

Assessment of disease activity and carpal erosions by MRI of the wrist in children with juvenile idiopathic arthritis

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Abstract

Résumé

L'IRM est un outil important pour évaluer l'activité et la progression structurale chez les patients atteints d'arthrite juvénile idiopathique (AJI). L'évaluation des érosions au poignet est difficile étant donné la présence de variations normales chez les enfants sains.

Objectifs : comparer les dépressions osseuses chez les patients atteints d'AJI et les différencier chez les enfants sains et valider le score RAMRIS d'érosions, de synovite et d'œdème osseux dans l'AJI.

Méthodes : L'IRM du poignet a été réalisée chez des enfants sains et atteints d'AJI âgés de 5 à 18 ans. Nous avons évalué le nombre de dépressions osseuses dans les os du carpe en utilisant des séquences coronales T1 et T2 saturées de graisse.

Résultats : Au total, 13 patients atteints d'AJI ont été inclus et 22 enfants sains. Le nombre de dépressions osseuses était significativement plus élevé dans le groupe AJI par rapport aux enfants en bonne santé dans les deux groupes d'âge ; pour la tranche d'âge 5-9 ans $6,55 \pm 2,25$ (n = 7) de dépressions osseuses ont été retrouvées dans le groupe AJI versus $2,15 \pm 1,12$ (n = 10) dans le groupe témoin (p = 0,03) ; dans le groupe des 10-18 ans, le nombre de dépressions osseuses dans le groupe AJI et le groupe des enfants sains était respectivement de $9,08 \pm 4,36$ (n=6) et $5,35 \pm 2,06$ (n = 12) (p = 0,02).

Conclusion : L'IRM du poignet représente une méthode prometteuse pour évaluer l'activité de la maladie dans l'AJI, en particulier chez les patients atteints d'arthrite du poignet et pour différencier les érosions des variations normales. Notre étude suggère que les érosions osseuses sur l'IRM du poignet sont plus fréquentes dans l'AJI contrairement aux enfants en bonne santé, et la synovite sur l'IRM est fortement corrélée avec l'activité de la maladie et l'impact fonctionnel.

Mots-clés : Variante normale. Enfants en bonne santé. Poignet. AJI. Érosion. IRM

الملخص

يعد التصوير بالرنين المغناطيسي أداة مهمة لتقييم النشاط والتقدم الهيكلي بالنسبة لمرضى التهاب المفاصل المجهول السبب لدى الأطفال (AJI). و يصعب تقييم التآكل على مستوى المعصم نظرًا لوجود اختلافات طبيعية لدى الأطفال الأصحاء.

الأهداف: مقارنة الانخفاضات العظمية لدى الأطفال المصابين بالتهاب المفاصل المجهول السبب وتمييزها لدى الأطفال الأصحاء والتحقق من معدل "رامريس" للتآكل و التهاب الغشاء المفصلي و وذمة العظام لدى هؤلاء الأطفال.

الطريقة: تم إجراء التصوير بالرنين المغناطيسي للمعصم بالنسبة للأطفال الأصحاء و كذا الأطفال المصابين بالتهاب المفاصل المجهول السبب والذين تتراوح أعمارهم بين 5 سنوات و 18 سنة. بحيث قمنا بتقييم عدد الانخفاضات العظمية على مستوى المعصم باستخدام متواليات T2 الاكليلية و T2 المشبعة بالدهون.

النتائج: تم تضمين مجموعة مكونة من 13 طفل مصاب بالتهاب المفاصل المجهول السبب و مجموعة ثانية تضم 22 طفلًا من الأصحاء. بحيث كان عدد الانخفاضات العظمية أعلى بشكل ملحوظ في مجموعة AJI مقارنة بمجموعة الأطفال الأصحاء في كلتا الفئتين العمريتين. بالنسبة للفئة العمرية التي تتراوح ما بين 5 و 9 سنوات، تم العثور على معدل 6.55 ± 2.25 ($n = 7$) من الانخفاضات العظمية في مجموعة AJI مقابل 1.12 ± 2.15 ($n = 10$) في المجموعة الضابطة ($p = 0.03$)؛ و في المجموعة التي تتراوح أعمارها بين 10 و 18 سنة، كان عدد الانخفاضات العظمية في مجموعة AJI ومجموعة الأطفال الأصحاء 9.08 ± 4.36 ($n = 6$) و 5.35 ± 2.06 ($n = 12$) ($p = 0.02$) على التوالي.

الخلاصة: يمثل التصوير بالرنين المغناطيسي على مستوى المعصم طريقة واعدة لتقييم نشاط مرض التهاب المفاصل المجهول السبب عند الأطفال خاصة بالنسبة للمرضى الذين يعانون من التهاب مفاصل المعصم والتميز بين التآكلات العظمية والتغيرات الطبيعية. و تشير دراستنا إلى أنه من خلال التصوير بالرنين المغناطيسي للمعصم فإن التآكلات العظمية جد شائعة عند الأطفال المصابين بالتهاب المفاصل المجهول السبب على عكس الأطفال الأصحاء ، وأن التهاب الغشاء المفصلي في التصوير بالرنين المغناطيسي يرتبط ارتباطًا وثيقًا بنشاط المرض والتأثير الوظيفي.

الكلمات الرئيسية: متغير عادي. أطفال أصحاء. معصم. AJI. تآكل. التصوير بالرنين المغناطيسي.

Abstract

MRI is an important tool for assessing activity and structural progression in patients with juvenile idiopathic arthritis (JIA). Assessment of erosions on the wrist is difficult given the presence of normal variations in healthy children.

Objectives: to compare bone depressions in JIA patients and differentiate them in healthy children and to validate the RAMRIS erosions, synovitis and bone edema score in JIA.

Methods: MRI of the wrist was performed in healthy children and those with JIA aged between 5 and 18 years. We evaluated the number of bone depressions in the carpal bones using coronal T1 and fat-saturated T2 sequences.

Results: A total of 13 patients with JIA were included and 22 healthy children. The number of bone depressions was significantly higher in the JIA group compared with healthy children in both age groups; for the age group 5-9 years 6.55 ± 2.25 (n = 7) of bone depressions were found in the JIA group versus 2.15 ± 1.12 (n = 10) in the control group (p = 0,03); in the group aged 10-18 years the number of bone depressions in the JIA group and the healthy children group were respectively 9.08 ± 4.36 (n=6) and 5.35 ± 2.06 (n = 12) (p = 0.02).

Conclusion: Wrist MRI represents a promising method for evaluating disease activity in JIA especially in patients with wrist arthritis and differentiating erosions from normal variations. Our study suggests that bone erosions on MRI of the wrist are more common in JIA unlike healthy children, and synovitis on MRI is highly correlated with disease activity and functional impact.

Keywords : Normal variant. Healthy children. Wrist. JIA. Erosion. MRI

Assessment of disease activity and carpal erosions by MRI of the wrist in children with juvenile idiopathic arthritis

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Background

Background :

Juvenile Idiopathic arthritis (JIA) is a heterogeneous group of chronic inflammatory rheumatism in childhood, of unknown origin. It is characterized by chronic synovial inflammation with a potential risk of destruction, joint damage and functional disability [1, 2, 3].

The appearance of erosions at the beginning of the disease is a factor of poor long-term prognosis since it is associated with a higher risk of progression of the disease [4, 5]. The wrist proved to be the most informative joint for detecting erosions with standard radiography, but the sensitivity for early disease is low [6,7,8,9].

Several studies have shown that *Magnetic Resonance Imaging* (MRI) has a greater sensitivity than conventional radiography especially for disease in early stages to detect bone erosions, and can be used as a strong tool imaging to visualize synovitis and bone edema as well as the assessment of bone and cartilage damage [6,10, 11].

The child's growing skeleton may have different appearances on MRI. In fact, numerous studies have shown that bone depressions on the wrist can resemble bone erosions and constitute a normal variation than a true disease in children [2,9].

The aim of our study was to compare bone depressions in JIA patients them in healthy children and to validate the RAMRIS erosions, synovitis and bone edema score in JIA.

Methods

Methods:

In the juvenile idiopathic arthritis population, we included children aged between 5 and 18 years with clinically active wrist involvement. The exclusion criteria was any general contraindication to MRI. The control group contains healthy children matched for age and sex and excluded from any history of cancer, musculoskeletal disorders, metabolic disorders, current infection, or recent wrist trauma. Both groups were asked to perform an MRI of the wrist after having the informed consent of their parents. Sociodemographic data, clinical and biological characteristics relating to JIA were collected.

The duration of the study between August 2017 and April 2018. MRI was performed without sedation. The MRI images were read by an expert rheumatologist in dedicated wrist MRI and with experience in juvenile idiopathic arthritis. Coronal and axial T1 Spine echo 3D sections were made before and after gadolinium with a thickness of 0,3 mm sections, coronal and axial STIR sections (Figure 1). Three elements were analyzed according to the RAMRIS scales [12]: erosions (range 0–10), bone edema (range 0-3) and synovitis severity (range 0-3) (Figures 2 & 3). We evaluated the number and aspect of bony depressions, focal or tubular depressions or is it a normal vascular depression

Statistics:

The children were grouped into two age groups because of the small sample size and the large interindividual variations in the number of bone depressions: group 1 (5 to 9 years), group 2 (10 to 18 years), in order to compare the number of bone depressions by age group between children with JIA and children in good health with the help of an independent t test. Statistical analysis was performed using SPSS 25 software. $P < 0.05$ was considered statistically significant.



Figure 1: **A**, Coronal gradient echo sequence 3-dimensional T1-weighted magnetic resonance image of the carpus in a patient with juvenile idiopathic arthritis. **B**, The bone erosion visible in the lunate in the coronal plane is confirmed on both axial and sagittal planes in the multiplanar reconstruction [6].

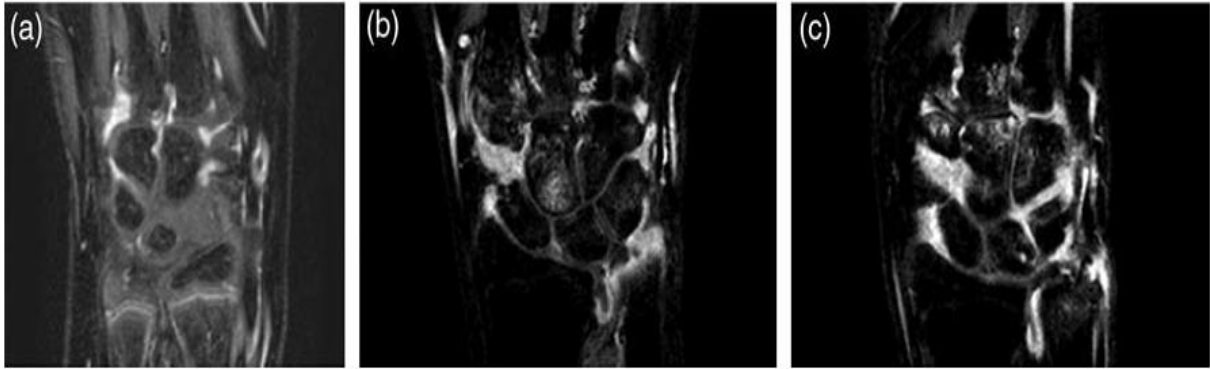


Figure 2: Wrist MRI in a 13-year-old JIA patient. Examples of radio-ulnar synovitis enhancement score 0 (panel a), score 1 (panel b), and score 2 (panel c) [13].



Figure 3: Wrist MRI in a 13-year-old girl with JIA. Examples of signal suggestive of diffuse BMO in most of the carpal bones as evident in coronal 3D T1-weighted turbo spin-echo sequence (a), coronal fat-saturated T2-weighted turbo spin-echo (b) and coronal, contrast-enhanced fat-saturated T1-weighted 3D gradient-echo (c) [13].

Results

Results:

A total of 13 patients with juvenile idiopathic arthritis were included (7 girls) and 22 healthy children (15 girls). The characteristics of the two cohorts are described in Table 1.

The number of bone depressions was significantly greater in the JIA group compared with healthy children in both age groups. For the age group 5-9 years 6.55 ± 2.25 (n = 7) of bone depressions were found in the JIA group versus 2.15 ± 1.12 (n = 10) in the control group with $P = 0,03$. In the group aged 10-18 years the number of bone depressions in the AJI group and the healthy children group were 9.08 ± 4.36 (n=6) and 5.35 ± 2.06 (n = 12) with $p = 0.02$ (Table 2).

Table 1: Sociodemographic and Clinical Characteristics of the Study Population

	JIA group n = 13	Healthy children group n = 22
Age (years) ¹	8,3±2,8	9,4±3,2
Female sex ²	7(60)	15(68)
AI ³	4(2-12)	-
SI ³	2(1-8)	-
Sedimentation rate ¹ (mm/1st hour)	15±5	-
VAS doctor ³	45(30-80)	-

JIA sub-group		
- Systemic	5	-
- Polyarticular	3	-
- Oligoarticular	3	-
- Arthritis and enthesitis	2	-

VAS = visual analogue scale; AI = articular index; SI= synovial index

1: Mean and standard deviation, 2: Number and percentage, 3: average and minimum – maximum

Table 2: Number of bone depressions assessed by MRI according to RAMRIS erosions in JIA and healthy children

	JIA	Healthy children	p
5-9 years-old	(n=7) 6,55±2,25	(N=10) 2,15±1,12	0,03
10-16 years-old	(n=6) 9,08±4,36	(n=12) 5,35±2,06	0,02

Spearman correlation was established between RAMRIS synovitis, erosion, and bone edema and with the clinic-biological characteristics of children with juvenile idiopathic arthritis (JIA). The good correlation found was between RAMRIS synovitis and clinic-biological characteristics: 0.41 ($p = 0.001$) for the articular index, 0.35 ($p = 0.03$) for the synovial index and 0.20 ($p = 0.02$) for the sedimentation rate; however, there was no correlation between RAMRIS bone edema and erosion RAMRIS with joint index, synovial index, physician's global visual analog scale (physician's GVAS), CHAQ and VS (table 3).

Table 3: Spearman correlation between RAMRIS synovitis, erosion, and bone edema with clinico-biological features of JIA

	RAMRIS synovitis	RAMRIS Bone edema	RAMRIS erosion
AI	0,41(p=0,001)	0,10(p=0,15)	0,15(p=0,25)
SI	0,35(p=0,003)	0,04(p=0,75)	0,24(p=0,09)
Physician's VAS	0,45(p=0,001)	0,16(p=0,21)	0,13(p=0,25)
CHAQ	0,32(p=0,02)	0,09(p=0,49)	0,10(p=0,15)
Sedimentation rate	0,20(p=0,02)	0,06(p=0,61)	0,09(p=0,31)

VAS = visual analogue scale; AI = articular index; SI= synovial index

Discussion

Discussion:

In children with JIA, signs of early bone destruction are difficult to assess and to differentiate from normal bone depressions using MRI sequences and OMERACT erosion definition [14]. In our study we compared the MRI results of the wrist of healthy children and those with juvenile idiopathic arthritis, and we found that bone depression at the level of the carp also exists in healthy children but the number of erosions was greater in the JIA group.

In the literature, some studies have evaluated the wrist by MRI in healthy adult patients showing the presence of change resembling bone erosions and mild synovitis in a number of healthy subjects controlled [15,16].

Muller LS et al [2] have mentioned in their study a high prevalence of MRI findings of bone edema, volume of joint fluid and erosions-like bone changes in carpal bones in a cohort of healthy children hence the need to interpret these results with caution in children with suspected juvenile idiopathic arthritis.

Regarding the correlation between the RAMRIS score and clinical-biological characteristics, Malattia C et al [17] found in their study that the RAMRIS erosion score was not correlated with measures of disease activity, however it was significantly correlated with radiographic damage and clinical indicators of damage such as JADAS. RAMRIS synovitis score was significantly higher in JIA with a higher wrist swelling score ($p < 0.0001$) and it was moderately correlated with clinical features of disease activity such as JADAS-71, the physician's global assessment and total number of swollen joints [17].

In our study, we found a statistically significant correlation between RAMRIS synovitis and the articular index and the synovial index and it was moderately significant for the sedimentation rate. However, there was no correlation

between RAMRIS bone edema and RAMRIS erosion and the clinico-biological features.

OMERACT RAMRIS defines bone erosion on MRI as focal bone loss in both planes with rupture of cortical in at least one plane. Boavida P et al [18] proposed to use another definition for erosion: pathological bone depression is associated with other MRI abnormalities including synovial enhancement, effusion and / or loss of joint space in standard radiography. They adopted this definition because they think that the definition of OMERACT should be revised especially to analyze the wrist MRI in children. Furthermore, the definitions of the OMERACT-RAMRIS criteria do not take into account the shape of the bone depression [14]. Boavida P et al [18] proposed that a tubular depression would be more likely to be interpreted as a vascular canal. A number of studies showed that some bony indentations resemble erosions are normal findings in the child's carp and they occur at typical locations especially at the level of the metacarpal bases and the intermetacarpal ligaments [19,20]. Ording Muller LS et al [14] had another perception that in cases of JIA, erosions can be developed at the level of these normal irregular surfaces creating larger bone depressions than those observed in healthy children.

Avenarius DFM et al [9] found that the majority of carpal depressions in a group of healthy children are stagnant and that new depressions appear with maturation of skelet, and they observed that 40% of bone depressions in the wrists of healthy children between the ages of 10 and 19 year-olds were covered with articular cartilage, while those not covered were located at or near the vascular canals or ligament attachments.

The supplementary irregularities of the bone surface, observed on the T1 sequence of the MRI, come from normal but irregular maturation of endochondral bone, which explains a peak in the number of bone depressions

in diverse carpal bones, especially the trapezium, the trapezoid, the scaphoid and the capitatum, just before bone maturation [9]. Older children in the Avenarius DFM et al [9] cohort had numerous bone depressions during follow-up and therefore the adult skeleton could also exhibit these characteristics.

Cartilage imaging may be essential and usable to distinguish between normal bone depression and true carpal erosion especially when they occur on the joint surface, where erosions are seen frequently in JIA [14,21,22]. The cartilaginous surface at the level of the proximal metacarpals could have a role in the diagnosis of true erosions only in the youngest children, because the cartilaginous covering is rarely observed in this area in children of advanced age [9], hence other studies are necessary in order to compare the cartilage coverage between healthy children and children with JIA. In our study, we found that in the group of healthy children, the surface irregularities did not cover the entire circumference of the carpal bone; we also noted that the maximum number of bone depressions was found in the group of children with juvenile idiopathic arthritis especially on the articular surface of the carpometacarpal joints and therefore these depressions are more likely to constitute real erosions. The correlation between RAMRIS synovitis score and clinico-biological measures is encouraging for assessing disease activity in JIA.

The limits of our study concern the small sample since it is a monocentric study, and secondarily the age difference of the 2 groups and this was minimized by dividing the subjects into two age groups for comparison. This study has strong points; it is the first study in our context which assesses erosions on MRI in JIA by a case-control study.

Conclusion:

MRI of the wrist of children is difficult to interpret because bone depressions, which are seen in healthy subjects, are a normal variant and should not be considered as signs of pathology of juvenile idiopathic arthritis.

Our study suggests that the number of erosions in children with JIA is greater than the group of healthy children and that the RAMRIS synovitis score is correlated with clinical and biological parameters of disease activity. Further large-scale studies are needed to confirm these results.

List of abbreviations :

JIA : juvenile idiopathic arthritis

MRI : *Magnetic Resonance Imaging*

VAS = visual analogue scale

AI = articular index

SI= synovial index

Declarations :

- Ethics approval and consent to participate: The parental consent was obtained.
- Consent for publication : all of the authors was invoved in this study and have given their consent for the publication.
- Availability of data and materials : All data generated or analyzed during this study are included in this article
- Competing interests : The authors declare that they have no competing interests
- Funding : Not applicable
- Authors' contributions : We declare that we participated at the study as following:

ME performed the statistical analysis and interpretation, and prepared the manuscript. SR performed and interpreted MRIs of patient, reviewed and interpreted the statistical analysis and participated in the critical review of the manuscript. All authors read and approved the final manuscript.

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