007 recommendation, this overarching principle now also reflects that the first step in hand OA management should focus on non-pharmacological therapies, which may be complemented by pharmacological and/or surgical options, although not necessarily for all patients with hand OA, depending on the level of symptoms.

Recommendations

In total, 10 recommendations were formulated (table 1). Table 1 also presents the LoE, GoR and LoA for each recommendation. Many of the 2007 recommendations were modified because new evidence has emerged since the previous SLR, and were formulated as recommendations rather than 'statements' reflecting the state of the evidence and/or expert opinion. Two recommendations are new (#8, #10), one recommendation was split into two (old #3 into new

#1 and #2), two recommendations were combined into one (old #7 and #8 into new #5), and one recommendation was deleted (old #4). The recommendation that was deleted concerned the use of heat and ultrasound, which was based on expert opinion and extrapolation from hip or knee OA studies.

Education and training in ergonomic principles, pacing of activity, and use of assistive devices, should be offered to every patient

Education and training in ergonomic principles and pacing of activity, formerly included in the recommendations under the term 'joint protection', is an important aspect of management, and has been shown to be efficacious in one study.²⁶ The term 'joint protection', although still often used, was viewed by the task force as an outdated concept, implying that one should protect the joints and refrain from using them. It was thus replaced by a more explicit statement of what the education and training should consist of. The use of assistive devices is an important and commonly used strategy to improve patient's self-management, and shown to be efficacious.^{29,30} No evidence is available that intensive programmes delivering this care are more effective or cost-effective than more simple strategies.³¹ This care can be delivered by any health professional specialised in these interventions (eg, an occupational or physical therapist or a trained nurse).

Exercises to improve function and muscle strength, as well as to reduce pain, should be considered for every patient

Although exercise was endorsed in the 2007 recommendations, no supporting evidence was available at that time. Since then, multiple trials (n=7) have been performed, and their results were summarised in a Cochrane review.³² It was shown that hand exercises have small beneficial effects on self-reported pain and function, joint stiffness and grip strength, while resulting in few and non-severe adverse effects. However, the interventions studied were heterogeneous, varying from home-based exercises after a single instruction session to multiple supervised sessions per week for several weeks, and also the frequency of exercising, number of repetitions per exercise, and type of exercises (eg, strengthening or stretching) were variable. Furthermore, the review authors debated whether the effects that were found constituted a clinically relevant improvement, and the beneficial effects were not sustained when patients stopped exercising. Exercises should aim at improving joint mobility, muscle strength and thumb base stability. Exercise regimens aimed at the first carpometacarpal (CMC-1) joint differ from those for interphalangeal joints.

Orthoses should be considered for symptom relief in patients with thumb base OA. Long term use is advocated

Since the 2007 recommendations many orthosis trials have been performed, of which five compared orthoses to usual care or a non-pharmacological intervention.³³⁻³⁷ These trials provide evidence for beneficial effects of a thumb base orthosis, especially on pain and to a lesser extent on function, but not on grip strength, when used for a prolonged period (at least 3 months). No improvements were evident when used for shorter periods. Long-term use is

thus advocated. The 2007 recommendations advised the use of orthoses to “prevent/correct lateral angulation and flexion deformity” in patients with thumb base OA, yet no evidence to date supports an effect of orthoses on angulation or deformity, and therefore the statement was reworded.

No straightforward advice can be given for the type of orthosis (short or long, custom-made or prefabricated, neoprene, thermoplast or other material) or instructions for use (eg, during activities of daily living, at night, constantly), as studies are heterogeneous and no consistent benefit of one type of orthosis over the other could be identified. Trials showing a long-term beneficial effect of orthosis use investigated a custom-made thermoplast long orthosis to be worn during activities of daily living,³⁵ and a custom-made neoprene long orthosis to be worn at night.³⁷

It is important to pay attention to prescribing a well-fitted orthosis, preferably custom-made by a specialised health professional. This will likely improve patients' compliance and increase long-term use.

Most trials were performed in patients with thumb base OA, and only one trial investigated night-time distal interphalangeal joint (DIP) orthoses, which did not prove to be efficacious, and is therefore not specifically recommended.³⁸

Topical treatments are preferred over systemic treatments because of safety reasons. Topical NSAIDs are the first pharmacological topical treatment of choice

Topical NSAIDs are recommended as a first-line pharmacological treatment, due to their favourable safety profile compared with oral analgesics and beneficial effects on pain and function.³⁹⁻⁴¹ Topical diclofenac gel showed small improvements in pain and function after 8 weeks compared with placebo in one high-quality study.⁴¹ Moreover, topical NSAIDs can show similar pain relief as oral NSAIDs.^{39,40} Pooled safety data from randomised clinical trials comparing topical diclofenac gel to placebo in patients with hand and knee OA also showed similar low rates of adverse effects in subgroups of low-risk versus high-risk patients (ie, age ≥ 65 years, and with comorbid hypertension, type 2 diabetes or cerebrovascular or cardiovascular disease).⁴² When a large number of joints are affected, systemic pharmacological treatment may be preferred. At present, no data is available on long-term effects of topical NSAIDs.⁴³

Capsaicin is another topical treatment, which is however known to be associated with frequent local adverse effects (burning and stinging sensation), and therefore success of blinding of the (positive) placebo-controlled trial investigating its efficacy is questionable.⁴⁴

Topical application of heat was regarded by the task force as a self-management strategy that patients can apply at home, with weak and conflicting evidence for a possible beneficial effect.⁴⁵⁻⁴⁷ It was therefore not included as a separate recommendation in this update. Cold packs, in case of inflammation during an OA flare, may also give symptomatic relief, though studies in hand OA have not been performed, and a single knee OA study comparing hot and cold application to usual care found no between-group differences.⁴⁸

Oral analgesics, particularly NSAIDs, should be considered for a limited duration for relief of symptoms

This recommendation is a combination of the 2007 recommendations concerning paracetamol and oral NSAIDs.

Oral NSAIDs effectively improved pain and function after 2-4 weeks in three high-quality studies.⁴⁹⁻⁵¹ However, adverse effects are well-known, especially in the elderly. No new evidence was identified compared with the 2007 recommendations. The advice to prescribe NSAIDs at the lowest effective dose, for a limited duration (preferably on-demand), with attention for the risk-benefit-ratio, especially in patients at high risk of gastrointestinal, cardiovascular or renal adverse effects, remains unchanged.

Paracetamol is prescribed by many health professionals, and also in the premeeting survey the vast majority of health professionals indicated that they prescribed paracetamol to their patients with hand OA. Patients' experience with paracetamol is known to be variable. It has generally been regarded as a safe treatment option, although lately its risk-benefit profile has been a topic of debate, even leading to controversy about including it in the National Institute for Health and Care Excellence (NICE) guidelines on OA.⁵² Three small trials, two only published as conference abstracts, have studied paracetamol (1000-3900 mg daily) in hand OA.⁵³⁻⁵⁵ In these trials, paracetamol was not superior over placebo or an active comparator. Two large meta-analyses of trials in patients with knee and hip OA found small effects on pain, with doubtful clinical significance.^{56,57} Evidence from these trials showed that paracetamol was associated with an increased risk of liver test abnormalities, although the clinical relevance of this finding is unknown, but not with increased risk of any other safety parameter.⁵⁷ A narrative review of long-term observational studies in the general adult population found a dose-response increased risk of mortality (n=2 trials), cardiovascular (n=4), gastrointestinal (n=1) and renal adverse effects (n=4). This should, however, be interpreted with caution, as these observational studies were associated with a large risk of bias (most importantly confounding by indication) and imprecision of measurement of paracetamol exposure (eg, reliance on self-reported medication use or prescription databases).⁵⁸ In conclusion, the efficacy of paracetamol in hand OA is still uncertain and likely to be small, and this drug is also not free from adverse effects, although for now there is no reason to refrain from prescribing paracetamol, preferably for a limited duration, in selected patients (eg, when oral NSAIDs are contraindicated). Tramadol (with or without paracetamol), was also regarded by the task force as an alternative oral analgesic, although currently no evidence in patients with hand OA is available to support its use.

Chondroitin sulfate may be used in patients with hand OA for pain relief and improvement in functioning

Chondroitin sulfate and glucosamine are among the most widely used over-the-counter nutraceutical products for OA. Chondroitin sulfate was shown to be effective for relief of hand OA symptoms in one well-performed trial, although in patients with knee and hip OA a clinically meaningful effect of glucosamine and chondroitin preparations has not been proven.⁵⁹⁻⁶¹ A single report of two (independent) placebo-controlled trials reported structure-modifying effects of chondroitin polysulfate (a preparation that is not commercially available), but not of chondroitin

sulfate.⁶² However, this evidence was judged unconvincing to promote chondroitin sulfate for structure modification. No placebo-controlled trials of glucosamine have been performed in patients with hand OA. Owing to the limited evidence available to support this recommendation, and even less convincing data from trials in knee and hip OA which led to discouragement of chondroitin sulfate and glucosamine use by NICE, this recommendation was formulated more as a suggestion than a recommendation to use.⁶³

In addition to the nutraceuticals discussed here, other so-called Symptomatic Slow Acting Drugs for Osteoarthritis ('SYSADOA') were included in the 2007 recommendation, namely avocado soybean unsaponifiables, diacerhein and intra-articular hyaluronan. Currently, however, there is no evidence for clinical efficacy of these preparations.¹⁶ The task force further agreed that at this moment in OA no drugs are available with disease-modifying properties, and therefore these substances should also not be advocated as such.

Intra-articular injections of glucocorticoids should not generally be used in patients with hand OA, but may be considered in patients with painful interphalangeal joints

This recommendation was completely revised, since the previous recommendation was largely based on expert opinion and new evidence could not confirm a beneficial effect of intra-articular glucocorticoids over placebo in patients with thumb base OA.⁶⁴⁻⁶⁶ In contrast, in one trial of patients with painful interphalangeal OA, intra-articular glucocorticoid injections were more effective than placebo for pain during joint movement and joint swelling.⁶⁷ The formulation 'should not generally be used' was chosen, since the task force recognised that in specific cases where, for example, clear joint inflammation is present, injection with glucocorticoids may still be a therapeutic option. Evidence pertaining specific subgroups that could benefit from intra-articular glucocorticoids, for example, patients with active joint inflammation due to a flare of the disease, is lacking. It is also unknown whether image-guided injections are more beneficial or safer than blind injections, although a Cochrane review of shoulder injections could not establish clinical advantages of guided injection.⁶⁸ Injections in small finger joints are preferably performed by a rheumatologist.

Patients with hand OA should not be treated with conventional or biological disease modifying antirheumatic drugs

This recommendation was newly added, after several studies have emerged demonstrating the lack of efficacy of csDMARD/bDMARD. In clinical practice, severe cases of inflammatory, often erosive, hand OA are occasionally prescribed csDMARDs or even bDMARDs. However, the 2007 recommendations did not include advice on the use of these drugs, and no evidence was available at that time. Trials investigating the efficacy of hydroxychloroquine,^{53,69,70} different TNF-inhibitors,⁷¹⁻⁷⁴ and anti-interleukin-1,⁷⁵ could not demonstrate efficacy of these antirheumatic drugs in patients with hand OA. Trials investigating methotrexate, sulfasalazine or colchicine have not been performed. Two trials investigated low-dose oral glucocorticoids (3-5 mg daily), one in combination with dipyridamole, yet reached conflicting conclusions.^{76,77} Evidence for short-term use of oral glucocorticoids is therefore still equivocal; at this moment, there is no reason to prescribe glucocorticoids for prolonged periods of time in patients with hand OA.

Surgery should be considered for patients with structural abnormalities when other treatment modalities have not been sufficiently effective in relieving pain. Trapeziectomy should be considered in patients with thumb base OA and arthrodesis or arthroplasty in patients with interphalangeal OA This recommendation was slightly modified compared with the 2007 recommendation on surgery. Trials with a placebo-controlled or sham-controlled group have not been performed, and so this recommendation remains mostly based on expert opinion.

In the first part of the updated recommendation, treatment failure has now been defined more specifically as 'not sufficiently effective in relieving pain', since surgical interventions are mostly effective to relieve pain, and are less effective in improving function (expert opinion). Surgery should only be considered in persistently symptomatic patients with structural abnormalities despite conventional treatments, including both non-pharmacological and pharmacological therapies. Second, the recommendation does not solely focus on the thumb base joint as before, since surgery can be a viable treatment option in cases with severe painful interphalangeal OA as well.

Surgical interventions vary for the different hand joints. In the CMC-1 joint, trapeziectomy is generally the surgical technique of choice. An updated Cochrane review of the evidence of surgery for thumb base OA found no consistent benefit of one surgical technique over the other, although in general more complicated interventions than simple trapeziectomy led to more adverse effects and were not more effective.⁷⁸ Complications reported in the studies included pain, instability, nerve dysfunction, superficial wound infections, tendon pulling sensation and chronic regional pain syndrome. Arthroplasty (typically silicone implants) is the preferred surgical technique for the proximal interphalangeal (PIP) joints, with the exception of PIP-2, for which arthrodesis may be considered. Arthrodesis is the recommended approach for the distal interphalangeal joints. No controlled trials of surgery for interphalangeal OA have been published so far.

It is important that patients receive rehabilitation postoperatively. Osteotomy was deleted from the recommendation, as it is an obsolete technique for treating hand OA.

Long-term follow-up of patients with hand OA should be adapted to the patient's individual needs A recommendation on follow-up was not included in the previous recommendations. Due to the lack of evidence for the cost-effectiveness of long-term follow-up, an evidence-based statement could not be made. Hand OA is a heterogeneous disease, and the spectrum of patients seen with hand OA is diverse, which resulted in a general recommendation. 'Individual needs' that may be taken into consideration when assessing the need for follow-up include severity of symptoms, presence of erosive disease, use of a pharmacological therapy that needs re-evaluation, and patient's wishes and expectations.

It was discussed whether long-term follow-up is always indicated for patients with erosive OA. In spite of evidence that these patients have more clinical and structural progression,^{79,80} the task force perceived that currently follow-up does not add a benefit. In the absence of a disease-modifying treatment, the goal of follow-up differs from the situation in many other rheumatic diseases. Follow-up will likely increase adherence to non-pharmacological therapies like exercise or orthoses, and provides an opportunity for re-evaluation of treatment (eg, revision of orthoses, or adjustment of pharmacological treatment). For most patients, standard radiographic follow-up is not useful at

this moment. Follow-up does not necessarily have to be performed by the rheumatologist. At what moment other health professionals should refer a patient back to the rheumatologist, should be considered at an individual patient level.

Research agenda

A research agenda was developed (table 2).

Table 2. Research agenda for hand OA

Theme	Research questions
Pathophysiology	Does treatment of inflammation lead to a decrease in structural progression?
Treatment strategy	- Which contextual factors influence treatment effects? - Assessing efficacy of stratified treatment based on contextual factors.
Trial methodology	Clear definition of study population to accommodate later subgroup analyses or stratification based on patient characteristics.
Outcomes	- Evaluation of outcome measures in hand OA, and use of existing outcome core sets for future hand OA trials. - Cost-effectiveness studies. - Defining treatment targets for disease-modifying drugs.
Education	- Evaluation of efficacy of education without concomitant exercise. - Definition of the desired content of education.
Exercise	- Assessment of most effective type of hand exercises, most optimal method of delivery, and most optimal frequency. - Assessment of methods to increase adherence to exercise.
Orthoses	- Assessment of orthosis design (material, which joints are supported), and instructions or frequency for use of orthoses. - Evaluation of daytime orthoses, night-time orthoses and a combination of daytime and night-time orthoses. - Placebo-controlled trial of orthoses for thumb base OA. - Evaluation of effect of use of orthoses on CMC-1 subluxation.
Topical treatments	Another placebo-controlled trial of topical NSAID.
Oral analgesics	- Placebo-controlled trial of paracetamol. - Placebo-controlled trial of tramadol.
Nutraceuticals	- Placebo-controlled trial of glucosamine. - Another placebo-controlled trial of chondroitin sulfate, also to assess possible effect on structural damage.
Intra-articular therapies	- Placebo-controlled trial of intra-articular glucocorticoids specifically in CMC-1 joints with OA inflammation - Image-guided injection versus blind injection
DMARDs	- Placebo-controlled trial of methotrexate. - Placebo-controlled trial of low-dose oral glucocorticoids.
Surgery	- Randomised controlled trial of most commonly used surgical interventions. - Assessment of best timing of referral to surgery. - Evaluation of whether early non-pharmacological interventions may prevent or delay surgery.
Follow-up	Investigation of trajectories in hand OA to define subgroups.
Implementation	Determination of optimal implementation of the guidelines in people with hand OA.

CMC-1, first carpometacarpal; DMARDs, disease-modifying antirheumatic drugs; OA, osteoarthritis.

DISCUSSION

This is the first update of the EULAR recommendations for the management of hand OA, containing five overarching principles and 10 recommendations. After a decade, it was timely to update the recommendations, as many new studies had emerged during this period. In light of this new evidence, many of the 2007 recommendations were modified and new recommendations were added. Furthermore, recommendations were formulated as recommendations rather than 'statements' reflecting the state of the evidence and/or expert opinion.

In this update, two patient research partners with hand OA were included as active members of the task force, while the 2007 task force did not include patient research partners. This is an important improvement, since patients are one of the important target-users of these recommendations, and in evidence-based clinical decision making, the patient perspective is valued as equally important to research evidence and clinical expertise.⁸¹

New in the 2018 update is also the use of overarching principles. This is in line with other EULAR sets of management recommendations. Some of the 2007 recommendations were in retrospect already more an overarching principle, and were (modified and) included in the 2018 update as such, for example, statements regarding individualised treatment, and combination of non-pharmacological and pharmacological treatment modalities.

Moreover, the 2018 update of the SLR summarising the evidence for the recommendations, is published as a separate manuscript.¹⁶ As pointed out in their discussion, Zhang *et al* did perform a systematic search of the literature to underpin the recommendations, but rather than reviewing all possible treatments, a limited number of key propositions were highlighted. The publication of the complete SLR, including a detailed description of its methodology and results, provides the interested reader with a full update of the currently available evidence concerning the management of hand OA and provides more insight in the size of the effects of different interventions compared with placebo or control treatment. It is important to note that the recommendations as presented in table 1 cannot be read and interpreted without the accompanying text, and this manuscript and the separately published SLR form an integral part, and should be considered together.

Guidelines for the management of OA from other large (international) societies, including the 2012 ACR recommendations and the NICE guidelines, mainly focus on large joint OA (ie, knee and hip).^{10,63} However, these recommendations cannot readily be extrapolated to the situation of OA in the hand because of the unique functionality of the hands compared with large joints, and emerging evidence for different risk factors and possibly even pathophysiological mechanisms of OA at different joint sites.

These recommendations are targeted at all health professionals who care for patients with hand OA. Since hand OA is a prevalent disease encountered by a variety of healthcare providers in primary and secondary care, this not only includes rheumatologists, but also for example general practitioners, orthopaedic and plastic surgeons, occupational and physical therapists and rehabilitation physicians. Furthermore, these recommendations aim to inform patients about their disease to support shared decision-making, as well as students. Other targeted stakeholders include pharmaceutical industry, policy makers and health insurance companies.

Efforts to implement these recommendations will be made by dissemination across national societies, online and by presentations in (inter)national congresses and educational sessions for healthcare providers. A slide deck to facilitate dissemination will be provided on the EULAR website. Evidence of optimal systematic implementation is lacking and this was highlighted in the research agenda.

Although a relatively long period passed between the first set of recommendations and the current update, it is expected that the next update of the recommendations may be needed sooner, as the field of hand OA is growing. Advances in research of OA pathophysiology as well as outcome measurement, increase the likelihood of finding new therapeutic options. The next update should be undertaken when sufficient new data are available, either on the current treatment options, or on new therapies.

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