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2023 EULAR recommendations on imaging in diagnosis and management of crystal-induced arthropathies in clinical practice

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ABSTRACT

Objective To formulate evidence-based recommendations and overarching principles on the use of imaging in the clinical management of crystal-induced arthropathies (CiAs).

Methods An international task force of 25 rheumatologists, radiologists, methodologists, healthcare professionals and patient research partners from 11 countries was formed according to the EULAR standard operating procedures. Fourteen key questions on the role of imaging in the most common forms of CiA were generated. The CiA assessed included gout, calcium pyrophosphate deposition disease and basic calcium phosphate deposition disease. Imaging modalities included conventional radiography, ultrasound, CT and MRI. Experts applied research evidence obtained from four systematic literature reviews using MEDLINE, EMBASE and CENTRAL. Task force members provided level of agreement (LoA) anonymously by using a Numerical Rating Scale from 0 to 10.

Results Five overarching principles and 10 recommendations were developed encompassing the role of imaging in various aspects of patient management: making a diagnosis of CiA, monitoring inflammation and damage, predicting outcome, response to treatment, guided interventions and patient education. Overall, the LoA for the recommendations was high (8.46–9.92).

Conclusions These are the first recommendations that encompass the major forms of CiA and guide the use of common imaging modalities in this disease group in clinical practice.

INTRODUCTION

Crystal-induced arthropathies (CiAs) are common conditions caused by the deposition of crystals within articular and periarticular tissues.[1 2] The three types of crystals that are mainly involved in the pathogenesis of these diseases are monosodium urate (MSU) in gout, calcium pyrophosphate (CPP) crystals responsible for CPP deposition (CPPD) and basic calcium phosphate (BCP) crystal (mostly hydroxyapatite crystals) associated with BCP deposition (BCPD) which may lead to different clinical phenotypes such as calcific tendinitis or the so-called Milwaukee shoulder syndrome.[3 4]

The epidemiology of CiAs is not well established, at least not for all of them, but they appear to be common diseases. The prevalence of gout ranges from 0.68% to 14% in adults depending on region and ethnicity.[5] In terms of prevalence, data for CPPD are even less clear and its diagnosis is quite challenging due to the variable clinical presentation and the difficulty of symptoms attribution to CPPD or concomitant conditions. Considering the presence of radiological chondrocalcinosis in selected populations, a prevalence of 13% has been reported across all age groups, but increases dramatically over the age of 70 years.[6] Finally, there are scarce epidemiological data on BCPD.[7]

Imaging has been increasingly used in the assessment of CiAs over the last two decades and has been included in the most recent recommendations for the classification and diagnosis of gout[8 9] and CPPD.[3 10] The imaging techniques included in these guidelines differ both in terms of intrinsic characteristics (ie, radiation exposure, cost, availability) and in terms of validation in the assessment of the various aspects of CiAs (ie, diagnostic performance for the identification of crystal deposition, assessment of structural damage and/or inflammation) making the choice of the most appropriate diagnostic test challenging. Furthermore, the choice of imaging technique becomes even more arduous when considering the multifaceted clinical presentation of CiAs and the different clinical questions arising in the different stages of the diseases.

The aim of this task force was to provide evidence-based recommendations for the use of commonly used imaging modalities: conventional radiography (CR), ultrasound, CT, dual-energy CT (DECT) and MRI for physicians involved in the clinical management (eg, diagnosis, monitoring and outcome prediction) of the three most common forms of CiA.

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Table 1 Research questions

RQ 1	What is the diagnostic value above other diagnostic tests of individual imaging modalities in gout?
RQ 2	What is the ability and added value of individual imaging modalities for monitoring inflammation, damage or crystal deposition in gout? In case there is additional value, how frequently and at which time points should imaging be applied to monitor inflammation, damage or crystal deposition in gout?
RQ 3	What is the ability and added value above other measures of individual imaging modalities to predict outcome (severity) in gout?
RQ 4	What is the ability and added value above other measures of individual imaging modalities to predict treatment effect in gout?
RQ 5	What is the diagnostic value, including differential diagnosis, above other diagnostic tests of individual imaging modalities in CPPD?
RQ 6	What is the ability and added value of individual imaging modalities for monitoring inflammation and damage (including crystal deposition) in CPPD? In case there is additional value, how frequently and at which time points should imaging be applied to monitor inflammation and damage in CPPD?
RQ 7	What is the ability and added value above other diagnostic measures of individual imaging modalities to predict outcome (severity) in CPPD?
RQ 8	What is the ability and added value above other measures of individual imaging modalities to predict treatment effect in CPPD?
RQ 9	What is the diagnostic value, including differential diagnosis, above clinical criteria of individual imaging modalities in BCPD (including calcific tendinitis of the supraspinatus tendon, calcific tendinitis of the Achilles tendon, Milwaukee shoulder syndrome and knee, etc)?
RQ 10	What is the ability and added value of individual imaging modalities for monitoring inflammation and damage (including crystal deposition) in BCPD? In case there is additional value, how frequently and at which time points should imaging be applied to monitor inflammation and damage in BCPD?
RQ 11	What is the ability and added value above other diagnostic measures of individual imaging modalities to predict outcome (severity) in BCPD?
RQ 12	What is the ability and added value above other measures of individual imaging modalities to predict treatment effect in BCPD?
RQ 13	What is the ability and added value above conventional measures of individual imaging modalities in guiding diagnostic aspiration and guiding delivery of drugs in CiA?
RQ 14	What is the ability and added value above standard care of individual imaging modalities to facilitate patient education and understanding of disease in CiA?

BCPD, basic calcium phosphate deposition; CiA, crystal-induced arthropathy; CPPD, calcium pyrophosphate deposition; RQ, research question.

METHODS

A task force was conceived by two convenors (PM and GF) and two methodologists (MAD'A and VN-C) after approval by the EULAR Council. The task force consisted of an expert group of 25 rheumatologists with specific expertise in imaging and/or CiAs, musculoskeletal radiologists, methodologists, a healthcare professional, two EMerging EUlar NETwork representatives and two patient research partners representing 11 countries according to the EULAR standard operating procedures.[11] The first objective was to formulate relevant clinical questions regarding the role of imaging in CiA, to identify and critically appraise the available evidence, and to develop recommendations based on both evidence and expert opinion. The first meeting of the task force was originally scheduled as a face-to-face (F2F) meeting, but was then transformed into a virtual event due to the restrictions imposed by the COVID-19 pandemic in the spring of 2021. At this meeting, members discussed key aspects related to the use of imaging in main CiAs and finally constructed and agreed upon research questions (RQs) by a consensus. The RQs (Q1–14) encompassed the full spectrum of use of imaging in clinical practice: diagnosing the three major CiAs, monitoring activity (inflammation) and damage, predicting outcome and response to treatment, guiding therapeutic or diagnostic interventions and using imaging as a tool to educate patients about their disease (table 1). All members disclosed their potential conflicts of interest prior to the start of the process. Four systematic literature reviews (SLRs) were conducted by two fellows (IG and GS) under the guidance of the methodologists (MAD'A and VN-C). The convenors, together with the methodologists and fellows, translated the RQs into the Population, Intervention, Comparator, Outcome format. The search strings were developed by an experienced information specialist (BW) and applied to MEDLINE, EMBASE and CENTRAL (through 31 March 2022). Original research articles including short or concise reports, letters including original (patient) data and SLRs in patients with CiA published in English were retrieved. Risk of bias (RoB) was assessed using validated instruments based on study type[12–14] as reported previously.[15]

The evidence revealed in the SLR was presented during the second meeting, which was an F2F meeting (with two participants (ND, WAS) joining virtually), held in Vienna, Austria in June 2022. Data were summarised in the form of standardised tables including the RoB assessment. The four SLRs which are published separately should be considered an integral part of these recommendations.[16] Task force members formulated the recommendations and overarching principles based on the published evidence in a process of expert opinion discussion and consensus. During the F2F meeting, recommendations and overarching principles were drafted and subsequently discussed and voted on. Consensus was reached as follows: accepted if >75% of the members voted in favour of the recommendation at the first round, >66% at the second round and >50% at the third round.[17] Following the F2F meeting, minor edits were discussed among the participants through email. Oxford Centre for Evidence-Based Medicine levels of evidence (LoE) and grades of recommendation (GoR) derived from the SLR were added to each recommendation.[18] Each task force member anonymously indicated the level of agreement (LoA) via REDcap (LoA, 0–10 Numerical Rating Scale ranging from 0='completely disagree' to 10='completely agree'). The LoE, GoR as well as the mean and SD of the LoA and the percentage of task force members with an agreement ≥8 were calculated. Based on the gaps in the evidence and unmet needs in research, a future research agenda was formulated. The manuscript was reviewed by the EULAR Council and a revised version was finally approved by all task force members and the Council.

RESULTS

A total of five overarching principles and 10 specific recommendations have been formulated. These are summarised in table 2 and discussed in detail below.

Overarching statements

These principles refer to points that apply to all CiAs and reflect good clinical practice, as well as the experience of the task force members, who are experts in this group of diseases.

Overarching statement A: CiAs are typically characterised by intermittent, acute episodes of inflammation, but may also

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Table 2 EULAR recommendations for the use of imaging in crystal-induced arthropathies in clinical practice

Overarching principles	LoE	GoR	LoA
A. Crystal-induced arthropathies are typically characterised by intermittent, acute episodes of inflammation, but may also exhibit a persistent disease course with or without superimposed flares.	n.a.	n.a.	9.83 (0.48) 100% ≥8
B. Imaging in crystal-induced arthropathies provides useful information on crystal deposition, inflammation and structural damage.	n.a.	n.a.	9.83 (0.48) 100% ≥8
C. The presence of imaging abnormalities, in particular, those related to crystal deposition, may not always be related to clinical manifestations.	n.a.	n.a.	9.79 (0.51) 100% ≥8
D. Patient information (medical history, physical/laboratory examination, synovial fluid/tissue analysis, etc) should be taken into account when imaging is considered in crystal-induced arthropathies.	n.a.	n.a.	9.75 (0.74) 96% ≥8
E. Imaging in crystal-induced arthropathies should be performed and interpreted by trained healthcare professionals.	n.a.	n.a.	9.92 (0.41) 100% ≥8
Recommendations			
1. When performing imaging in crystal-induced arthropathies, both symptomatic areas and disease-specific target sites (ie, MTP1 joint in gout, knee and wrist in CPPD, shoulder in BCPD) should be considered.	1a*	A†	9.71 (0.55) 100% ≥8
2. In the diagnostic assessment of gout, ultrasound and DECT are both recommended imaging modalities.	1a	A	9.75 (0.61) 100% ≥8
3. When characteristic features of monosodium urate crystal deposition on ultrasound (ie, double contour sign or tophi) or on DECT are identified, synovial fluid analysis is not needed to confirm a diagnosis of gout.	1a	A	8.79 (1.82) 87% ≥8
4. In the diagnostic assessment of CPPD, conventional radiography and ultrasound (or CT if axial involvement is suspected) are recommended imaging modalities.	1a‡	A§	9.63 (0.92) 96% ≥8
5. In the diagnostic assessment of BCPD, imaging is necessary; conventional radiography or ultrasound is the recommended modality.	2b	C	9.08 (1.69) 87% ≥8
6. In gout, ultrasound and DECT can be used to monitor crystal deposition and in case of ultrasound, also inflammation. Both modalities provide additional information on top of clinical and biochemical assessment. In case ultrasound/DECT are not available, conventional radiography can be used to assess structural damage due to gout. The decision on when to repeat imaging depends on the clinical circumstances.	2b	B	9.33 (1.17) 96% ≥8
7. In CPPD and BCPD, serial imaging is not recommended, unless there is an unexpected change in clinical characteristics.	2a	B	9.42 (1.21) 96% ≥8
8. In gout, assessing the amount of monosodium urate crystal deposition by ultrasound or DECT may be used to predict future flares.	2b	B	8.46 (1.67) 79% ≥8
9. If synovial fluid analysis is required in the assessment of crystal-induced arthropathies, ultrasound guidance should be used in cases where aspiration based on anatomical landmarks is challenging.	5	D	9.71 (0.55) 100% ≥8
10. Showing and explaining imaging findings of crystal-induced arthropathies to people with such conditions may help them understand their condition and improve treatment adherence in gout.	2b	C	9.38 (0.92) 96% ≥8

Numbers in column 'LoA' indicate the mean and SD (in parentheses) of the LoA (range 0–10 with 0='completely disagree' to 10='completely agree'), as well as the percentage of task force members with an agreement ≥8.
*1a for gout, 1a for CPPD, 5 for BCPD
†1a for US, 1a for CR, 1b for CT
‡A for gout, A for CPPD, C for BCPD
§A for CR, A for US, B for CT
BCPD, basic calcium phosphate deposition; CPPD, calcium pyrophosphate deposition; CR, conventional radiography; DECT, dual-energy CT; GoR, grades of recommendation; LoA, level of agreement; LoE, level of evidence; MTP1, first metatarsophalangeal; n.a, not applicable; US, ultrasound.

exhibit a persistent disease course with or without superimposed flares.

Although the different diseases grouped together under the umbrella of CiA are heterogeneous with regard to the pathognomonic crystals, the course of these diseases bears similarity, in that these are chronic diseases, present even during asymptomatic periods. They are however often accompanied by rapid bouts of acute inflammation evoked by crystal deposition, and these episodes are often interspersed with symptom-free phases, that is, as seen in intercritical gout[8] or calcific tendinitis. However, they can also manifest as chronic arthropathies with varying levels of activity over time as seen in CPPD disease, gout or calcific periarthritis in case of BCPD disease. This has relevance with regard to the choice of the imaging technique, and its use, strongly related to the clinical course of the disease (ie, acute, chronic), its duration and the clinical situation in which it is used (ie, diagnosis, monitoring).

Overarching statement B: imaging in CiAs provides useful information on crystal deposition, inflammation and structural damage.

Imaging techniques can be used in CiA to visualise and detect each pathological finding. CR and DECT provide better assessment of structural damage and DECT provides a quantitative assessment of crystal deposition and may also visualise bone marrow oedema,[19] while ultrasound is useful to assess inflammation, early joint damage and provides semiquantitative assessment of crystal deposition. Considering that for some CiAs very little is known about the processes responsible for the development of the disease or their association with clinical symptoms, imaging has great potential in addressing many clinical questions beyond the available clinical or laboratory evidence.

Overarching statement C: the presence of imaging abnormalities, in particular, those related to crystal deposition, may not always be related to clinical manifestations.

Pathological lesions that are characteristic of certain CiAs may be depicted by imaging, but may not cause clinical symptoms over longer periods of time, such as the asymptomatic form of CPPD as defined in the 2011 EULAR recommendations,[3] or cases of asymptomatic calcific tendinitis.[7] In addition, smaller tophi in gout, or crystal aggregates or crystal deposits in cartilage

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may not necessarily lead to clinical manifestations and are seen as asymptomatic MSU crystal deposition (see Gout, Hyperuricaemia and Crystal-Associated Disease Network nomenclature on disease labels).[20 21]

Overarching statement D: patient information (medical history, physical/laboratory examination, synovial fluid/tissue analysis, etc) should be taken into account when imaging is considered in CiAs.

In general, imaging can rarely be used to reach a diagnosis on its own, and that the information gained through the use of such techniques should be interpreted within the overall picture, that is the gestalt of the disease. Medical history and synovial fluid analysis are important criteria for both the 2015 American College of Rheumatology/EULAR classification criteria[9] as well as the 2018 EULAR recommendations for the diagnosis of gout.[8] Similarly, the 2011 EULAR recommendation for CPPD includes both synovial fluid and tissue analysis to detect crystal deposits, as well as characteristic clinical features.[3] Diagnostic/classification criteria are lacking for BCPD; however, these diseases are generally diagnosed clinically with acceptable accuracy. Indeed, in a patient with acute joint symptoms and clear, macroscopic evidence of tophaceous gout or evidence of pathognomonic crystals on synovial fluid analysis or tissue analysis, imaging may not be necessary. In case imaging is employed, the clinical scenario will typically guide the choice and order of imaging examinations performed. Another crucial aspect to consider for diagnosis and/or appropriate monitoring is the anatomical site to be examined by imaging.

Overarching statement E: imaging in CiAs should be performed and interpreted by trained healthcare professionals.

Task force members, in particular musculoskeletal radiologists, strongly felt that the complex and multifaceted nature of CiAs necessitates expertise in performing and analysing imaging findings. However, published literature is scarce about the predictable benefit of expertise in interpreting imaging examinations[22 23]; this issue should be clarified by future studies and has been added to the research agenda. When CT or DECT is considered, the basic principles of radiation protection, that is, justification, optimisation and limitation of radiation dose, must be always contemplated, as prescribed in the European Directive 2013/59/Euratom.[24]

Recommendation 1: when performing imaging in CiAs, both symptomatic areas and disease-specific target sites (ie, first metatarsophalangeal in gout, knee and wrist in CPPD, shoulder in BCPD) should be considered.

The task force deemed important to point out that in addition to areas that show clinical symptoms, also those commonly involved in individual CiAs should be examined by imaging. The term area was purposefully chosen to make it clear that CiAs commonly involve periarticular and other soft tissue structures such as tendons or ligaments which may also be targets of imaging. DECT and ultrasound can be used to identify MSU deposits in joints not showing clinical symptoms at the time of the examination, as seen in intercritical gout[25 26] but also in patients with asymptomatic hyperuricaemia or other rheumatic and musculoskeletal diseases.[27–31]

Recommendation 2: in the diagnostic assessment of gout, ultrasound and DECT are both recommended imaging modalities.

The majority of the studies for the diagnostic RQ on gout investigated either ultrasound or DECT with few studies on CR or CT.[16] Considering the overall evidence on the diagnostic use of various imaging techniques concerning gout, the task force considered it pertinent to specify these two techniques as the preferred modalities as opposed to CR or CT where the evidence was much less. Either one of these techniques can provide information that is helpful for making the diagnosis of gout, and the choice of technique should depend on the clinical scenario, in addition to availability and operator expertise. In general, early disease will warrant investigation with ultrasound rather than DECT, due to the capability of ultrasound to depict synovitis. In case of ultrasound, the term crystal deposition covers a plethora of findings, particularly double-contour sign and tophus, while for the purpose of DECT, crystal deposition is an overall term.[32] The overwhelming evidence of diagnostic utility for ultrasound in gout was demonstrated for crystal deposition, in particular double contour and tophi, rather than inflammation or bone erosion, while the evidence for DECT naturally concerns only crystal deposition. The task force acknowledges that access to DECT, and probably to a lesser extent to ultrasound, may be limited in certain countries and, at least the former, mostly available in academic or tertiary centres.[33] In such situations, or in case of financial or insurance-related limitations, modalities that are not specifically mentioned in the recommendation, but for which there is evidence and low cost, such as CR, may be applied.

Recommendation 3: when characteristic features of MSU crystal deposition on ultrasound (ie, double-contour sign or tophi) or on DECT are identified, synovial fluid analysis is not needed to confirm a diagnosis of gout.

While evidence of MSU deposition in synovial fluid or tissue analysis remains the diagnostic hallmark, it has been recognised that this may not always be possible, due to unsuccessful arthrocentesis or lack of facilities/expertise to analyse joint fluid.[34] Other expert groups have acknowledged this, as evidenced also by recent classification criteria which consider imaging evidence of crystal deposition among the criteria in patients with imaging signs typical for gout or CPPD disease but lacking confirmation of relevant crystals of synovial fluid analysis in an appropriate clinical scenario suggestive of the disease (8–10). The decision on whether to perform arthrocentesis should be evaluated in the clinical context; however, as a general rule, this should be always attempted, whenever feasible, especially for ruling out other causes of acute arthritis, such as septic arthritis, regardless of whether there is previous evidence for gout (for instance, positive DECT and hyperuricaemia). Indeed, gout may coexist with septic arthritis or CPPD, which would again necessitate synovial fluid to rule out/confirm differential diagnoses. It should be noted that while ultrasound may be useful to identify synovitis in gouty flares, there is only limited evidence for the use of DECT in visualising inflammation. However, both are capable of visualising MSU deposits, which have diagnostic utility in gout. Imaging findings should be interpreted carefully, taking into account the fact that they are not entirely specific (ie, double-contour sign is more typical of gout, but may be present in CPPD and also in asymptomatic hyperuricaemia).[29–31 35] Overall, the task force felt that the higher the number of typical lesions present and in case of gout or CPPD, the larger the variety of findings (ie, double contour and synovitis with tophi), the more certain the diagnosis of CiA will be; this however needs to be demonstrated in future studies.

Recommendation 4: in the diagnostic assessment of CPPD, CR and ultrasound (or CT if axial involvement is suspected) are recommended imaging modalities.

While the diagnosis of CPPD can be made in the absence of imaging, by demonstrating the presence of CPP crystals in synovial fluid or tissue, diagnostic imaging is usually required and performed in CiAs and indeed in most cases of CPPD. The overwhelming majority of the studies for the diagnostic RQ on CPPD

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assessed using CR or ultrasound. Either one of these techniques may be used; however, there were very few studies comparing both methods. While early disease may favour ultrasound due to its superior resolution for demonstrating smaller deposits, certain areas, such as the menisci or articular discs, are not accessible due to the lack of acoustic window.[36] Both techniques were used primarily for assessing peripheral joints. Throughout all techniques and sites, the evidence retrieved referred to CPP deposits, specifically in fibrocartilage and hyaline cartilage, while there was very limited evidence on other lesions, such as synovitis.[16] Despite having strong face validity, the SLR did not reveal evidence for the diagnostic utility of conventional CT in CPPD; however, the task force felt it important to highlight its utility in case of axial involvement, such as in the case of crowned dens syndrome, which is a diagnosis based on constellation of clinical, biochemical and imaging findings, and where conventional CT has an important role and remains the preferred imaging modality.[37 38]

Recommendation 5: in the diagnostic assessment of BCPD, imaging is necessary; CR or ultrasound is the recommended modality.

Due to the difficulties in forming a diagnosis based purely on clinical presentation and also on the fact that the analysis of BCP crystals is very difficult, diagnosis of BCPD is clearly dependent on diagnostic imaging. Either CR or ultrasound may be helpful for diagnosing BCPD and may provide information on joint or periarticular involvement.[39] The choice of technique will mainly depend on availability. Ultrasound allows a more precise localisation of BCP deposits both in individual joint components and in periarticular structures, while CR typically provides comprehensive information on the joint as a whole.

Recommendation 6: in gout, ultrasound and DECT can be used to monitor crystal deposition and in case of ultrasound, also inflammation. Both modalities provide additional information on top of clinical and biochemical assessment. In case ultrasound/DECT are not available, CR can be used to assess structural damage due to gout. The decision on when to repeat imaging depends on the clinical circumstances.

While there is evidence on its use for depicting bone marrow oedema, unlike ultrasound, DECT is not capable of visualising synovitis and thus has very limited utility in early gout, when the load of MSU crystal depositions is typically lower.[40] While there was unequivocal evidence for its utility to detect change in crystal deposition, its use in monitoring at this time is limited by cost and accessibility issues, but can be considered in clinical practice in patients with gout flares despite adherence to treat-to-target urate-lowering therapy. Ultrasound findings of crystal deposition, such as tophi, double-contour signal as well as aggregates, were shown to be sensitive to change[41] over 1 year. A smaller number of studies have also demonstrated that inflammation seen on ultrasound may also be used to follow up gout. Structural damage seen in gout, such as bone erosions can be assessed in CR, particularly in long-standing disease.[16] However, since it does not provide information on crystal deposition or inflammation, the use of CR is limited mostly to long-standing disease. Whether monitoring gout with imaging is superior to monitoring it without imaging needs to be demonstrated in further studies. Based on the very limited evidence available, the task force felt that 1 year is a reasonable time frame to monitor imaging changes in gout.[41] Repeated imaging may also be useful in case of suspected association with an additional rheumatic and musculoskeletal disease (eg, osteoarthritis or inflammatory arthritides, etc).

Recommendation 7: in CPPD and BCPD, serial imaging is not recommended, unless there is an unexpected change in clinical characteristics.

The SLR found no evidence on the utility of imaging for the monitoring of CPPD or BCPD in clinical practice, and the task force agreed that serial imaging generally should not be recommended for these indications. However, in certain cases, such as rapid progression of symptoms, imaging may be useful to determine whether it relates to disease severity or may help identify additional diagnosis. In addition, imaging studies monitoring patients with calcium crystal deposition diseases would be fundamental for further understanding of the natural history of these diseases.

Recommendation 8: in gout, assessing the amount of MSU crystal deposition by ultrasound or DECT may be used to predict future flares.

After initiation of urate-lowering therapy, reduction of crystal deposition or tophi on ultrasound or DECT may be used to predict flares in gout.[42] LoE for this recommendation is low as very few studies tried to address this question. Regarding the risk of flare during urate-lowering therapy, the USEFUL 2 Study demonstrated that a decrease of >50% in tophus size on ultrasound 6 months following initiation of urate-lowering therapy correlated with a reduced risk of gout flare.[43] Much less is known regarding imaging and risk of development of gout in asymptomatic hyperuricaemia in patients with confirmed crystal deposition in joints. However, given the potential of imaging in assessing crystal deposition burden in joints, it is very likely that in the future, both ultrasound and DECT will be used frequently for monitoring deposition and predicting flares.

Recommendation 9: if synovial fluid analysis is required in the assessment of CiAs, ultrasound guidance should be used in cases where aspiration based on anatomical landmarks is challenging.

Synovial fluid should be acquired whenever possible in the workup of CiAs in order to secure diagnosis. While routine interventions targeting peripheral joints or periarticular structures can be performed using anatomical landmarks, in case of a challenging procedure, imaging guidance is preferable.[44] While fluoroscopy is a valid alternative, ultrasound is the preferred modality for guiding interventions due to the absence of ionising radiation and better visualisation of soft tissue structures.[45 46]

Recommendation 10: showing and explaining imaging findings of CiAs to people with such conditions may help them understand their condition and improve treatment adherence in gout.

A small number of studies using DECT have investigated and shown the benefit of presenting both personal images or medical illustrations to patients with gout.[16] Task force members agreed that such an approach may help patients with CiA better understand their condition and improve treatment adherence.[47 48]

FUTURE RESEARCH AGENDA AND IMPLEMENTATION PLAN

Many important aspects of CiAs still need to be defined, and sculpting the appropriate role of imaging requires further studies. The task force has listed the most important topics for future research on the applications of imaging in CiAs in Box 1. and developed and implementation plan (online supplemental file 1).

DISCUSSION

While previous guidelines on gout and CPPD disease developed by EULAR include imaging, mainly as a diagnostic tool, the purpose of the current recommendations is to guide physicians including rheumatologists, orthopaedic surgeons, radiologists,

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Box 1 Future research agenda

- ⇒ To further investigate which imaging findings (imaging modality, anatomical location and type of pathology) provide the best clinical utility for early and accurate diagnosis of crystal-induced arthropathies
- ⇒ To assess the diagnostic performance of emerging advanced imaging techniques (eg, multienergy photon-counting CT) in crystal-induced arthropathies
- ⇒ To assess change in patient diagnosis in suspected crystal-induced arthropathies depending on imaging findings
- ⇒ To further investigate the utility of DECT and ultrasound in monitoring crystal deposition and inflammation (eg, synovitis, bone marrow oedema) in gout
- ⇒ To determine whether disease monitoring with imaging has a benefit over disease monitoring without imaging
- ⇒ To determine the type and number of lesions required to make a diagnosis of gout, CPPD or BCPD according to each imaging technique
- ⇒ To further investigate which imaging findings (imaging modality, anatomical location and type of pathology) best predict the disease course (structural progression, pain, functional ability, health-related quality of life) and treatment response in crystal-induced arthropathies
- ⇒ To assess the relationship between imaging findings and treatment response in crystal-induced arthropathies
- ⇒ To investigate the role of imaging in revealing the natural history of crystal-induced arthropathies and the type of crystal (eg, CPP vs BCP) involved
- ⇒ To evaluate the utility of presenting and discussing imaging findings to patients with crystal-induced arthropathy to manage their disease

BCP, basic calcium phosphate; BCPD, BCP deposition; CPP, calcium pyrophosphate; CPPD, CPP deposition; DECT, dual-energy CT.

specialists in physical medicine and rehabilitation or sports medicine as well as general practitioners in applying imaging techniques for all common CiAs and encompass the full spectrum of imaging in clinical practice, namely in diagnosis, monitoring disease activity and prediction of outcome and treatment response. In addition, they may also benefit healthcare providers in making management decisions concerning imaging in patients with CiA. The populations of interest included both patients with suspected (diagnostic RQs) and established (monitoring and prediction RQs) disease of the three most common forms of CiA. From its beginning, the task force acknowledged the heterogeneous clinical phenotype of these diseases and considered this characteristic when formulating the recommendations.

Recommendations were primarily based on available research evidence, with the exception of recommendation 9, which, lacking available data, relied only on expert opinion. Although the evidence for some recommendations was scarce, experts scored the LoA for each recommendation using data from the quality assessment.

What emerges from this work is the inequality of the available data both in terms of CiA studied and of the imaging techniques used, despite the increasing interest in both the disease and the use of imaging. Gout was the disease in which the role of both traditional and advanced imaging techniques was most frequently investigated. On the other hand, very few studies have investigated the use of imaging in BCPD.[16] The task force acknowledges that a large body of evidence is still needed to optimise the use of imaging in the routine clinical practice of CiAs. However, the research is rapidly growing, and it is likely that these recommendations will need to be revisited in a near future when the results of ongoing and new studies will become available. In the meanwhile, these practical recommendations, developed by a panel of international experts in the field, will allow clinicians, not only rheumatologists, but also orthopaedic surgeons, and commonly general practitioners, who deal with CiAs to guide the decision-making process in daily clinical practice using the most appropriate techniques, thereby improving patient care in this disease group. Although radiologists (with the exception of those performing interventions) do not treat patients, they also need to be aware of such guidelines to recommend the use of the most appropriate imaging techniques in patients with CiAs.

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