Recommendation

EULAR-PReS points to consider for the use of imaging in the diagnosis and management of juvenile idiopathic arthritis in clinical practice

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ABSTRACT
To develop evidence based points to consider the use of imaging in the diagnosis and management of juvenile idiopathic arthritis (JIA) in clinical practice. The task force comprised a group of paediatric rheumatologists, rheumatologists experienced in imaging, radiologists, methodologists and patients from nine countries. Eleven questions on imaging in JIA were generated using a process of discussion and consensus. Research evidence was searched systematically for each question using MEDLINE, EMBASE and Cochrane CENTRAL. Imaging modalities included were conventional radiography, ultrasound, MRI, CT, scintigraphy and positron emission tomography. The experts used the evidence obtained from the relevant studies to develop a set of points to consider. The level of agreement with each point to consider was assessed using a numerical rating scale. A total of 13 277 references were identified from the search process, from which 204 studies were included in the systematic review. Nine points to consider were produced, taking into account the heterogeneity of JIA, the lack of normative data and consequent difficulty identifying pathology. These encompassed the role of imaging in making a diagnosis of JIA, detecting and monitoring inflammation and damage, predicting outcome and response to treatment, use of guided therapies, progression and remission. Level of agreement for each proposition varied according to the research evidence and expert opinion. Nine points to consider and a related research agenda for the role of imaging in the management of JIA were developed using published evidence and expert opinion.

INTRODUCTION
Juvenile idiopathic arthritis (JIA) is a heterogeneous group of conditions with onset under the age of 16 years with unknown aetiology and persistence of symptoms for over 6 weeks.[1] Imaging plays an important role in diagnosis and monitoring of patients with JIA, but until recently there were few studies in this area.

A European League against Rheumatism (EULAR)—Pediatric Rheumatology European Society (PReS) task force was convened to produce evidence and consensus-based recommendations on the use of imaging in the diagnosis and management of JIA in clinical practice for use by secondary care professionals caring for children with JIA, to help define standards of care for appropriate imaging.

METHODS
An expert group of paediatric rheumatologists, rheumatologists with imaging expertise, radiologists, methodologists and a fellow (16 people, representing 9 countries) participated. The task force used a rigorous procedure as described in the updated EULAR standardised operating procedures.[2][3] Full methodological details are given in the online supplementary material S1.

At an initial meeting, members developed questions relevant to key aspects of the use of imaging in JIA. Eleven research questions were agreed by consensus, encompassing the role of imaging in making a diagnosis, detecting inflammation and damage, predicting outcome and response to treatment, the use of guided treatment, monitoring disease progression, and remission (see online supplementary text research questions S2). A detailed systematic search of the published literature was performed on studies involving the use of imaging in children with JIA. Imaging modalities included were X-ray described as conventional radiography (CR), ultrasound (US), MRI, CT, scintigraphy and positron emission tomography. Included studies were evaluated for risk of bias and applicability using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS)-2 tool.[4] Following presentation of the literature review at a second meeting, experts produced points to consider (PTC) with final agreement by a process of discussion and consensus. The available evidence for each recommendation was scored according to the Oxford Centre for Evidence-Based Medicine level of evidence.[5] The experts anonymously scored their level of agreement for each proposition using a 0–10 numerical rating scale (0=do not agree at all, 10=fully agree). Scores reflected research evidence and clinical expertise.[2] An agenda for future research was also agreed upon following presentation of the literature review.

Three patient representatives (one child and two young adults with a diagnosis of JIA) and two parents of children with JIA participated in the development of the PTC at a Patient and Public Involvement event; further details are given in the online supplementary material S1.

RESULTS
The database search (November 2013) resulted in 13 277 records leaving 10 925 articles after

Table 1 Points to consider, level of evidence, grade of recommendation and level of agreement

Point to consider	Level of evidence	Grade of recommendation	Level of agreement, mean NRS 0–10 (range)
1 US and MRI are superior to clinical examination in the evaluation of joint inflammation; these techniques should be considered for more accurate detection of inflammation, in diagnosis and assessing extent of joint involvement.	3b	C	9.07 (6–10)
2 When there is clinical diagnostic doubt, CR, US or MRI can be used to improve the certainty of a diagnosis of JIA above clinical features alone.	3b	C	9.43 (9–10)
3 If detection of structural abnormalities or damage is required, CR can be used. However MRI or US may be used to detect damage at an earlier time point than CR.	3b	C	8.71 (5–10)
4 In JIA imaging may be of particular benefit over routine clinical evaluation when assessing certain joints, particularly the use of MRI in detecting inflammation of the TMJ and axial involvement.	3b	C	9.64 (8–10)
5 Imaging in JIA may be considered for use as a prognostic indicator. Damage on CR can be used for the prediction of further joint damage. Persistent inflammation on US or MRI may be predictive of subsequent joint damage.	4	C	9.07 (5–10)
6 In JIA, US and MRI can be useful in monitoring disease activity given their sensitivity over clinical examination and good responsiveness. MRI should be considered for monitoring axial disease and TMJ.	3b	C	9.07 (7–10)
7 The periodic evaluation of joint damage should be considered. The imaging modality used may be joint dependent.	3b	C	8.29 (5–10)
8 US can be used for accurate placement of intra-articular injections.	3b	C	9.64 (8–10)
9 US and MRI can detect inflammation when clinically inactive disease is present; this may have implications for monitoring.	3b	C	8.86 (5–10)

The level of evidence and grade of recommendation are based on the Oxford Centre for Evidence-Based Medicine system.[5]
Level of evidence scale, 1a–5; grade of recommendation scale; A–D. NRS, numerical rating scale (0–10; 0=do not agree at all, 10=fully agree).
CR, conventional radiography; JIA, juvenile idiopathic arthritis; TMJ, temporomandibular joint; US, ultrasound.

deduplication. Four hundred and thirty-three articles were included for detailed review once exclusions were made based on title or abstract. All full text articles written in English were retrieved for review, of which 244 articles were excluded leaving 189 articles for inclusion. The hand search identified 15 additional articles, resulting in a total of 204 articles for inclusion (see flow chart in the online supplementary figure S4). Articles that were relevant to multiple research questions were included in the review as necessary. The number of articles included per question is shown in the online supplementary table S5.

The task force produced nine PTC which are presented with the level of evidence, grade of recommendation and level of agreement in table 1. The task force felt that the supporting data was not sufficient to produce 'recommendations' so they were categorised as 'points to consider'. Scores for risk of bias and applicability of the included studies according to QUADAS-2, a full reference list for articles included in each recommendation, and feedback given at the Patient and Public Involvement meeting are given in the online supplementary text S6 S7 and S8.

Overarching principles

The task force produced general statements that should be considered when interpreting the PTC. These principles cover the imaging needs of inflammatory arthritis is children and assume that other important differentials such as infection have been ruled out.

▶ 'JIA' is an umbrella term for all forms of inflammatory arthritis that begins before the age of 16 years, persists for more than 6 weeks and is of unknown origin. This heterogeneous group of diseases is currently classified according to the International League of Associations for Rheumatology classification.[6] There is a lack of information on imaging related to JIA categories at present.

▶ There is a paucity of data on the joint-specific imaging features present during growth and skeletal development in healthy children. Understanding normative data is essential for interpretation of imaging abnormalities. For example, some physiological features of recently ossified bones can be misinterpreted as cortical erosions, cartilage thickness may vary with skeletal maturation and vascularity of epiphyses will change with ageing.

▶ Joint inflammation at certain developmental time points may cause specific structural changes, further challenging imaging assessment.

▶ The appropriateness and feasibility of different imaging modalities differs with age, related to radiation exposure and requirement for sedation. Every effort should be made to avoid unnecessary radiation exposure. However, there is a long established experience with the use of CR to demonstrate damage.

▶ Patient experience with different imaging modalities is affected by their age and development. It is important to provide a 'child friendly' environment.

Points to consider
Making a diagnosis of JIA
PTC 1: US and MRI are superior to clinical examination in the evaluation of joint inflammation; these techniques should be considered for more accurate detection of inflammation, in diagnosis and assessing extent of joint involvement.

Sixty-five studies compared clinical examination with imaging in the detection of inflammation in various joints, 40 with US, 27 with MRI, 5 with CR and 1 with positron emission tomography (table 2). The data is represented according to detection rates; for example, how many times more (>one fold) or less (<one fold) does imaging detect inflammation over clinical examination; this has the potential to increase false positive results. In general, US and MRI were able to detect joint inflammation more frequently than clinical examination; for example

Table 2 Point to consider 1: Summary of included studies comparing imaging with CE in the detection of joint inflammation

Ultrasound US knees vs CE 13 studies[13 14 33 34 38 76–83]	Detection rate, mean (range) US vs CE	MRI MRI knees vs CE studies[13–15 36 72 84–87]	Detection rate, mean (range) MRI vs CE	CR CR knees vs CE 3 studies[13 15 85]	Detection rate, mean (range) CR vs CE
Synovitis/effusion (12 studies)[13 14 34 38 76–83]	1.19-fold (0.14–3.67-fold)	Synovitis vs clinical swelling (3 studies)[14 85 86]	1.02-fold (0.96–1.12-fold)	Joint distension vs swelling (3 studies)[13 15 85]	0.69-fold (0.45–1.0-fold)
		Effusion vs swelling (5 studies)[13–15 36 85]	1.07-fold (0.75–1.33-fold)		
Effusion (1 study)[33]	Agreement k=0.54 CE missed a significant no. of effusions	Effusion vs pain (1 study)[13]	1.45-fold (1.33–1.57-fold)		
PD vascularity (2 studies)[38 82]	1.63-fold (0.96–2.71-fold)	Synovial volume vs CRP (1 study)[87]	r=0.51–0.80 p=0.000–0.036	Joint distension vs pain (1 study)[13]	1.57-fold
		Synovial hypertrophy vs pain (1 study)[84]	r=0.68–0.74		

US hip vs CE 5 studies[13 16 78 88 89]		MRI hip vs CE 5 studies[13 15 90–92]		CR hip vs CE 1 study[15]	
Synovitis/effusion (5 studies)[13 16 78 88 89]	0.85-fold (0.13–1.39-fold)	MRI inflammation (4 studies)[13 15 90 91]	0.88-fold (0.50–1.78-fold)	Joint distension vs clinical effusion (1 study)[15]	0.80-fold
Synovitis/effusion vs LOM (1 study)[89]	Association p=0.006				
Synovitis/effusion vs pain (1 study)[89]	Association p=0.103	Synovial enhancement (1 study)[91]	0.94-fold		

US hands/wrists vs CE 4 studies[38 40 93 94]		MRI hands/wrists vs CE 2 studies[19 95]		CR hands/wrists vs CE 1 study[93]	
Synovitis/effusion (3 studies)[38 93 94]	0.93-fold (0.47–1.33-fold)	Synovitis volume vs total hand swelling score (1 study)[95]	r=0.52–0.72 p<0.05	Joint distension vs clinical effusion (1 study)[93]	0.63-fold
PD vascularity (2 studies)[38 40]	0.96-fold GS synovitis had weaker correlation with clinical disease activity than PD	Synovitis volume vs LOM (1 study)[95]	r=0.76 p<0.05		
Flexor/extensor tenosynovitis (1 study)[40]	Significant association with clinical disease activity	Synovitis score vs wrist swelling score (1 study)[19]	MRI score significantly higher with higher swelling score p<0.00001		

US ankles/feet vs CE 5 studies[38 79 96–98]		MRI ankles/feet vs CE 1 study[99]	
Synovitis/effusion (3 studies)[38 79 96]	0.97-fold (0.86-1.04-fold)	Tibiotalar synovitis (1 study)[99]	1.00-fold
PD vascularity (1 study)[38]	0.57-fold	Subtalar synovitis (1 study)[99]	3.33-fold

US TMJ vs CE3 studies[25 100 101]		MRI TMJ vs CE 8 studies[25 41 42 102–106]	
Synovitis/effusion (2 studies)[25 100]	11.7-fold (0.35–23.0-fold)	Synovitis (6 studies)[25 41 42 104–106]	2.46-fold (1.10–5.91-fold)
		Synovitis vs reduced MIO (4 studies)[25 102 103 105]	Significantly correlated Reduced MIO best predictor of active MRI changes
		Acute changes (1 study)[41]	71% asymptomatic 63% normal CE

Continued

Table 2 Continued				
US enthesitis vs CE **3 studies**[107–109]		**MRI enthesitis vs CE** **1 study**[110]		
US enthesitis vs CE **3 studies**[107–109]		**MRI enthesitis vs CE** **1 study**[110]		
Enthesitis (3 studies)[107–109]	0.79-fold (0.53–1.09-fold)	Enthesitis (1 study)[110]	0.50-fold	
US VARIOUS MULTIPLE JOINTS vs CE **9 studies**[48 50 64 111–117]		**MRI VARIOUS MULTIPLE JOINTS vs CE** **1 study**[110]		**CR VARIOUS MULTIPLE JOINTS vs CE** **1 study**[118]
Synovitis/effusion (6 studies)[48 111–114 116]	1.85-fold (1.00–3.33-fold)	Synovitis/effusion (1 study)[110]	1.08-fold	Soft tissue swelling vs clinical swelling (1 study)[118] 1.05-fold
Association US changes vs swelling (1 study)[48]	SH: r=0.63 Effusion: r=0.66 PD: r=0.50			
Association synovitis vs CE (2 studies)[50 117]	Swelling: r=0.50 LOM: r=0.40 Pain: r=0.21 CE missed inflammation in 25.2% joints			
		MRI cervical spine vs CE 1 study[20]		
		Synovitis/SH (1 study)[20]	4.25-fold	
		MRI SIJ vs CE 2 studies[23 119]		
		Sacroiliitis (2 studies)[23 119]	0.93-fold CE was normal in 22.9% patients with MRI sacroiliitis	

CE, clinical examination; CR, conventional radiography; CRP, C reactive protein; GS, grey scale; LOM, limitation of movement; MIO, maximal incisional opening; PD, power Doppler; SIJ, sacroiliac joint; SH, synovial hypertrophy; TMJ, temporomandibular joint; US, ultrasound.

Recommendation

the mean (range) detection rate for synovitis and effusion at the knee was 1.19-fold (0.14–3.67-fold) for US and 1.02-fold (0.96–1.12-fold) for MRI knee synovitis.

PTC 2: When there is clinical diagnostic doubt, CR, US or MRI can be used to improve the certainty of a diagnosis of JIA above clinical features alone.

The diagnosis of JIA is mainly based on clinical features and the exclusion of other causes of chronic arthritis. However this point illustrates the role of imaging when there is diagnostic doubt; no specific imaging signatures for JIA have been described yet, but imaging is helpful to narrow the differential diagnosis. Four studies compared imaging features in suspected/proven JIA with either controls or other disease entities, including infectious arthritis, acute lymphoblastic leukaemia and haemophilia.[7–10] US detected more joint inflammation than clinical examination; two studies specifically described US improving the diagnostic certainty in subjects with suspected JIA.[11 12]

Detecting damage
PTC 3: If detection of structural abnormalities or damage is required, CR can be used. However MRI or US may be used to detect damage at an earlier time point than CR.

Thirty-seven studies compared joint damage (erosions, joint space narrowing (JSN), deformity) detected by imaging with clinical findings suggestive of underlying damage, such as tenderness, limitation of movement and crepitus. In general, all imaging modalities appeared to detect less joint damage than suggested by clinical examination; for example the mean (range) detection rate for cartilage loss at the knee was 0.32-fold for US, 0.63-fold (0.20–1.0-fold) for MRI and 0.46-fold (0.23–0.71-fold) for CR when compared with pain.[13–15] This reflects the poor sensitivity of pain as an indicator of underlying damage.

When the imaging modalities are directly compared MRI and US detected more joint damage than CR, particularly at the hip (MRI vs CR detection rate, mean (range) 1.54-fold (1.08–2.0-fold); US vs CR detection rate, mean 2.29-fold), and at the wrist (MRI vs CR detection rate, 1.36-fold (1.0–2.0-fold)).[13 15–19]

Imaging specific joints
PTC 4: In JIA imaging may be of particular benefit over routine clinical evaluation when assessing certain joints, particularly the use of MRI in detecting inflammation of the temporomandibular joint (TMJ) and axial involvement.

Cervical spine MRI appears better at detecting inflammation than clinical examination; one study showed 20% of patients had pain and/or limitation of movement whereas 85% had MRI inflammatory changes suggesting that cervical spine involvement in JIA is often clinically silent.[20] MRI and CR have shown better detection rates than clinical examination for structural changes in the cervical spine (4.5-fold and mean, range 2.29 (1.58–3.0-fold)), respectively.[21 22] Abnormal sacroiliac joint (SIJ) imaging is also demonstrated despite a high rate of normal examination; for example, normal SIJ examination in 42.9% and 22.9%, in patients with CR and MRI sacroiliitis, respectively.[23 24]

Muller et al[25] compared TMJ clinical examination and US with MRI changes, and found that examination correctly identified 58% patients with active MRI TMJ arthritis compared with 33% for US, and missed inflammation in 42% and 67%, respectively. They described reduced maximal incisal opening to be the best predictor of active MRI changes.[26] Full data comparing the various imaging modalities with clinical examination of the TMJ is given in the online supplementary text S9.

Prognosis
PTC 5: Imaging in JIA may be considered for use as a prognostic indicator. Damage on CR can be used for the prediction of further joint damage. Persistent inflammation on US or MRI may be predictive of subsequent joint damage.

Thirteen observational studies examined the relationship between baseline imaging and subsequent radiographic and clinical outcome; 11 with CR and 2 with MRI at baseline. The statement on US inflammation is therefore based on expert opinion; the findings are given in full in table 3. In general, CR damage in the 1st year has a moderate correlation with functional deterioration according to Steinbocker class, Childhood Health Assessment Questionnaire and physician/parent disability scores at 5 years, as well as with CR progression at 5 years.[27–29] A baseline CR wrist adapted Sharp van der Heijde score >1 was shown to be predictive of CR progression at 5 years (OR, 8.2), and patients with erosions and/or JSN in the first 6 months of the study spent more time with clinically active disease and were less likely to achieve clinical remission on medication.[30 31] Just one study described the correlation of baseline MRI wrist synovial volume with MRI erosive progression at 1 year; this found a moderate correlation, and all patients with high synovial volume at baseline had erosive progression.[32]

Monitoring inflammation
PTC 6: In JIA, US and MRI can be useful in monitoring disease activity given their sensitivity over clinical examination and good responsiveness. MRI should be considered for monitoring axial disease and TMJ.

Data comparing imaging with clinical examination in detecting joint inflammation is discussed in PTC 1, and specific information on imaging the TMJ and for axial involvement is summarised in PTC 4. This section will consider the comparison of the ability of imaging to detect inflammation, responsiveness of imaging to change in inflammation, and which joints should be assessed.

Comparison of the ability of imaging to detect inflammation
Several studies compared US with MRI in the detection of inflammation, particularly at the knee.[13 14 33 34] These studies have shown MRI to be better in detecting knee inflammation than US (mean detection rate 1.20-fold, range 0.63–1.56-fold) and in particular MRI was better than US in differentiating pannus from effusion.[13] Knee MRI with contrast enhancement was more reliable at localising and differentiating synovial hypertrophy from synovial fluid particularly when there was <5 mm of synovial hypertrophy, but the addition of contrast did not provide additional information in the assessment of inflammatory bone marrow lesions.[35–37] Comparison of power Doppler with grey-scale wrist US has resulted in conflicting results, whereas the use of contrast significantly increased knee US synovial pixel intensity in those with symptomatic disease (p=0.004) and asymptomatic disease (p=0.0001), but not in those in clinical remission.[38–40]

Studies comparing TMJ US with MRI have shown a poor correlation between these modalities, with US missing 67–75% of TMJ MRI inflammation.[25 41] The use of MRI contrast enhancement improved the detection of MRI TMJ inflammation from 35.7% to 86.7%.[42] One study examined the CR findings in patients with TMJ MRI synovitis and found significant correlation with abnormal condyle morphology and accentuated antegonial notching on CR, and joints with both of these changes

Table 3 Point to consider 5: Summary of included studies describing the prognostic value of the imaging modalities

Reference	No. of subjects	Duration of follow-up (months)	Radiological or clinical assessment	Outcome assessed	Correlation	
Baseline CR predictive factors						
Susic et al[120]	87	48	Wrist involvement	CHAQ-DI	Significant correlation p<0.01	
			Hip involvement		Significant correlation p<0.001	
			JADI-A		Significant correlation p<0.01	
Ravelli et al[29]	96	min. 60	CR wrist changes at: baseline in 1st year in 1st 5 years	No. of joints with LOM	Baseline: low r=0.16 1st year: low r=0.35 1st 5 years: moderate r=0.59	
				JADI-A	Baseline: low r=0.21 1st year: moderate r=0.53 1st 5 years: moderate r=0.60	
				Steinbocker functional class	Baseline: low r=0.21 1st year: moderate r=0.48 1st 5 years: moderate r=0.55	
				CR progression at 5 years	Baseline: low r=0.38 1st year: moderate r=0.61 1st 5 years: high r=0.89	
Pederzoli et al[30]	130	min. 60	CR wrist a SH score > 1	CR progression at 5 years	Significant predictor OR 8.2	
Magni-Manzoni et al[28]	94	54			Baseline Poznanski score	CR progression in 1st yr
			Baseline Poznanski score	Yearly CR progression	r=0.88 p=0.47	r=0.62, p<0.001 OR 14.32, p<0.0001
			CR wrist progression in 1st year	Final Poznanski score	r=0.58 p<0.0001	r=0.59, p<0.0001 OR 6.49, p=0.0006
				CHAQ	r=0.20 p=0.14	r=0.39, p=0.003 OR 8.42, p=0.002
Bertamino et al[27]	148	max. 132	CR hip progression in 1st year	CHAQ	r=0.24, p=0.1	
				SJC	r=0.03, p=0.86	
				TJC	r=0.06, p=0.65	
				No. of joints with LOM	r=0.46, p=0.0005	
				Steinbocker functional class	r=0.50, p=0.005	
				JADI-A	r=0.45, p=0.01	
				Physician disability score	r=0.40, p=0.05	
				Parent disability score	r=0.53, p=0.007	
Oen et al[121]	136	min. 60	Early (<2 years) erosions/JSN	CHAQ	No correlation	
Selvaag et al[122]	197	36	Baseline swelling/osteopenia	CR erosive progression	OR 7.95, p<0.001	
					Less patients with CR progression had CHAQ of 0, p=0.045	

Table 3 Continued

Reference	No. of subjects	Duration of follow-up (months)	Radiological or clinical assessment	Outcome assessed	Correlation
Ringold et al[31]	104	29.9	Early (<6 months) erosions/JSN vs normal	Time with active disease CRM	More time with active disease p<0.001 Less chance of CRM, RR=0.34, p<0.001
			RF +ve vs −ve		More time with active disease p=0.07
Oen et al[54]	88	Early (<2 years) Late (1–20.8 years)	Late vs early JSN	CHAQ	Significant correlation Explains 17.7% of variation in CHAQ
			Joint pain		Explains 32.4% of variation in CHAQ
Habib et al[123]	68	–	ACPA	CR erosions	Significant correlation p=0.004
Arvidsson et al[124]	103	324	Baseline/early TMJ involvement	Micrognathia	66.7% patients with micrognathia had baseline TMJ involvement; 33.3% had CR TMJ involvement within 2 years
Baseline MRI predictive factors					
Malattia et al[32]	58	12	Baseline wrist synovial volume	MRI erosive progression	Correlation r=0.42 p<0.02 All patients with high synovial volume had erosive progression
			Baseline CRP		Correlation r=0.40 p<0.02
Gardner-Medwin et al[125]	10	12	Baseline synovial hypertrophy in a clinically normal joint	Disease extension from monoarthritis	100% patients developed clinical arthritis in other joints

ACPA, anticyclic citrullinated peptide antibody; aSH, adapted Sharp van der Heijde score; CHAQ-DI, Childhood Health Assessment Questionnaire disability index; CR, conventional radiography; CRM, clinical remission on medication; CRP, C reactive protein; JADI-A, Juvenile Arthritis Damage Index for articular damage; JSN, joint space narrowing; LOM, limitation of movement; RF, rheumatoid factor; +ve, positive; −ve, negative; RR, relative risk; SJC, swollen joint count; TJC, tender joint count; TMJ, temporomandibular joint.

on CR were 7.5 times more likely to have MRI synovitis (OR 7.55, 95% CI 1.66 to 34.4, p=0.009).[43]

Responsiveness of imaging to change in inflammation

US and MRI have been shown to have good responsiveness to change in inflammation, as measured by standardised response means (SRM, ≥0.20 small change, ≥0.50 moderate, ≥0.80 good). The mean (range) SRM for MRI wrist synovitis was good at 1.27 (0.51 to 1.69) and demonstrated ability to discriminate between different levels of clinical responder categories, whereas the SRM for MRI wrist bone marrow oedema was small at 0.22.[19 32 44] Similar levels of SRM have been described for MRI knee synovial hypertrophy (0.68–0.70) and bone marrow oedema (0.15).[45 46] A comparison of MRI wrist synovitis score with US showed higher MRI responsiveness (1.61) when compared with US grey-scale (0.87) and US power Doppler (0.71).[47]

Which joints to assess

Studies describing the frequency of US joint inflammation in JIA have shown these changes to be most common in the knee (~30%) and wrist (~20%), then ankle, proximal interphalangeal joint and metatarsophalangeal joint (~10% each).[48 49] US power Doppler activity was most common in the wrist (~35%).[48 49] One study examined the frequency of US peripheral synovitis and found changes more commonly in the metatarsophalangeal joint (61.9%) than in the metacarpophalangeal joint (39%), with the first metatarsophalangeal joint and second metacarpophalangeal joint most frequently affected (20% and 13%, respectively).[50]

Monitoring damage

PTC 7: The periodic evaluation of joint damage should be considered. The imaging modality used may be joint dependent.

As for PTC 6, this section will consider the comparison of the ability of imaging to detect damage, responsiveness of imaging to change in damage, and which joints should be assessed. Data comparing imaging with clinical examination in detecting joint damage and comparing CR with MRI and US in detecting damage is discussed in part in PTC 3.

Comparison of the ability of imaging to detect damage

El-Miedany et al[14] examined the role of MRI, US and CR in the detection of knee JSN and described a 3.14-fold detection rate of MRI compared with US, 4.40-fold for MRI compared with CR and 1.4-fold for US compared with CR. The addition of contrast to MRI enhanced the appreciation of depth of cartilage involvement by 1.42-fold. Data describing the detection of wrist erosive changes have shown a detection rate for MRI compared with US of 1.92-fold, MRI compared with CR of 1.36-fold and US compared with CR of 1.0-fold.[17–19 40]

In terms of detecting damage of the TMJ, Muller et al[25] showed that MRI condylar damage was detected in 25% of their cohort, whereas US detected only 17% (1.47-fold). Weiss et al[41] also described a poor correlation between these modalities, with only 50% agreement (detection rate 2.44-fold).

Responsiveness of imaging to change in damage

Several studies examined the responsiveness of imaging to detect change in damage at the wrist, particularly with CR and MRI. The rate of change in CR score (Larsen, Sharp, Poznanski) appears to be greatest in the 1st year, which is mainly due to progression in JSN.[28 51] This seems to slow after the 1st year, whereas the rate of erosive change is steady from baseline to

year 3; the rate of progression overall slows after 3rd third year. In general, the rate of JSN exceeds that of erosions and total score.[29] When compared with CR, Malattia et al[44] described the relative efficacy of MRI compared with CR erosion score to be <1 at year 1; that is, MRI was less responsive than CR in detecting erosive progression; the fact that cartilage assessment was not included in the MRI scoring systems might explain this result. A study of TMJ condylar changes showed that MRI identified significantly more changes than CR (p≤0.003), and MRI was superior to CR in following condylar changes over time: MRI condylar changes at baseline were found in 58.6% compared with 80% at year 2; CR condylar changes were stable at baseline and year 2 at 30%.[52]

Which joints to assess

Studies describing the distribution of CR changes in 'early' (within 2 years of disease onset) and 'late' (up to 20.8 years of follow-up) disease have shown JSN to be most common in early disease in the wrist (20%), hips (16%), cervical spine (5%), ankles (4%) and knees (3%) compared with 34%, 25%, 38%, 15% and 6%, respectively in late disease.[53 54] Rostom et al[55] observed CR hip disease to start after 4 years of disease, whereas 80% had developed hip disease at 6 years, and 100% after 14 years. Other studies describing radiological features of JIA found most CR changes in the hands (57%), knees (47%), ankles (27%) and feet (36%), with erosions mainly in hands (18%) and feet (25%).[56] The hands and feet were the area most likely to show CR damage progression at 6 months and 5 years.[57 58]

Guided treatment

PTC 8: US can be used for accurate placement of intra-articular injections.

Studies summarising the role of imaging for guiding intra-articular steroid injections are given in online supplementary text S10, along with additional data on the use of imaging to assess and monitor efficacy of steroid injections. All studies used triamcinolone injections; doses and preparations varied according to the age of the patient and the joint being injected. Young et al[59] used US to assess the accuracy of needle placement for steroid injections at various sites (joints and tendon sheaths), and described that US allowed accurate visualisation of the injection point in all 1444 injections. A study by Parra et al[60] used CT to establish if US-guided TMJ injections had been accurately placed; needle placement was shown to be acceptable in 91% (75% required no needle adjustment, 16% required minor adjustment) and unacceptable in 9% where the needle required major readjustment. A study of the efficacy of TMJ injections used MRI to assess needle placement accuracy according to the location (intra-articular or extra-articular) of the injected material on MRI acquired after injection; MRI confirmed that 65% of injections were accurately placed.[61] A similar study using postinjection MRI of the SIJ described technical success in 100%.[62]

Remission

PTC 9: US and MRI can detect inflammation when clinically inactive disease is present; this may have implications for monitoring.

Several studies addressed the discrepancy between clinical remission and inflammation seen on US and MRI; these are summarised in the online supplementary text S11. Evidence of ongoing US synovitis has been described in 56.1–94.1% of patients with clinically inactive joints, and 32% of patients with

inactive disease showed US signs of synovial hypertrophy, effusion and power Doppler activity.[63–65] In clinical remission, US grey-scale synovitis was seen in up to 84.1% of joints, and power Doppler activity in up to 48.6% of joints, with a non-significant trend to more US inflammation in clinical remission on medication compared with clinical remission off medication.[39 66–71] MRI knee inflammation has been demonstrated in up to 50% of patients in clinical remission and bone marrow oedema in 33.3% patients with clinically inactive joints.[72–74] Recent pilot studies have demonstrated that patients with subclinical US or MRI inflammation are more likely to develop active disease and disease progression, even within 6 months of follow-up.[64 70 74 75]

Research agenda

The group formulated a research agenda based on areas identified with a lack of currently available evidence, shown in box 1.

DISCUSSION

These EULAR-PReS considerations for imaging provide important and novel advice for JIA in clinical practice. There is still significant research needed in this field, in particular consensus on understanding normative data to allow the interpretation of imaging abnormalities, agreement on appropriate MRI protocols and definitions of bone marrow oedema, synovitis and erosions, and suitability of the imaging modalities for detecting changes at specific joints. Our data is limited by the lack of specific information for each JIA disease subtype; this is reflected in the research agenda.

There are significant conceptual differences between imaging in adult and paediatric conditions, and consideration must be given to the appropriateness and feasibility of different imaging modalities which differs with age and developmental stage, as well as to economic issues such as the cost-effectiveness of the

intervention. Repeated unnecessary exposure to radiation from imaging should also be considered. We appreciate that access to individual imaging modalities may be insufficient to allow full implementation of these PTC; however most of the points include the use of US which is generally readily available. An economic evaluation was not included in the process as the primary aim was to discuss the clinical implications of imaging; overall the cost of implementing the PTC should be low.

After dissemination of the PTC by means of publication and presentation at European meetings, we would propose to perform a survey of awareness and their use, for example:

▶ Do you have access to musculoskeletal US and MRI routinely?
▶ Are you aware of and implementing the EULAR-PReS JIA imaging PTC?
▶ Have the PTC changed your clinical practice?

The task force agreed that it was not appropriate to create audit or implementation tools as the strength of data was only sufficient to develop PTC rather than recommendations.

In summary, we have developed nine PTC on the role of imaging in various clinical aspects in JIA. We would recommend that a similar rigorous process is followed to reassess the available data after an interval of 5 years.

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Box 1 Research agenda

1. What are the age-specific changes in imaging, including age-specific intervals for imaging, development of an atlas of age-specific normal images and a registry as mechanism for pooling of data
2. Development of validated scoring systems including pathology definition (eg, differentiating reversible structural abnormalities from damage), imaging acquisition protocols and quantification
3. What are the imaging characteristics of the subtypes of JIA, and which target sites should be imaged?
4. What is the clinical significance of imaging-detected subclinical disease in diagnosis, monitoring and remission?
5. What is the usefulness of imaging-guided injection over non-imaging guided injection?
6. What is the prognostic value of specific imaging features, for example BM oedema?
7. Can imaging be used to assess and monitor disease progression and response to treatment including the development of structural damage?
8. What is the feasibility, cost and appropriate training for using US and MRI in JIA in clinical practice?

JIA, juvenile idiopathic arthritis; BM, bone marrow; US, ultrasound.

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