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Conventional radiography in juvenile idiopathic arthritis: Joint recommendations from the French societies for rheumatology, radiology and paediatric rheumatology

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Abstract

Background Juvenile idiopathic arthritis (JIA) can cause structural damage. However, data on conventional radiography (CR) in JIA are scant.

Objective To provide pragmatic guidelines on CR in each non-systemic JIA subtype.

Methods A multidisciplinary task force of 16 French experts (rheumatologists, paediatricians, radiologists and one patient representative) formulated research questions on CR assessments in each non-systemic JIA subtype. A systematic literature review was conducted to identify studies providing detailed information on structural joint damage. Recommendations, based on the evidence found, were evaluated using two Delphi rounds and a review by an independent committee.

Results 74 original articles were included. The task force developed four principles and 31 recommendations with grades ranging from B to D. The experts felt strongly that patients should be selected for CR based on the risk of structural damage, with routine CR of the hands and feet in rheumatoid factor-positive polyarticular JIA but not in oligoarticular non-extensive JIA.

Conclusion These first pragmatic recommendations on CR in JIA rely chiefly on expert opinion, given the dearth of scientific evidence. CR deserves to be viewed as a valuable tool in many situations in patients with JIA.

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s00330-018-5304-7) contains supplementary material, which is available to authorized users.
Key Points

- CR is a valuable imaging technique in selected indications.
- CR is routinely recommended for peripheral joints, when damage risk is high.
- CR is recommended according to the damage risk, depending on JIA subtype.
- CR is not the first-line technique for imaging of the axial skeleton.

Keywords  Juvenile idiopathic arthritis  · Conventional radiography · Recommendations · Structural damage · Erosions

Abbreviations

ACPA  Anti-Citrullinated Protein Antibody
CR  Conventional radiography
DMARDs  Disease-modifying Antirheumatic drugs
ERA  Enthesitis-related arthritis
EULAR  European League Against Rheumatism
GRADE  Grading of Recommendations, Assessment, Development and Evaluation
ILAR  International League Against Rheumatism
JIA  Juvenile idiopathic arthritis
jPsA  Juvenile psoriatic arthritis
JSN  Joint space narrowing
MRI  Magnetic resonance imaging
oJIA  Oligoarticular juvenile idiopathic arthritis
OMERACT  Outcome Measures in Rheumatology
PReS  Paediatric Rheumatology European Society
PICO  Population, Intervention, Comparison, Outcome
pJIA  Polyarticular juvenile idiopathic arthritis
RA  Rheumatoid arthritis
RF  Rheumatoid factor
SFIPP  French Society for Paediatric and Prenatal Imaging
SFR  French Society for Radiology
SFR  French Society for Rheumatology
sJIA  Systemic juvenile idiopathic arthritis
SLR  Systematic literature review
SOFREMIP  French Society for Paediatric Rheumatology and Internal Medicine
TMJ  Temporo-mandibular joint
US  Ultrasound

Introduction

Juvenile idiopathic arthritis (JIA) is a heterogeneous group of chronic inflammatory joint conditions that can cause structural damage [1]. Seven mutually exclusive subtypes of JIA are defined in the 2001 Edmonton classification developed by the International League Against Rheumatism (ILAR) [2]. This classification has been challenged and modifications suggested, such as exclusion of systemic-onset JIA (sJIA) due to its similarity to autoinflammatory diseases [3, 4].

The prevalence of joint damage among patients with JIA has been estimated at 8–27% in extended oligoarticular JIA (oJIA), 35–67% in polyarticular JIA (pJIA) and up to 80% in rheumatoid factor (RF)-positive pJIA [5, 6]. The main treatment objectives in JIA are to control the pain and to prevent structural damage. Joint space narrowing (JSN), bone erosions and demineralization are radiographic findings shared between JIA and adult rheumatoid arthritis (RA). Changes specific to the paediatric population are early growth plate closure, epiphyseal deformity and growth asymmetry [7].

Conventional radiography (CR), magnetic resonance imaging (MRI) and ultrasound (US) are the imaging modalities most often used to evaluate joint inflammation or structural damage [8]. MRI and US hold considerable promise but are still under evaluation in JIA. CR remains the most readily available imaging technique for detecting and monitoring structural damage. However, potential limitations of CR in JIA include the risk of radiation-induced harm to the patient, interpretation difficulties raised by skeletal immaturity, and the delayed development of structural joint damage. Furthermore, because JIA is rare, little is known about the potential effects of synthetic or biological disease-modifying anti-rheumatic drugs (DMARDs) on structural joint damage [9–11]. Thus, whereas recommendations based on large studies are available for the radiographic assessment of chronic inflammatory joint disease in adults [12, 13], no similar guidelines have been developed for JIA. A task force was recently convened by the European League Against Rheumatism (EULAR) – Paediatric Rheumatology European Society (PReS) to develop recommendations about imaging studies for diagnosing and managing JIA [14]. Although this undertaking acknowledged, for the first time, that an assessment of imaging studies in JIA was needed, the task force neither focussed on CR nor provided specific guidance for everyday practice.

We established a multidisciplinary task force to develop guidelines on the use of CR for the diagnosis and follow-up of each JIA subtype in everyday practice. Our project was supported by the French Society for Rheumatology (SFR), French Society for Paediatric Rheumatology and Internal Medicine (SOFREMIP), French Society for Paediatric and Prenatal Imaging Imaging.
Methods

Field of research

We considered the following situations, at diagnosis and during follow-up, in each of the following five subtypes of JIA (oJIA, pJIA with and without RF and/or anti-citrullinated peptide antibody (ACPA), juvenile psoriatic arthritis (jPsA), and enthesitis-related arthritis (ERA)) Undifferentiated arthritis, as a heterogeneous subset related to one or several subtypes, and systemic JIA, having a peculiar articular course and structural prognosis, were left aside. Experts also focused on juvenile monoarthritis. Special attention was directed to the cervical spine, hip and temporo-mandibular joints (TMJs).

Recommendation development process

The task force comprised 16 JIA experts (eight rheumatologists, five paediatricians, two paediatric radiologists experienced in skeletal disease and one patient organisation representative). We used the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) method [15, 16] for elaborating, evaluating, disseminating and implementing recommendations elaborated by the EULAR and the Outcome Measures in Rheumatology (OMERACT) group [17, 18], and the Population, Intervention, Comparison, Outcome (PICO) process to frame the research questions.

We considered structural radiographic abnormalities: JSN, erosions, pseudo-joint space widening for sacro-iliac joint [19, 20] and ankylosis [12]. A research fellow (PM) assisted by two experts in systematic review methodology (CGV, methodologist; and VDP, convenor) performed a systematic literature review by searching PubMed, Scopus/Elsevier, and the Cochrane Library. Original articles including clinical trials, retrospective cohort studies, other retrospective studies, and case-control studies published between 1980 and December 2016 were identified. The following indexing was used: ‘juvenile idiopathic arthritis’ OR ‘juvenile rheumatoid arthritis’ OR ‘juvenile chronic arthritis’ OR ‘juvenile psoriatic arthritis’ OR ‘enthesitis-related arthritis’ OR ‘juvenile spondyloarthritis’ AND ‘radiography’ OR ‘X-ray’ (see Appendix 1 for details). The quality of evidence and grades of recommendation were determined according to the standards of the Oxford Centre for Evidence-Based Medicine [21]. Recommendations were graded A to D depending on the level of the underlying evidence (from 1A to 4) [18].

The task force debated and formulated a preliminary set of recommendations based on the systematic literature review supplemented, when necessary, by their expert opinion. This set was then evaluated by a panel of 14 independent French-speaking experts. Modifications were debated by the task force. The final recommendations were then rated on a 10-point scale by the task force and independent panel through a Delphi process.

Results

Systematic literature review

Of the 118 publications identified by the literature search, 74 [5, 6, 9–11, 19, 20, 22–88] original articles, as well as one abstract [89] and one online recommendation [90], were included (Fig. 1, Table 1).

Recommendations

The experts elaborated four overarching principles and 31 recommendations. Table 2 lists the recommendations.

Overarching principles

Radiation exposure was taken into account (principle B), according to French Society for Radiology recommendations [90] (Appendix 2). Much of the cartilage is still radiotransparent in children younger than 5 years of age. In this age group, the need for CR must be evaluated with great care (principle C) [91].

Other imaging modalities such as US and MRI are increasingly used in JIA. Although promising, they are not discussed herein. They will be the focus of specific recommendations (principle D).

Oligoarticular JIA (oJIA)

1. **CR should not be performed routinely as a diagnostic investigation in oJIA.** The literature review identified ten studies in which CR was performed, even in patients younger than 4 years. Among them, one focussed specifically on oJIA [35] and nine investigated several JIA subtypes but reported data separately for oJIA [6, 24, 27, 36–38, 40, 42, 43]. The usefulness of CR is limited by the incomplete ossification of the epiphyses, most notably in the youngest age groups [33]. Therefore, when the diagnosis is definitive, CR is not recommended.

2. and 3. During follow-up, CR should be performed on affected joint(s) that remain symptomatic after 3 months. By ‘symptomatic joints*”, we mean painful and/or swollen joints and/or joints that are limited in motion. In patients with persistently symptomatic* joints, the reiteration of CR during follow-up is at the discretion of the physician. Several studies
showed evidence of radiographic progression early in the natural history of oJIA [24, 27, 35, 38].

4. In patients with clinically inactive disease (CID), CR should not be performed routinely. The diagnosis of CID relies on physician judgement, aided by validated tools [92–94]. No data are available on radiographic disease progression in clinically silent joints in patients with oJIA.

5. In patients with extended oJIA, the recommendations for pJIA should be applied. The number of affected joints is strongly associated with structural damage in oJIA [35].

6. In patients with structural damage, the selection and timing of specific imaging techniques to further assess the damaged joint during follow-up is guided by clinical considerations.

Joints with structural damage must undergo specific CR evaluations during the patient’s growth.

Polyarticular JIA (pJIA)

7. and 8. Routine CR of the wrists, hands and forefeet is strongly recommended at the diagnosis of polyarticular JIA with positive RF/ACPA. CR of other joints than wrists, hands and forefeet, is recommended at the diagnosis for symptomatic joints only. Prospective studies were reviewed, with special attention to early pJIA. Erosions and JSN occurred preferentially at the hands, wrists and feet [11, 31, 43, 48–51], joints that were sometimes asymptomatic [31] CR at the diagnosis provides a reference for assessing disease progression. It is supported by ‘adult’ recommendations [13] for rheumatoid arthritis, which has a similar structural evolution.

9. and 10. In new-onset RF/ACPA-negative pJIA with adverse prognostic factors, CR at diagnosis should be performed as for RF/ACPA-positive pJIA. Box 1 lists the factors of adverse prognostic significance in pJIA [31, 44, 50, 51]. These factors are associated with a pattern of joint damage over time similar to that seen in RF/ACPA-positive pJIA [38].

Box 1: Factors of adverse prognostic significance in polyarticular juvenile idiopathic arthritis (pJIA)

| Factor                                      |
|---------------------------------------------|
| Early involvement of wrists                |
| Symmetric arthritis                        |
| Distal, small-joint arthritis              |
| Elevated ESR/CRP                           |
| Pre-existing radiographic abnormalities     |

ESR, erythrocyte sedimentation rate; CRP, serum C-reactive protein level

11. In new-onset, RF/ACPA-negative pJIA without adverse prognostic factors, at diagnosis, CR should be confined to symptomatic joints. This recommendation is based on expert opinion.

12. In RF/ACPA-positive pJIA, CR of the hands, wrists and forefeet is strongly recommended 1 year after disease onset, and when transitioning from paediatric to adult healthcare. At other time points, the use of CR during follow-up is at the discretion of the physician. Prospective studies found evidence of joint damage even in asymptomatic joints [31]. Patients with long-standing disease had high prevalences of joint erosions (30–70 % in historical studies) [5, 28, 38, 40, 44, 48, 54], close to those in adults with RA [48]. In RA, joint destruction at asymptomatic sites is a major predictor of adverse outcomes [13, 95]. However, radiographic progression with erosions in asymptomatic joints is not well documented in JIA and may have been underestimated. In a study of 471 joints in 67 patients with polyarticular JIA, radiographs showed erosions at the hands and feet in 36 % and 39 % of
Table 1  Details of the studies identified by the systematic literature review

| Article | Design | JIA subtype | Number of patients | Imaging findings used as outcome | Imaging technique | Purpose |
|---------|--------|-------------|--------------------|----------------------------------|-------------------|---------|
| Maldonado-Cocco 1980 [46] | Prospective | JRA | 100 | Primary | CR | To assess the frequency of carpal ankylosis |
| Williams and Ansell 1985 [54] | Retrospective | RF+ pJIA | 81 | Primary | CR | To assess peripheral radiographic progression |
| Poznanski 1991 [26] | Narrative review | JRA | NA | NA | CR | To develop a first score for assessing radiographic damage |
| Harel 1993 [10] | Prospective | JRA | 23 | Primary | CR | To assess effects of MTX on radiographic progression evaluated based on carpal length |
| Ravelli 1998 [11] | Retrospective | pJIA | 26 | Primary | CR | To assess carpal length changes during MTX therapy in pJIA (with bilateral wrist involvement) |
| Guillaume 2000 [35] | Prospective | oJIA | 207 | Secondary | CR | To identify prognostic factors in oJIA |
| Al-Matar 2002 [36] | Retrospective | oJIA | 205 | Secondary | CR | To identify early features associated with poor outcome in oligoarticular-onset JIA |
| Flato 2002 [30] | Prospective | oJIA, SEA, JPsA, IBD-associated arthritis | 314 | Primary | CR | To assess factors associated with radiographic sacroiliitis in JIA |
| Haeumer 2002 [64] | Prospective | JPsA, oJIA | 87 | No | NA | To compare clinical features of JPsA and oJIA, including patterns of joint involvement, and to discuss classification |
| Laiho 2002 [70] | Cross-sectional | JCA | 159 | Primary | CR | To evaluate radiographic inflammatory changes in the cervical spine |
| Mason 2002 [49] | Cross-sectional | Polarticular JRA | 60 | Primary | CR | To assess the frequency of in hand/wrist CR damage at diagnosis |
| Oen 2002 [39] | Narrative review | JIA | NA | NA | NA | To identify outcome predictors, including radiographic findings |
| Bowyer 2003 [40] | Cross-sectional | oJIA, pJIA, sJIA | 703 | Secondary | CR | To assess health status 1 and 5 years after disease onset |
| Doris 2003 [45] | Cross-sectional | JRA | 60 | Primary | CR | To assess inter- and intra-observer variability of two scoring systems (Larsen/modified Larsen), comparison to MRI |
| Flato 2003 [50] | Case-control | JRA | 268 | Secondary | CR | To assess long-term prognostic factors |
| Magni-Manzoni 2003 [51] | Prospective | pJIA, extended oJIA, sJIA, JPsA, ERA | 94 | Primary | CR | To assess the rate of radiographic progression (Poznanski score) |
| Oen 2003 [38] | Retrospective | JRA | 216 | Primary | CR | To assess radiographic damage in early and advanced disease |
| Oen 2003 [37] | Retrospective | JRA | 393 | Secondary | CR | To identify early predictors of long-term outcome |
| Ravelli and Martini 2003 [6] | Narrative review | All subtypes | NA | NA | NA | To identify early predictors of outcomes, including radiographic outcomes |
| Tsitsami 2003 [68] | Retrospective | oJIA, JPsA, UA | 185 | Secondary | CR | To evaluate associations between a familial history of psoriasis and the outcome of oligoarticular JIA |
| Van Rossum 2003 [31] | Prospective | pJIA, oJIA, extended oJIA | 67 | Primary | CR | To describe radiographic features |
| Twilt 2004 [73] | Cross-sectional | JIA (all subtypes) | 97 | Primary | CR | To evaluate the prevalence of radiographic damage on the OPG |
| Mason 2005 [5] | Prospective | Polynarticular JRA | 12 | Primary | CR | To assess radiographic progression after 2 years |
| Van Rossum 2005 [29] | Prospective | pJIA, oJIA | 66 | Primary | CR | To assess sensitivity of Dijkstra radiographic score |
| Helenius 2006 [83] | Prospective | Adult: RA, AS, SPA, MCTD | 67 | Primary | CR, MRI | To describe clinical, radiographic and MRI findings in rheumatic diseases |
| Rossi 2006 [33] | Prospective | pJIA | 25 | Primary | CR | To assess the reliability of the Sharp and Larsen radiographic scoring systems |
| Flato 2006 [58] | Case / control | ERA/oJIA, pJIA | 55/55 | Secondary | CR | To compare clinical, functional and radiological features in ERA versus other JIA subtypes |
| Selvaag 2006 [28] | Prospective | sJIA, pJIA, oJIA, ERA | 137 | Primary | CR | To assess radiographic findings at diagnosis and 3-years later |
| Billi 2007 [82] | Prospective | sJIA, RF+ and RF- pJIA, oJIA, ERA, JPsA | 100 | Secondary | CR | To describe clinical, orthodontic, OPG and lateral cephalogram in 46 patients |
| Gilliam 2008 [44] | Retrospective | RF+ and RF- pJIA, oJIA, sJIA | 68 | Secondary | CR | To evaluate associations of markers, including radiographic changes, to disease severity |
| Habib 2008 [47] | Cross-sectional | pJIA, sJIA, oJIA | 68 | Secondary | CR | To determine the prevalence and significance of ACPAs in JIA |
| Article                        | Design    | JIA subtype            | Number of patients | Imaging findings used as outcome | Imaging technique | Purpose                                                                                     |
|------------------------------|-----------|------------------------|--------------------|---------------------------------|------------------|--------------------------------------------------------------------------------------------|
| Nielsen 2008 [9]             | Retrospective | extended oJIA, sJIA, pJIA, PsA | 40                 | Primary                         | CR               | To evaluate the radiographic outcome (Poznanski score) during etanercept therapy             |
| Pedersen 2008 [84]           | Prospective | JIA (subtype not specified) | 15                 | Primary                         | CR, MRI          | To describe clinical, CR and MRI features; to compare CR to MRI                             |
| Rostom 2008 [57]             | Cross-sectional | JIA (all subtypes)       | 121                | Primary                         | CR               | To determine the prevalence of clinical and radiological hip involvement                    |
| Müller 2009 [77]             | Prospective | JIA (all subtypes)       | 30                 | Primary                         | US, MRI          | To compare clinical examination/US to MRI                                                  |
| Burbul 2009 [62]             | Retrospective | PsA, oJIA, pJIA           | 106                | No                              | NA               | To compare clinical features in PsA to other JIA subtypes with similar patterns of joint disease – including growth abnormalities |
| Endén 2009 [71]              | Cross-sectional | sJIA, pJIA/ fibromyalgia (control) | 134/24             | Primary                         | CR               | To describe growth and cervical vertebrae size in JIA (vs. control)                         |
| Flato 2009 [63]              | Retrospective | PsA, oJIA, pJIA           | 336                | Secondary                        | CR               | To compare PsA features (including radiographic sacro-iliitis) and outcomes to other JIA subtypes |
| Lin 2009 [60]                | Cross-sectional | Juvenile AS               | 47 juvenile AS, 122 adult AS | Secondary                        | CR               | To compare clinical, laboratory and radiographic features between juvenile and adult-onset AS |
| Tafaghodi 2009 [34]          | Retrospective | JIA (all subtypes)        | 174                | Primary                         | CR               | To assess radiographic characteristics of JIA (118 patients) vs. ALL (56 patients)         |
| Arvidsson 2010 [76]          | Prospective | JRA                     | 60                 | Primary                         | CR, CT           | To assess TMJ imaging during follow-up for long-standing JIA                                |
| Pagnini 2010 [20]            | Prospective | ERA                     | 59                 | Primary                         | CR, MRI          | To identify predictors of sacroiliitis                                                     |
| Stoll 2010 [19]              | Retrospective | ERA, PsA, JPsA            | 143                | Primary                         | CR, MRI          | To identify risk factors for sacroiliitis                                                  |
| Cannizzaro 2011 [85]         | Retrospective | oRA, RF+ and RF- pJIA, PsA, ERA, sJIA | 223                | Secondary                        | CR, MRI          | To determine the incidence of TMJ involvement in different JIA subtypes                    |
| Kjellberg 2011 [72]          | Case-control | pJIA, oJIA, PsA, ERA, UA  | 82                 | Primary                         | CR               | To compare radiographic cephalometry findings in JIA and healthy controls                   |
| Ravelli 2011 [24]            | Retrospective | oJIA, RF- negative pJIA, PsA, UA  | 971                | Secondary                        | CR               | To compare disease characteristics depending on ANA status                                  |
| Stoll 2011 [65]              | Retrospective | PsA                    | 87/303             | No                              | NA               | To compare clinical features of oJIA vs. PsA                                              |
| Stoll 2011 [66]              | Narrative review | PsA                   | NA                 | No                              | NA               | To identify features of PsA, in comparison with other subtypes of JIA                       |
| Bertilsson 2012 [41]         | Prospective | JCA                     | 132                | Secondary                        | CR               | To prospectively investigate the characteristics and outcome predictors over 5 years of follow-up |
| Lipinska 2012 [27]           | Prospective | oJIA, sJIA, sJIA         | 74                 | Secondary                        | CR               | To assess the Steinbrocker score depending on ACPA status                                    |
| Berhilsson 2013 [42]         | Prospective | JCA                     | 132                | Secondary                        | CR               | To evaluate long-term outcomes, after 17 years of follow-up                                 |
| Chen 2012 [56]               | Cross-sectional | Juvenile- onset AS       | 67                 | Secondary                        | CR               | To compare clinical, laboratory and radiographic features of juvenile-/adult-/late-onset AS |
| Ozawa 2012 [52]              | Cross-sectional | pJIA, sJIA              | 40                 | Secondary                        | CR               | To compare radiological and laboratory findings in pJIA and sJIA                            |
| Abramowicz 2013 [75]         | Retrospective | JIA                    | 51                 | Primary                         | MRI              | To identify prevalence of synovitis on MRI, TMJ imaging and clinical predictive factors     |
| Elhai 2013 [48]              | Prospective | pJIA                    | 43                 | Primary                         | CR               | To compare radiological outcomes of pJIA at transition vs. matched RA patients              |
| Elhai 2013 [69]              | Cross-sectional | pJIA/RA                | 57/58              | Primary                         | CR               | To compare the frequency of cervical spine radiographic damage between long-standing pJIA and RA |
| Jadon 2013 [59]              | Systematic review | Juvenile-onset AS       | NA                 | NA                              | CR               | To compare clinical, social and radiographic features of adult- vs. juvenile-onset AS      |
| Omar 2013 [53]               | Cross-sectional | oJIA, pJIA, sJIA        | 54                 | Secondary                        | CR               | To assess correlations linking ACPA presence to the JADAS and Sharp van der Heijde scores   |
| Article | Design | JIA subtype | Number of patients | Imaging findings used as outcome | Imaging technique | Purpose |
|---------|--------|-------------|--------------------|----------------------------------|-------------------|---------|
| Cedströmer 2013 [78] | Retrospective | oJIA, sJIA, pJIA, JPsA, ERA | 266 | Secondary | CR | To describe clinical findings and disease activity and their associations with CR abnormalities |
| Giancane 2014 [43] | Prospective | RF+ and RF- pJIA, sJIA, extended oJIA, UA, JPsA | 186 | Primary | CR | To assess radiographic outcomes during follow-up (1–10 years) |
| Jaremko 2014 [61] | Cross-sectional | Juvenile AS | 26 | Primary | CR, MRI | To compare the usefulness of CR and MRI for sacro-iliac joint evaluation at diagnosis of juvenile AS |
| Rodriguez-Lozano 2014 [32] | Cross-sectional | sJIA, RF+ and RF- pJIA, JPsA, extended oJIA | 60 CR | NA | CR | To assess the inter-observer reliability of CR interpretation |
| Abramowicz 2014 [74] | Retrospective | oJIA, pJIA, JPsA | 30 | Primary | CR, MRI | To identify radiographic findings associated with TMJ synovitis on MRI |
| Górska 2014 [79] | Cross-sectional | oJIA, pJIA | 26 | Primary | CR | To describe orthodontic and radiographic findings |
| Koos 2014 [80] | Case-control | oJIA, RF- negative pJIA, ERA, JPsA/non-JIA controls | 23/23 | Primary | Cone Beam CT | To describe pathological changes in TMJs |
| Koos 2014[81] | Cross-sectional | JIA (all subtypes)/controls | 134/134 | Primary | MRI | To evaluate the reliability of clinical symptoms for diagnosing TMJ synovitis |
| Ringold 2014 [55] | Recommendations | pJIA | NA | NA | CR | To develop CARRA recommendations for treating new-onset pJIA |
| Colebatch-Bourn 2015 [87] | Recommendations | All subtypes | NA | NA | CR, US, MRI | EULAR recommendations/ all imaging techniques |
| Ravelli 2015 [23] | Narrative review | JPsA | NA | NA | No | To assess the classification of JPsA and its relation to oJIA |
| Chan 2016 [22] | Prospective | JPsA and non-psoriatic JIA | 57 | No | No | To discuss the classification of JPsA |
| Jadon 2016 [88] | Prospective | Adult AS and PsA | 402 | Primary | CR | To compare radiographic features of AS vs. PsA with axial disease |
| Kavanaugh 2016 [25] | Phase III clinical trial | Adult PsA | 405 | Primary | CR | To assess the efficacy of golimumab on radiographic progression in adult PsA |
| Kristensen 2016 [86] | Systematic review | All subtypes | NA | NA | MRI | To identify clinical predictors of TMJ involvement, needing imaging assessment |
| Weiss 2016 [67] | Prospective | JSpA | 40 | Primary | CR, MRI | To evaluate the prevalence of sacroiliitis, compared to physical examination findings |
| Guide du bon usage des examens d’imagerie (French online recommendation) [90] | Recommendations | JSpA | NA | NA | CR | To develop recommendations about CR for focal limb pain |
| Ravelli 2014 [89] (ACR Pediatric Rheumatology Symposium) | Clinical trial | pJIA | 87 | Primary | CR | To assess the effect of tocilizumab on pJIA after 2 years, using the van der Heijde and Poznanski scores |

ACPA anti-citrullinated protein antibody, ALL acute lymphoblastic leukaemia, ANA antinuclear antibody, AS ankylosing spondylitis, CARRA Childhood Arthritis and Rheumatology Research Alliance, CR conventional radiography, IBD inflammatory bowel disease, JADAS Juvenile Arthritis Disease Activity Score, JCA juvenile chronic arthritis (former EULAR criteria), JRA juvenile rheumatoid arthritis (former ACR criteria), JPsA juvenile psoriatic arthritis, JSpA juvenile spondyloarthritids, MCTD mixed connective tissue disease, MTX methotrexate, NA not applicable, oJIA oligoarticular juvenile idiopathic arthritis, OPG orthopantomogram, pJIA polyarticular juvenile idiopathic arthritis, SEA seronegative spondyloarthritis and arthropathy, sJIA systemic juvenile idiopathic arthritis, UA undifferentiated arthritis
Table 2  Recommendations about CR as a diagnostic and follow-up investigation in non-systemic JIA, with scores for agreement among experts, levels of evidence and grade

| Recommendations | Mean agreement score (±SD) | Level of evidence | Grade |
|----------------|-----------------------------|-------------------|-------|
| **Overarching principles** |                           |                   |       |
| A. A CR assessment is necessary in JIA. | 9.30 (±1.26) | - | - |
| B. The potential risks associated with exposure to ionising radiation must always be considered when using CR. | 9.70 (±0.70) | - | - |
| C. CR is difficult to interpret in skeletally immature patients, particularly those <5 years of age. | 8.95 (±1.73) | - | - |
| D. Other imaging techniques, such as US and MRI, are being developed in JIA, and will be discussed in specific recommendations. | 8.95 (±1.85) | - | - |
| **Oligoarthritis (oJIA)** |                           |                   |       |
| 1. CR should not be performed routinely as a diagnostic investigation. | 8.20 (±1.94) | 3 | C |
| 2. During follow-up, CR should be performed on affected joint(s) that remain symptomatic* after 3 months | 9.10 (±2.17) | 4 | D |
| 3. In patients with persistently symptomatic* joints, the reiteration of CR during follow-up is at the discretion of the physician. | 9.15 (±1.04) | 4 | D |
| 4. In patients with inactive disease, CR is not recommended. | 9.45 (±0.83) | 4 | D |
| 5. In patients with extended oJIA, the recommendations for pJIA should be applied. | 9.30 (±0.92) | 3 | C |
| 6. In patients with structural damage, the selection and timing of specific imaging techniques to further assess the damaged joint during follow-up is guided by clinical considerations. | 9.15 (±1.04) | 4 | D |
| **Polyarthritis (pJIA)** |                           |                   |       |
| 7. Routine CR of the wrists, hands, and forefeet is strongly recommended at the diagnosis of polyarticular JIA with positive RF/ACPA. | 9.30 (±1.26) | 2B, 3 | B |
| 8. CR of other joints than wrists, hands, and forefeet, is recommended at the diagnosis for symptomatic* joints only. | 9.00 (±1.49) | 2B, 3 | B |
| 9. In new-onset RF/ACPA-negative pJIA with adverse prognostic factors, CR at diagnosis should be performed as for RF/ACPA-positive pJIA (recommendation #7). | 8.55 (±2.46) | 3 | C |
| 10. Adverse prognostic factors are early wrist involvement, distal involvement, symmetric arthritis, high CRP/ESR, and bone erosions. | 9.35 (±0.81) | 2B | B |
| 11. In new-onset, RF/ACPA-negative pJIA without adverse prognostic factors, at diagnosis, CR should be confined to symptomatic* joints. | 8.15 (±2.28) | 4 | D |
| 12. In RF/ACPA-positive pJIA, CR of the hands, wrists, and forefeet is strongly recommended - 1 year after disease onset | 8.30 (±1.72) | 2B | B |
| - and when transitioning from paediatric to adult healthcare | 8.85 (±0.99) | 4 | D |
| At other time points, the use of CR during follow-up is at the discretion of the physician. | 9.25 (±0.85) | 4 | D |
| 13. Routine CR of other joints is not recommended. | 9.40 (±0.75) | 4 | D |
| 14. During the follow-up of RF/ACPA-negative pJIA with adverse prognostic factors, CR should be performed as for RF/ACPA-positive pJIA (recommendation #12). | 9.00 (±2.03) | 3 | C |
| 15. During the follow-up of RF/ACPA-negative pJIA without adverse prognostic factors, the use of CR is at the discretion of the physician. | 9.50 (±1.17) | 4 | D |
| 16. CR can be repeated in patients who remain symptomatic longer than 3 months. | 8.25 (±2.10) | 4 | D |
| 17. In patients with structural damage, the selection and timing of specific imaging techniques during follow-up is guided by clinical considerations. | 9.35 (±0.81) | 4 | D |
| **Enthesitis-related arthritis (ERA)** |                           |                   |       |
| 18. In patients with axial ERA, CR of the spine and hip joints should be performed only when needed for the differential diagnosis. | 8.05 (±2.42) | 4 | D |
| 19. During the follow-up of axial ERA, CR should be considered only for the hip joints, depending on the clinical course and availability of US and/or MRI. | 8.90 (±1.33) | 3 | C |
| 20. CR is not recommended for multifocal enthesitis. | 9.10 (±0.97) | 4 | D |
| 21. In patients with isolated enthesitis, CR can be considered as a tool for establishing the differential diagnosis. | 8.35 (±2.43) | 4 | D |
cases, respectively [31]. Our literature review identified some data on the best times for CR. One study suggested a higher risk of radiographic progression within the first year after disease onset [51]. The experts felt that CR contributed to ease the transition from paediatric to adult healthcare [96].

13. Routine CR of other joints is not recommended. No data were found on which to base specific recommendations.

14. During the follow-up of RF/ACP A-negative pJIA with adverse prognostic factors, CR should be performed as for RF/ACP A-positive pJIA (see recommendation #12).

15. During the follow-up of RF/ACP A-negative pJIA without adverse prognostic factors, the use of CR is at the discretion of the physician. No scientific data were available on which to base specific recommendations.

16. and 17. CR can be repeated in patients who remain symptomatic* longer than 3 months. In patients with structural damage, the selection and timing of specific imaging techniques during follow-up is guided by clinical considerations. The experts emphasized the need for careful attention to joints with active disease. In prospective studies, the time interval separating CR assessments of the same joints ranged from 8 months to 24 years. The 3-month interval in this recommendation was based on expert opinion.

18. In patients with axial ERA, CR of the spine and hip joints should be performed only when needed for the differential diagnosis. Axial manifestations may arise at the spine, hips and sacro-iliac joints. A radiographic view specifically designed to assess the sacro-iliac joints is not recommended, as the results are not interpretable in skeletally immature patients and radiation exposure is significant [20]. In patients with axial inflammatory pain, MRI (for both sacro-iliac and hip joints) and US (for the hip joint) may be more relevant [67].

19. During the follow-up of axial ERA, CR should be considered only for the hip joints, depending on the clinical course and availability of US and/or MRI. ERA is associated with a high prevalence of hip joint arthritis [30, 56, 58–60]. MRI or US are non-irradiating methods capable of detecting hip joint effusion; in addition, MRI can detect bone oedema. Therefore, in the future, MRI and US may deserve consideration as first-line imaging techniques. CR, however, is appropriate for monitoring known structural damage and deformities.

20. and 21. CR is not recommended for multifocal enthesitis. In patients with isolated enthesitis, CR can be
Considered as a tool for establishing the differential diagnosis. When isolated enthesitis is suspected, CR may contribute to the differential diagnosis (e.g. with post-traumatic changes or osteochondritis); otherwise, CR is unhelpful for assessing peri-articular manifestations.

Psoriatic juvenile arthritis (jPsA)

22. No specific recommendation can be made about CR in juvenile psoriatic arthritis. Scientific data are scarce [62–66, 68]. The definition of this entity is still debated [68]. Traditionally, two subtypes are described, an axial inflammatory disease resembling axial ERA and a peripheral joint disease resembling oJIA [66].

23. Guidance may be taken from the recommendations above, depending on the clinical presentation, or from recommendations issued for adults.

Situations of specific interest

Monoarthritis 24. At the diagnosis of acute monoarthritis, CR of the involved joint should be performed, with two perpendicular views. The French Society for Radiology [90] strongly recommends CR of any site of focal bone pain in paediatric patients, with the goal of excluding a tumour, osteomyelitis, or a haematological malignancy [34, 97].

25. At the diagnosis of acute monoarthritis, comparative CR of the contralateral joint is unnecessary. Because cartilage thickness varies within individuals, comparison to the healthy contra-lateral joint is uninformative [26, 33].

Cervical spine 26. In patients with persistent neck pain related to JIA, MRI is preferable over CR.

27. When MRI is unavailable, CR is recommended only for the cervical spine and should consist only of a lateral view.

28. In patients with JIA who have neurological symptoms of spinal cord compression and neck pain, cervical MRI must be performed, on an emergency basis.

In a cohort study of oJIA, 2.4 % of patients had cervical spine damage at the diagnosis [35]. Cervical spine erosions and ankylosis are common in advanced pJIA [42, 71]. Evidence-based data are too scarce to recommend any specific pattern of radiological follow-up. Atlanto-axial diastasis may be normal in paediatric patients, and dynamic CR is therefore irrelevant. MRI is the most sensitive imaging technique, and is mandatory when spinal cord compression is suspected [98].

Temporomandibular joints 29. CR of the TMJs is not recommended when cross-sectional imaging is available.

TMJ damage is common in JIA, with the prevalence ranging across studies from 17 % to 87 % [73]. The TMJ cartilage is thin and condylar erosions therefore develop early. The panoramic radiograph is often normal at disease onset. Cross-sectional imaging offers better diagnostic performance. Imaging of the TMJs is not usually performed on a routine basis but is required in the event of pain, mouth-opening limitation or audible cracking of the TMJs [74, 76–81, 83, 84]. MRI is considered the best imaging technique, although distinguishing the normal appearance from abnormal changes can be challenging [99, 100]. Cone-beam computed tomography allows three-dimensional reconstructions [101]. The usefulness of US TMJ imaging is under debate [77, 102].

Hip joint 30. Routine CR of the hip joint is not recommended in patients with pJIA.

31. When CR of a symptomatic hip joint is performed, a single view should be obtained, i.e. either an antero-posterior view or a frog leg view.

In RF/ACPA-positive pJIA, hip joint damage is common [48] but CR of the hip joint is associated with a high level of ionising radiation exposure, so the hip is not among the joints for which routine CR is recommended. When available, MRI should be performed instead of, or in addition to, CR. If CR is performed, either an antero-posterior or a frog leg view is recommended, to visualise both hip joints and to allow the detection of bone erosions and/or avascular necrosis.

Discussion

CR is the most widely available imaging procedure worldwide. In paediatric patients, this advantage should be weighed against the heightened risks of radiation exposure and difficulty in interpreting joint radiographs before skeletal maturity is achieved. In addition, in JIA, radiographically visible joint damage takes time to develop, limiting the usefulness of CR. Specific recommendations about CR in paediatric patients are therefore needed, a fact that prompted the present work.

Obstacles to the development of recommendations about CR in JIA included the paucity of strong evidence about structural disease progression in JIA and the pooling of JIA subtypes in many studies. The low incidence of JIA contributes to explain the dearth of data. To maximise the usefulness of our recommendations to all physicians caring for patients with JIA, we focussed on CR and separated the five non-systemic, non-undifferentiated subtypes of JIA. Importantly, these recommendations are based not only on recently published data, but also, in many cases, on expert opinion, due to the paucity of paediatric studies. As a result, many of our recommendations are low grade, and in some cases obtaining guidance from recommendations for adults would seem to be the only option. However, the level of agreement among the multidisciplinary experts sitting on our panel was high.
Structural damage requires evaluation in JIA, especially in pJIA and extended oJIA, which carry the highest risk of adverse outcomes. In the treatment plans for pJIA developed by the CARRA, CR changes are considered an important outcome and their yearly assessment is suggested [55]. However, the risk associated with exposure to ionising radiation during CR is of major concern, as pointed out by the representative of the patient organisation during our study. Little evidence is available on which to base an objective quantification of this risk. Our experts considered that the risk was substantial for CR of the pelvis and lumbar spine but was too small at peripheral sites to constitute an argument against using CR. To minimise radiation exposure, the experts recommended having CR performed at centres with expertise in paediatric radioprotection.

Research is needed in a broad range of areas to fill the knowledge gaps we identified when developing our recommendations (Box 2). More specifically, most paediatric clinical trials failed to assess potential treatment effects on structural damage. Also, data on structural damage just before the transition to adult healthcare are needed, since treatment recommendations for adults are based on structural damage.

Box 2: Research agenda

- Follow-up of a cohort of patients with recent-onset RF/ACPA-positive polyarticular JIA, with annual CR for 10 years to identify predictors of structural joint damage
- Comparison of radiographic disease progression in oligoarticular JIA in patients with and without antinuclear antibodies
- Comparison of joint MRI, US, and CR as tools for detecting structural damage in patients younger than 5 years of age
- Evaluation of joint damage at the transition from paediatric to adult healthcare in each JIA subtype
- Improvement of the definition of juvenile psoriatic arthritis, to obtain homogeneous populations for studies of imaging techniques

We considered neither MRI nor US, both of which are under evaluation in JIA. Both are non-irradiating, and US is also widely available and inexpensive, although it requires specific training. US is now performed almost routinely in adults with joint disease. In paediatric patients, however, differentiating normal from abnormal findings by MRI and US can be challenging [100, 103]. Furthermore, very few physicians are specifically trained in paediatric US. The OMERACT and Health-e-Child Radiology groups are currently working together to standardise MRI protocols and interpretation in JIA [104–106].

In conclusion, CR still appears relevant in many situations in patients with JIA. CR is a widely available and inexpensive investigation that has an acceptable safety profile and can provide essential information about the structural course of the disease. Until validation studies of other imaging techniques, such as MRI and US, are completed, CR will remain the investigation of reference for assessing structural joint damage in patients with JIA.

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Compliance with ethical standards

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Statistics and biometry No complex statistical methods, were necessary for this paper.

Ethical approval Institutional Review Board approval was not required; the methodology entirely relies on literature review and expert opinion.

Informed consent Informed consent was not required because no human subjects were involved.

Methodology

- Retrospective
- Literature review, and expert consensus seeking through a Delphi process
- Performed at one institution

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