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A firm grip on hand OA: 20 years of progress and prospects

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In the past two decades the field of hand osteoarthritis (OA) has moved from resignation to action. Despite progress, such as the recognition of the phenotypic heterogeneity of hand OA (including inflammation- and/or metabolic syndrome-associated hand OA) and the standardization of imaging and treatment outcomes, challenges remain in achieving truly disease-modifying therapies.

In 2009, we published an article in *Nature Reviews Rheumatology* (formerly *Nature Clinical Practice Rheumatology*), titled 'Time for new outcome measures in hand osteoarthritis?', that called for a transformation in the assessment and management of hand osteoarthritis (OA)[1]. Despite its longstanding portrayal as a natural consequence of ageing rather than a disease, and its frequent perception as inevitable, this prevalent disease (the hand is the second most common site of OA, after the knee) affects the quality of life of the patient to an extent similar to that of RA, and pain associated with hand OA is a substantial burden, owing to a lack of efficacious treatments. In 2009, hand OA was often considered a 'second-class' discipline within rheumatology, lacking effective disease-modifying treatments and appropriate assessment tools. In the 16 years since our call to action[1], what advances have been made? In this Comment, we summarize the scientific, clinical and methodological advances that have shaped research on hand OA and highlight the remaining challenges in this field.

Diagnostic criteria

Since 2009, there have been advances in the diagnosis and assessment of hand OA, largely attributable to the analysis of data collected from hand OA cohorts (such as the HOSTAS, DIGICOD and NOR-HAND cohorts). In 2024, EULAR published new classification criteria in the form of a 15-point clinical-radiological score[2], with two main objectives: first, to enable earlier diagnoses; and second, to improve patient stratification. The aim of the criteria was to distinguish hand OA that affects the thumb base or the interphalangeal joints from OA of both the thumb and interphalangeal joints.

Clinical assessment

Concurrently, core disease-assessment tools have been refined. Nevertheless, the most widely used conventional pain and function scales (such as the visual analogue scale, the Australian/Canadian Hand OA Index, and the functional index for hand OA) are limited in their capacity to encompass pivotal clinical dimensions of patient impairment and subjective experience. Despite its importance, grip strength has received scant attention from the scientific community. Loss of grip strength can impair a wide range of professional, domestic and recreational activities.

Inflammatory activity, as indicated by the presence of soft tissue swelling, joint stiffness and the duration of such symptoms, is now widely acknowledged as a hallmark of hand OA. Its evaluation is mandatory in both ambulatory clinical practice and clinical research. Assessing synovitis (soft tissue swelling), pain flare and ultrasonography Doppler signals is pivotal for evaluating inflammation. Patients with hand OA who have synovitis in at least one joint exhibit more-severe structural damage and symptoms. Inflammation has been shown to predict worse clinical and radiographic outcomes[3,4].

Aesthetic discomfort has emerged as another important domain to assess in hand OA. A 2012 study emphasized the need for a specific tool for quantifying aesthetic discomfort[5]. Indeed, the use of specific assessments for this feature (for example, using a visual scale) has now become common, confirming the considerable impact of this domain on quality of life. Efforts have focused on standardizing objective endpoints for aesthetic damage to develop a validated tool.

Imaging

Substantial advances have been made in imaging hand OA. MRI has emerged as a pivotal tool for musculoskeletal imaging that enables the visualization of all joint structures and the detection of lesions, such as synovitis, early erosions and bone oedema, that are not visible on conventional radiographs. MRI images are scored with a validated quantitative scoring system, ensuring standardized assessments across readers[6]. Similarly, ultrasonography has been developed that can accurately identify osteophytes and synovial inflammation and assess synovitis[3]. The presence of synovitis or bone oedema in imaging studies has been associated with painful flare-ups and accelerated radiographic progression[4]. Artificial intelligence can also be used to analyse radiographic images and facilitate the automatic differentiation between OA hands and healthy hands, which could lead to more-objective screening and monitoring. Nevertheless, contemporary practice still relies on radiographic scores as the main instruments for evaluating disease severity and progression[6].

Hand OA phenotypes and personalized medicine

Hand OA is not a homogeneous entity; research has refined its classification into subgroups. For example, the erosive form of hand OA, which is diagnosed by central erosions in the interphalangeal joints on radiography, is associated with a more-severe phenotype[2,7] and is predictive of faster and more-severe structural progression[3,4]. This phenotype is also called 'inflammatory hand OA', owing to the occurrence of local inflammatory flare-ups (redness, swelling and pain in the fingers), although not all instances of erosive hand OA are accompanied by such symptoms. Inflammatory phases are characteristic of disease progression for a considerable number of patients; however,

clinical trials of systemic DMARDs (such as anti-TNF, anti-IL-6 or anti-IL-1 antibodies) have not demonstrated clear efficacy, which suggests a pathophysiology distinct from that of chronic inflammatory arthritis[8].

Personalized medicine approaches have also underscored the heterogeneity of clinical presentations. A multifactorial analysis of symptoms within the DIGICOD cohort identified five patient profiles, from those exhibiting mild symptoms to those experiencing considerable pain and aesthetic discomfort[7]. This study confirms that negative aesthetic perception is higher in patients with erosive damage and nodular deformities. Furthermore, systemic factors seem to influence symptoms; metabolic syndrome has been associated with high pain intensity in hand OA, irrespective of the location of the affected joint[9]. In addition, an inflammatory gut phenotype has also been associated with erosive hand OA and increased pain severity[10]. These findings suggest a metabolic phenotype, consistent with the concept of 'metabolic OA', in which low-grade inflammation associated with adiposity exacerbates pain. Several comorbidities have been associated with hand OA; coronary heart disease has been associated with worse clinical outcomes[11], and a greater incidence of hand OA has been reported in patients with HIV, especially in cases of metabolic syndrome[12].

Treatments

In the absence of curative treatments, the management of hand OA has long been limited to providing symptomatic relief through analgesics, topical and oral NSAIDs, orthoses and physical therapy, as stated in the 2019 EULAR recommendations[13]. According to the objective of these recommendations, the methodology for conducting clinical trials in hand OA has been refined, and assessment tools and outcomes have been better specified. Since 2009, a few pharmacological avenues have emerged; for example, a multicentre randomized controlled trial demonstrated that 6 months of methotrexate (20 mg weekly) significantly reduced pain compared with placebo in patients with hand OA with synovitis[8]. This result provides proof of concept that disease-modifying treatments, such as methotrexate, might have a role in inflammatory hand OA. By contrast, in another trial of patients with erosive hand OA, 10 mg of methotrexate weekly showed no superiority over placebo for pain relief[8]. Nevertheless, methotrexate could be a promising treatment for hand OA with synovitis and inflammation. Inflammation should be a target for hand OA; however, anti-inflammatory therapeutics, such as colchicine and hydroxychloroquine, have shown minimal efficacy when compared with placebo[8]. Despite these setbacks, the field of therapeutic research remains open to novel avenues. Results from a 2024 study indicated that targeting osteoclasts with denosumab might slow radiographic progression of erosive hand OA, but with no substantial pain reduction[14]. This result underlines the potential of bone-protection strategies for destructive forms of hand OA. A 2024 review of nonpharmacological and pharmacological treatments identified 65 published randomized trials on hand OA between June 2017 and December 2023, compared with 25 studies between 1994 and 2000, indicative of a growing number of studies performed[15].

Conclusion

The conceptualization of hand OA has undergone a substantial transformation. The severity of hand OA is now more widely recognized, new diagnostic and assessment tools have emerged, and the diversity of phenotypes is better understood. Concurrently, considerable progress has been made in the domain of outcome measures, including the development of standardized imaging scores, improvement in the reliability of functional tests, and the consideration of morning stiffness, synovitis assessments, aesthetic concerns and quality of life. Nevertheless, more-reliable, validated and sensitive assessment tools are urgently needed in clinical research. A set of common endpoints for hand OA is currently being developed by international initiatives (such as OMERACT). Given these challenges, the rheumatology community needs to intensify efforts across several domains, including a reorientation of research agendas to study not only the development of new therapeutics but also the improvement of tools for assessing hand OA (Supplementary Box 1).

The rheumatology community should also translate the progress made over the past 20 years into tangible clinical benefits for patients, building on that progress. To achieve this objective, targeted therapeutic interventions based on comprehensive assessments of inflammatory, erosive or metabolic phenotypes must be integrated with patient-centred evaluation methodologies. This integrated research approach is mandatory to identify effective treatment strategies that improve outcomes for people with hand OA.

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Competing interests

The authors declare no competing interests.

Additional information

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