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ASSESSMENT OF DISEASE ACTIVITY AND CARPAL EROSIONS BY MRI OF THE WRIST IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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ABSTRACT – ***Objective:*** 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. We aimed 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.

Patients and 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 *vs.* 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).

Conclusions: 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.

INTRODUCTION

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 [1-3].

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 [6-9]. 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 and differentiate them in healthy children and to validate the RAMRIS erosions, synovitis and bone edema score in JIA.

PATIENTS AND METHODS

In the juvenile idiopathic arthritis population, we included children aged between 5 and 18 years with clinically active wrist involvement. The exclusion criteria were 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 was from August 2017 to 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. 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). We evaluated the number and aspect of bony depressions, focal or tubular depressions or is it a normal vascular depression.

STATISTICAL ANALYSIS

Statistical analysis was performed using SPSS 25 software (SPSS Inc., Armonk, NY, USA). $p<0.05$ was considered statistically significant. 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.

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.

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.

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 *vs.* 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 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 analogue 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)

Legend: VAS = visual analogue scale; AI = articular index; SI= synovial index.

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 [13]. 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 [14,15]. Müller 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 et al [16] found 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 [16]. 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 et al [17] 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 [13]. Boavida et al [17] 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 [18,19]. Ording Muller et al [13] 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 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 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 [13,20,21]. 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, which was minimized by dividing the subjects into two age groups for comparison. This study has strong points since it is the first study in our context which assesses erosions on MRI in JIA by a case-control study.

CONCLUSIONS

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.

Consent to participate and Ethics approval:
The parental consent was obtained, the approval of the Ethics Committee was not applicable.

Consent for publication:
All of the authors were involved in this study and gave their consent for the publication.

Availability of data and materials:
All data generated or analyzed during this study are included in this published article.

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The authors declare that they have no competing interests.

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Authors' contributions:
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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