

Imaging of Juvenile Idiopathic Arthritis

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Introduction

Juvenile idiopathic arthritis (JIA) is a heterogeneous condition including all forms of chronic arthritis of unknown origin, duration ≥ 6 weeks and with onset before 16 years of age. It is characterized by chronic synovial inflammation with potential risk of developing progressive joint destruction and serious functional disability [1-4]. It affects around 1 in 1,000 children under the age of 16 [5-8]. Typically, the child presents with a history of morning stiffness, vague pain and one or more swollen joints.

Recent research has shown that adult disease is seen in up to 75% of those having suffered JIA during childhood [9]. Moreover, the temporomandibular joint (TMJ) is involved in up to 70% of patients; in a high proportion it is overt and thus not treated specifically [10]. This may lead

to pubertal growth disturbances of the TMJs, including restricted mandibular growth [9, 11, 12], with development of malocclusion and facial deformities [13]. Assessment of the TMJs, with treatment of those testing positive, has therefore become an important issue in management of children with JIA. The new understanding of JIA being more aggressive than previously believed and the introduction of new disease-modifying drugs have led to earlier and more aggressive treatment, and have fuelled the search for more accurate disease markers to better monitor therapeutic response.

Classification

Based on clinical and laboratory findings, JIA is currently subdivided to include [14-16] (Table 1):

Table 1. Subgroups of juvenile idiopathic arthritis

Subset of JIA	Frequency (%)	Age at onset	Clinical characteristics	Male/females
Oligo	27-56	Early childhood, peak 2-4 years	Four or fewer joints involved the first 6 months; lower extremity more often affected, generally good prognosis, worse prognosis if more than four joints affected after 6 months (extended oligo JIA); risk of developing iridocyclitis	F>>>M
Poly, RF negative	11-28	Early peak 2-4 years, late peak 6-12 years	Four or more joints involved the first 6 months, absence of IgM RF; heterogeneous disease with three subsets; prognosis varies with the disease subset	F>>M
Poly, RF positive	2-7	Late childhood to adolescence	Four or more joints involved the first 6 months, IgM RF positive; resembles adult rheumatoid arthritis. Involvement of small joints; progressive and diffuse joint involvement	F>>M
Entethesis-related arthritis	3-11	Late childhood to adolescence	Characterized by entesitis and arthritis. Often HLA-B27 positive; commonly hip involvement at presentation; often a mild and remitting course but may progress with sacroiliac and spinal joint involvement, resembling ankylosing spondylitis	M>>F
Psoriatic	2-11	Early peak 2-4 years, late peak 9-11 years	Arthritis and psoriatic rash or psoriasis in closefamily; controversial definition, resembles oligoarthritis, but more often with dactylitis and involvement of both small and large joints	F>M
Systemic	4-17	Throughout childhood	Arthritis and quotidian fever plus one or more of the following symptoms: characteristic rash, hepatomegaly, splenomegaly, lymphadenopathy, serositis; variable course; 5-8% develop macrophage activation syndrome	F=M

Subgroups described in [14-16]

F female, JIA juvenile idiopathic arthritis, M male, RF rheumatoid factor

- Oligoarthritis: one to four joints affected in the first 6 months of disease. This category is further divided into persistent oligoarthritis (with no more than four involved joints during the disease course) and extended oligoarthritis, involving more than four joints after the first 6 months.
- Polyarthritis: more than four joints affected within the first 6 months.
- Systemic arthritis: arthritis accompanied by systemic illness including fever.
- Psoriatic arthritis: arthritis associated with psoriasis.
- Enthesitis-related arthritis: these patients are often HLA-B27 positive.

This classification is unsatisfactory because many of the identified subgroups appear to be too inhomogeneous. Furthermore, it is difficult to distinguish, early in the disease course, between patients who are most likely to develop joint damage, and who therefore require a more aggressive treatment at an early stage, and patients who will have a mild disease course. Finally, in clinical trials, drug efficacy is judged only on clinical parameters, since measures that can allow the early identification of the progression of joint damage, and therefore of drug efficacy on disease progression, are not available in children.

Imaging

The role of imaging is to secure the diagnosis, to assess the extent, severity and activity of the disease, and to help monitor therapeutic response and potential complications to steroid therapy and immobilization, such as compression fractures and avascular necrosis. During the past decade there has been a shift from traditional radiography towards newer techniques such as ultrasound and magnetic resonance imaging, thus without proper evaluation of their accuracy and validity.

Radiographs can show periostitis, bone erosion, cartilage loss [indirectly, through joint space narrowing (JSN)], osteoporosis and joint misalignment (Figs. 1-4), but cannot visualize synovium, joint effusion, articular cartilage, bone marrow, or ligaments and tendons directly. Plain radiographs have particularly low sensitivity for disease in early stages (Table 2) [17-24].

Joint damage evaluation has traditionally been performed by radiographic scoring methods assessing JSN and erosions; however, they are quite inaccurate, in part due to the growing skeleton [25]. Wrist disease has been associated with a more severe course of arthritis and a poorer functional outcome, and is the only joint in which suitable radiographic measures of disease progression have been reported. Much effort has been spent recently on validating existing scoring systems or devising new ones, of which a modified version of the Sharp/van der Heijde wrist score has gained most acceptance (Table 2). The original Sharp/van der Heijde score is based on the assessment of JSN in 15 different



Fig. 1. Radiograph in 4-year-old girl with juvenile idiopathic arthritis, shows periarticular soft tissue swelling of the left fourth finger, proximal interphalangeal joint, periarticular osteoporosis and periostitis along the proximal phalanx (arrows)

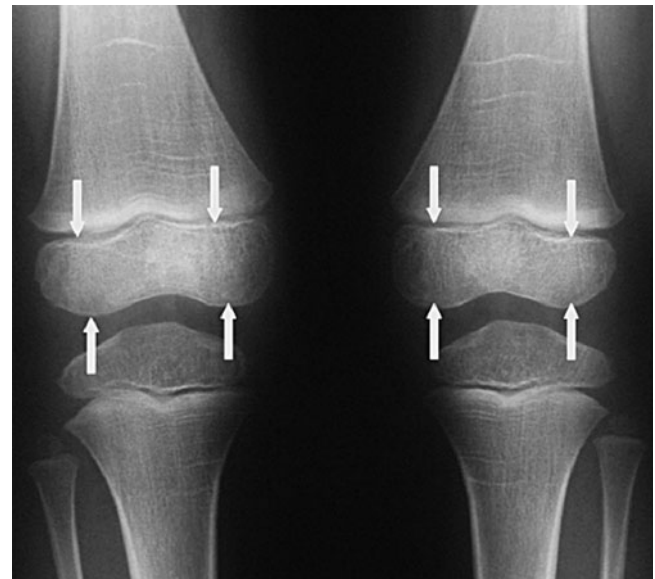


Fig. 2. A 5-year-old boy with active juvenile idiopathic arthritis of the right knee for 3 months. Radiograph shows accelerated growth of the knee epiphysis, as compared with the right normal side (arrows)

locations, and bone erosion in 16 locations for each hand/wrist, separately. JSN is scored from 0 to 4, and bone erosion from 0 to 5, and the scores are summarized to make a total score ranging from 0 to 280 [26]. Notably, carpal/metacarpal changes in younger children tend to present as bony deformation, ranging from mild squaring to severe compression, rather than definite erosions as often seen in adults (Fig. 3). This has been



Fig. 3. A 4-year-old girl with juvenile idiopathic arthritis and wrist affection. Radiograph shows squaring of the metacarpal epiphysis (arrows)

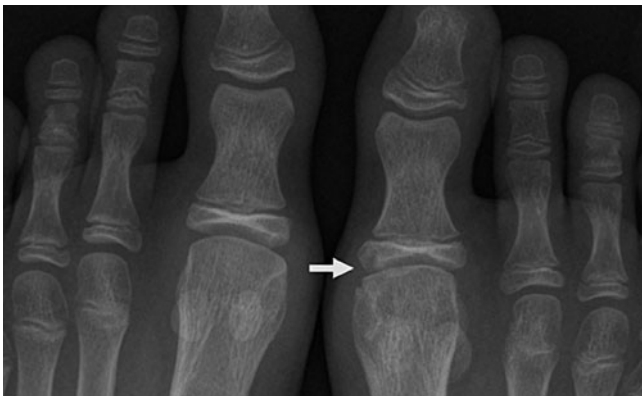


Fig. 4. Juvenile idiopathic arthritis in a 12-year-old boy. Radiograph shows destructive change of the metatarsophalangeal joint of the first left toe, with joint space narrowing and small erosions (arrow)

accounted for in Sharp/van der Heijde's scoring system in that both entities are considered pathological and scored in a similar fashion.

Rossi and colleagues noted that JSN tends to predominate over erosive change in JIA, and that erosion tends to involve locations other than those seen in adult rheumatoid arthritis [19]. For these reasons Ravelli et al. added another five locations to those described by Sharp/van der Heijde (second to fourth metacarpal bases, the capitate and the hamate), giving a total score of 330 [18]. When scoring is preceded by a meticulous standardization process, accuracy appears to be appropriate for clinical use.

Ultrasound (US) performs better than clinical examination in the diagnosis and localization of inflammatory change, such as joint effusion, bursal fluid collection and synovitis [27, 28] (Figs. 5-9). US can visualize inflammatory change relatively accurately, while assessment of chronic change is less feasible [29]. A structured assessment of synovitis and tenosynovitis, and classification of the findings, has been devised; however, the technique needs further validation [30] (Table 1). A few small uncontrolled studies have described improved sensitivity for detection of bone erosions in joints with the use of US as compared with conventional plain radiography; however, firm conclusions cannot be drawn from these studies. US may also demonstrate changes to cartilage.

Magnetic resonance imaging (MRI) can visualize both active JIA change, such as soft tissue and synovial inflammation, effusion, bone marrow edema and chronic change. Additional contrast-enhanced series can help quantify the inflammation process, and also differentiate pannus from joint effusion [20]. Furthermore MRI is the only technique for assessment of bone marrow edema [21].

The protocol should include pulse sequences for assessment of the synovium (T2-weighted and fat-saturated/gadolinium enhanced T1-weighted images) and cartilage

Table 2. Classification systems for active inflammatory change and chronic, structural change in juvenile idiopathic arthritis

Classification system	Active, inflammatory change		Chronic, structural change	
	Detection of pathology	Scoring system	Detection of pathology	Scoring system
Clinical parameters	Joint swelling, relatively low sensitivity	Inaccurate	Joint malalignment, late finding	Inaccurate
Radiography	Unfeasible		Feasible	Lack of accurate scoring systems, adapted version of the Sharp/van der Heijde wrist score
Ultrasound	Effusions, synovial hypertrophy, tenosynovitis, feasible	Relatively accurate	Relatively unfeasible	Inaccurate
MRI	Effusions, bone marrow edema, synovial, hypertrophy with hyperaemia, tenosynovitis, feasible	For wrist; devised by HeC, relatively accurate [20, 21]	Relatively unfeasible	For wrist; devised by HeC, relatively inaccurate [16, 22-24]



Fig. 5 a, b. **a** Hand radiograph in a 12-year-old girl with longstanding juvenile idiopathic arthritis (poly, rheumatoid factor positive) shows severe osteoporosis, crowding of the carpals and squaring of the metacarpal epiphysis. **b** A normal hand is shown for comparison

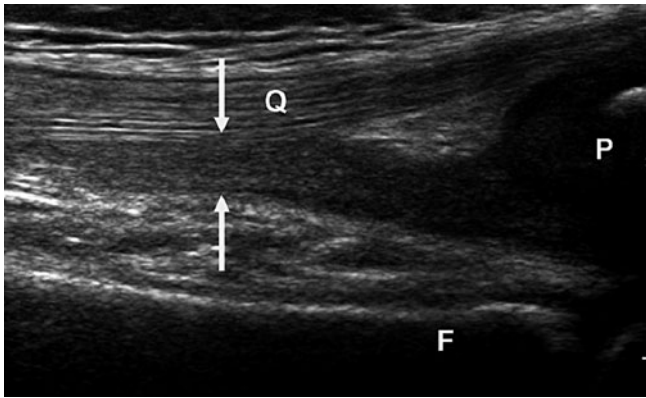


Fig. 6. Sagittal ultrasound view of the left knee joint in a 5-year-old girl with juvenile idiopathic arthritis shows synovial hypertrophy within the suprapatellar recess (between arrows) without an effusion (verified by compression technique). *F* distal femur, *P* patella, *Q* quadriceps tendon

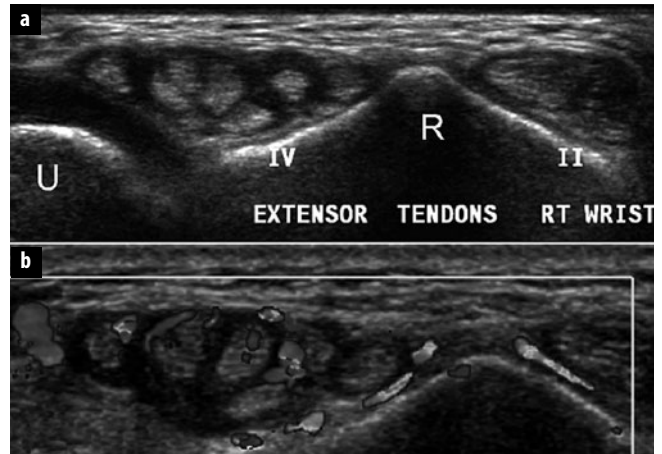


Fig. 8 a, b. Axial ultrasound view (standard view) of the dorsal right wrist in a 7-year-old girl with juvenile idiopathic arthritis shows tenosynovitis of the extensors (compartments 2-4) (**a**) and verified by hyperemia on color Doppler (**b**). *R* distal radius, tubercle of Lister; *U* distal ulna (for color reproduction see p 317)

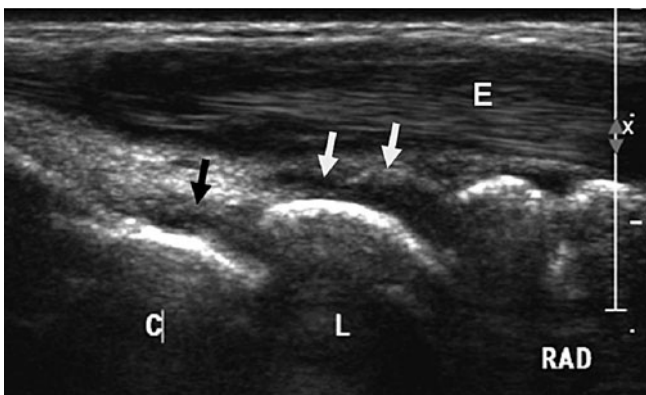


Fig. 7. Sagittal ultrasound view (standard view) of the dorsal wrist in a 6-year-old girl with juvenile idiopathic arthritis shows synovial hypertrophy and small effusions in the radiocarpal (white arrows) and midcarpal joints (black arrow). *C* capitate, *E* inflamed extensor tendons, *L* lunate, *RAD* distal radius (for color reproduction see p 317)

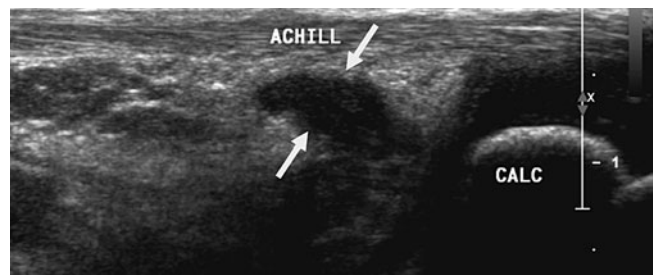


Fig. 9. Sagittal ultrasound view of the posterior ankle in a 9-year-old boy with enthesitis-related arthritis shows a swollen prepatellar bursa (arrows). *ACHILL* Achilles tendon, *CALC* calcaneus (for color reproduction see p 317)



Fig. 10 a-d. Coronal magnetic resonance images of the wrist in a 12-year-old girl with juvenile idiopathic arthritis, including a T1-weighted image [three-dimensional (3D) spin echo] showing no erosion (**a**), a T2 fat-saturated image showing a sliver of fluid in the radioulnar joint (within normal variation) (**b**), a T1-weighted (3D spoiled gradient recalled echo sequence) before (**c**) and after (**d**) intravenous contrast administration, showing mildly increased synovial enhancement around the distal scaphoid, the trapezoid and the trapezium, consistent with focal inflammation



Fig. 11 a, b. Sagittal magnetic resonance images of the right knee in a 12-year-old boy presenting with a swollen, painful knee. **a** T1 fat-saturated image (water excited) showing a swollen, prepatellar recess. **b** Contrast-enhanced image showing vivid enhancement of a mildly thickened synovium, consistent with synovitis. The clinical picture suggested juvenile idiopathic arthritis

and bone [T1/proton density weighted and three-dimensional (3D) spoiled gradient recalled echo sequences] in different planes (Figs. 10, 11).

The value of MRI as an advanced method to evaluate disease activity and disease damage in adults with rheumatoid arthritis is under active investigation by a research consortium called Outcome Measures in Rheumatology Clinical Trials (OMERACT). However, the results drawn from OMERACT studies are not directly applicable to children, because adult rheumatoid arthritis is different from JIA and because the growing skeleton of children needs a different approach (Fig. 12). Indeed, in children ossification is incomplete and joint

space width varies with age [16, 22]. Thus, despite technical progress in the imaging of cartilage, as development of ultrashort TE sequences, driven equilibrium, Fourier transform (DEFT) imaging, and steady-state free precession (SSFP) sequences for the detection of subtle surface irregularities and tiny focal defects of the articular cartilage, diffusion weighted techniques to assess degradation of collagen fibers, delayed gadolinium-enhanced cartilage imaging (dGEMRIC) to detect changes in cartilage proteoglycan content, and T2 relaxation time mapping to detect integrity of collagen in the extracellular matrix, the potential helpfulness of these techniques is yet to be seen. The same goes for sophisticated analysis



Fig. 12. Coronal T1-weighted image in a healthy 11-year-old boy shows bony depressions in the base of the fourth metacarpal and in the lunate (arrows) – within normal variation

of 3D image data to provide articular surface contour mapping, and 3D rendering as well as volumetric quantification of articular cartilage to evaluate the progression and response to treatment in patients with chronic arthritis. Progress in the assessment of synovitis, including dynamic contrast-enhanced MRI to assess the degree of inflammation, is also flawed with methodological difficulties, although voxel-by-voxel analysis of signal intensity versus time curves has proven more accurate than the region-of-interest approach in adults with rheumatoid arthritis. Other techniques for assessment of inflammation using semiautomated or automated segmentation program techniques of dynamic contrast-enhanced MRI have also been described [31, 32]. Thus, although MRI is a potential powerful imaging tool to assess joint inflammation and the progression of joint damage, standardized, validated, and feasible assessment systems are lacking.

During the years 2006 to 2010 we, as part of a large European-Union-funded multicenter study, devised a new scoring system for wrist involvement in JIA, assessing both active and chronic change, based on MRI and radiography combined. Based on a large cohort of around 350 patients aged from 5 to 15 years, we have examined feasibility and accuracy for all the different components within a scoring system, namely bone erosions, bone marrow edema, synovitis (effusion, synovial hypertrophy, increased enhancement) and tenosynovitis. In general, the accuracy, i.e., inter- and intraobserver agreement,

seems to be better for active than for chronic change (Table 2), and thorough standardization of the scoring method prior to assessment appears to be crucial. One major problem in assessing bone erosions and bone marrow change on MRI in particular was the lack of normal references (Fig. 10). Thus, during the project, such standards were created based on a population of 89 healthy children aged 5-15 years [16, 22]. Informed by these findings, we had to adjust some of the definitions used for pathological change.

In conclusion, imaging is crucial for the assessment, grading and follow-up of children with JIA. Plain radiography still plays an important role in the diagnostic work-up and in monitoring chronic change. US performs better than clinical examination in the diagnosis and localization of inflammatory change, but accurate scoring systems are lacking. US can also guide joint injections. MRI is an important tool for the detection and grading of active change, and is a promising technique for future assessment of chronic change. At present, the assessment of chronic change is flawed by the wide variation of normal bone size and shape, and the results drawn from the “adult OMERACT studies” are not directly applicable to children.

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