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Preliminary Definitions for Sacroiliac Joint Pathologies in the OMERACT Juvenile Idiopathic Arthritis MRI Score (OMERACT JAMRIS-SIJ).

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TITLE PAGE

Preliminary Definitions for Sacroiliac Joint Pathologies in the OMERACT Juvenile Idiopathic Arthritis MRI Score (OMERACT JAMRIS-SIJ).

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Abstract

Objective: To develop definitions for the assessment of MRI pathologies of the sacroiliac joints (SIJ) in juvenile idiopathic arthritis (JIA).

Methods: An OMERACT consensus-driven methodology consisting of iterative surveys and focus group meetings within an international group of rheumatologists and radiologists.

Results: Two domains, inflammation and structural, were identified. Definitions for bone marrow edema, joint space inflammation, capsulitis and enthesitis were derived for joint inflammation; sclerosis, erosion, fatty lesion and ankylosis were defined for assessing structural joint changes.

Conclusion: Preliminary consensus-driven definitions for inflammation and structural elements have been derived, underpinning the ongoing development of the JAMRIS-SIJ score.

INTRODUCTION

Juvenile idiopathic arthritis (JIA) is a chronic inflammatory disease that affects joint function, resulting in significant effects on quality of life by limiting physical and psychosocial integration ¹. JIA has an estimated worldwide prevalence of 0.07 to 4.01 cases and an incidence rate of 0.008 to 0.226 cases per 1000 children per year respectively, highlighting the global disease burden and the need for new clinical trials for JIA management ².

Magnetic Resonance Imaging (MRI) has been reported to be sensitive in detecting early inflammatory changes in the sacroiliac joints (SIJ) in JIA long before radiography, thus allowing for intervention before the onset of irreversible joint damage ³. Clinical assessment of the SIJ is limited by its location and anatomy ⁴. The quantification of interval change of pediatric SIJs using an MRI-based scoring method may serve as an important objective outcome measure ⁵. New JIA clinical core set recently endorsed at the OMERACT 2018 conference includes joint inflammation and damage domains as variables in the middle circle, recommending these as important measurement domains in JIA clinical trials. Improving these outcome measures calls for an international, multidisciplinary

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effort towards development and validation of a suitable and specific measurement instruments to quantify disease and assess treatment effects in JIA. A recent systematic review by Swami et al., 2018 (in press) of existing MRI-based SIJ scoring systems reported the lack of established MRI instruments for assessment of SIJ in the pediatric population. Conversely, SIJ MRI scoring systems are well developed and validated in adults⁶⁻⁹. Current attempts to extrapolate adult SIJ MRI scoring systems into the pediatric group reported significant feasibility and reliability but the construct validity remains a limitation, although clinical assessment of disease activity and damage also remains problematic in the pediatric population^{10,11}. Given the lack of standards for normality and pathology in growing SIJ, there is an urgent need for the development and validation of a pediatric-specific MRI scoring system for SIJ⁵. We used the Outcome Measures in Rheumatology (OMERACT) consensus-driven methodology for iteratively developing definitions as a prelude to the development of an MRI-based scoring system for the assessment of SIJ in JIA, and as a first step we aimed to decide on the main domains and elementary pathology definitions of the MRI-based scoring system.

METHODS

CONCEPTUAL FRAMEWORK OF THE OMERACT JAMRIS-SIJ

The OMERACT JAMRI Working Group developed the JAMRIS-SIJ as an outcome measure for the quantification of interval changes in the SIJ of children and adolescents with JIA in effectiveness trials. The components of this newly developed scoring system should identify and define the measured construct, and they need not correlate with each other. Thus the conceptual framework of the construct and measurement components are in keeping with a formative model¹². This model together with OMERACT Filter 2.0^{13, 14} shall guide the instrument's validation framework and specify the use and interpretation of the JAMRIS-SIJ in the context of other concurrently used outcome measures in clinical trials.

MEASUREMENT DOMAINS OF THE OMERACT JAMRIS-SIJ

After Working Group discussion and review of the existing literature, joint inflammation and structural change were selected as they measured/evaluated separate measurement constructs for the assessment of active and chronic SIJ disease in JIA. This separation is in keeping with known pathophysiology and disease history and follows from the domains in adult SIJ and other inflammatory

arthritis scoring system that have shown to be valid and feasible in the adult population^{6,7}.

DEVELOPING DEFINITIONS

An anonymous survey (Appendix 2) containing multiple choice, dichotomous and open-ended questions was developed to select constructs, component definitions, MRI data acquisition protocol and scoring method of an ideal pediatric SIJ MRI scoring system. The survey questions and component definitions were developed based on published adult SIJ MRI scoring systems^{7,8}.

Respondents provided suggestions to enrich the components and component definitions template, applying relevant content expertise¹⁵.

The survey response was analyzed and presented to the OMERACT JAMRI special interest group meeting during the Radiological Society of North America (RSNA) scientific conference in November 2017 in Chicago, IL, U.S.A. for refinement of definitions and consensus upon final definitions. In May 2018, the preliminary JAMRIS-SIJ was presented to a broader group of experts at the OMERACT meeting in Terrigal, Australia for additional input. As well, a Steering Committee constituted of members from the adult SIJ study group was formed to align pediatric definitions with existing definitions for the adult OMERACT SIJ MRI

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scale. After two iterations of video conferences held in August and September 2018, final deliberations and consensus of items and definitions of the JAMRIS-SIJ were reached. Each item definition was voted for agreement among the members of OMERACT JAMRI Working Group as summarized in table 1. A consensus was deemed to have been achieved if greater than 70% agreement was reached among voting attendees at the session in the absence of greater than 15% present or more in strong disagreement¹⁴. The final results were then presented to the entire OMERACT JAMRI SIJ working group for endorsement. A summary of the consensus framework is presented in appendix 1.

The study was approved by the Sickkids Research Ethics Board, REB Number 1000059077 and participation was voluntary with implied consent.

RESULTS

This study reported for the first time an all-inclusive definition of SIJ MRI lesion components without the use of contrast for acquisition of MRI sequences. This allows for the avoidance of unnecessary use of contrast in pediatric imaging due to concerns of potential brain accumulations, and nephrogenic systemic fibrosis¹⁶. Twenty-eight International multidisciplinary experts from North America (N=15), Europe (N=10) South Asia (N=2), and South America (N=1) participated in the

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study. The study group characteristics are summarized in appendix 2. The SickKids research ethics board approved the utilization of anonymized images for the surveys, and research agreements were made among collaborating centers. Participating experts voluntarily elected to collaborate in the study.

The consensus items and definitions of the OMERACT JAMRIS-SIJ are presented in table 1, with representative SIJ MRIs in Figure 1 and 2. Joint inflammation and structural changes are constructs defined separately on SIJ MRIs acquired using a dedicated acquisition protocol and defined according to the components. To reiterate the complexities and pitfalls of interpreting the growing/maturing SIJ, the group decided to include a statement of “overarching consideration” for all definitions and a caveat for the interpretation of bone marrow edema in Table 1. These contextual considerations will require pediatric-specific experience in image interpretation. The working group acknowledge that cartilage and bone marrow development are ongoing process in children resulting in changes that occur due to physiologic maturity unique to sex and age¹⁷⁻¹⁹. Transformation between hematopoietic and fatty marrow occur with advancing age, with early skeletal maturation in girls than boys^{18, 20}.

DISCUSSION

This study aimed at facilitating the development of a pediatric-specific MRI scoring system for measuring disease activity and structural joint changes in the SIJ of JIA. The study identified components that encompass both constructs, active joint inflammation and structural joint changes in JIA, through an iterative consensus process that allowed for both anonymized and in-person discussions and consensus quantification. The experts agreed that the preliminary JAMRIS-SIJ definitions have an acceptable face and content validity, allowing for a comprehensive measurement of the underlying construct¹³. Data-driven assessment of the lesion definitions is to follow.

However, as stated above, the aim of this process is to develop an outcome measure, not a diagnostic tool. The Working Group decided there is a need for defining an internal comparator to differentiate variations due to MRI acquisition and inter-subject variation. The sacral interforaminal area, the iliac crest, ischial pubic synchondrosis and triradiate cartilage can be used where available as normal reference for bone marrow signal¹⁰.

Notwithstanding consensus of the lesion definitions, there are areas of disagreement. The definition of erosion remains a contentious topic, as erosion

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may be solitary or in association with other lesions. Also, erosion changes in appearance as inflammation resolves (spontaneously and after treatment) and that linear fat metaplasia in the joint space (backfill) is a feature of post-inflammatory erosion⁶. Evaluation of SIJ MRI with several time points is needed when validating the definition.

An imaging atlas to accompany the definitions, age and sex related changes, and other common pitfalls will be developed by the expert group to improve the usability of the JAMRIS-SIJ. Such atlas should enable definition of thresholds between normality and abnormality of SIJ in the pediatric population. Further studies are required to define the minimum data acquisition protocol, measurement scale and methods for the preliminary OMERACT JAMRIS-SIJ.

CONCLUSION

We have reported the lesion component definitions for a preliminary pediatric MRI SIJ scoring system according to OMERACT standards – the OMERACT Juvenile Arthritis MRI SIJ scoring system (OMERACT JAMRIS – SIJ) – for the assessment of inflammatory and structural joint changes in JIA. The results of this consensus-driven methodologic and technical survey conducted among a multidisciplinary international expert group are the first step towards the development of the

OMERACT JAMRIS-SIJ scoring system. Further development is needed, including derivation of lesion scoring method and component score, determination of MRI data acquisition protocol, exercises to systematically evaluate reliability, responsiveness, and feasibility of the lesion definitions.

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Table 1. Consensus definitions of components of the Juvenile Arthritis Magnetic Resonance Image Sacroiliac Joint Scoring System (JAMRIS-SIJ)

Statement of Overarching consideration for all definition - "[...] *in comparison to physiological changes normally seen in MRIs of age and sex matched children, and visible in two planes where available"	
Caveat for Bone Marrow Edema- "[...] † compared to the signal intensity of the iliac crest, edges of the vertebrae, and triradiate cartilage where available".	
Feature	Definition
Inflammation MRI Components	
Bone Marrow Edema (BME)	An ill-defined area of high bone marrow signal intensity† within the subchondral bone in the ilium or sacrum on fluid sensitive sequences*
Joint Space Inflammation	Increased signal on fluid sensitive or contrast-enhanced T1 weighted images within the joint space of the cartilaginous portion of the SIJ*
Capsulitis	High signal on fluid sensitive and/or post-contrast enhancement involving the SIJ capsule*
Enthesitis	High signal in bone marrow and /or soft tissue on a fluid sensitive sequences or a contrast-enhanced T1 weighted sequence at sites where ligaments and tendons attach to a bone*
Structural MRI Components	
Sclerosis	A substantially wider than normal area of low subarticular bone signal on T1 weighted and fluid sensitive images (of ≥ 5mm in adolescents) *
Erosion	Bony defect (or irregularity with associated bone marrow edema, sclerosis, or fatty lesion) at the osteochondral interface involving both contour and signal on both T1 weighted and fluid sensitive images*
Fatty Lesion	Homogenous increased signal intensity on T1 weighted non-FS image in subchondral bone with a distinct border of the lesion*
Ankylosis	Presence of signal equivalent to regional bone marrow continuously bridging a portion of the joint space between the iliac and sacral bones*

Symbols: (*) Denotes the overarching consideration for each component definitions in the JAMRIS-SIJ.

“+”: Denotes the caveat for the definition of BME.

"[...]": Denotes the insertion of sentence that is denoted by the symbols "(*)" "(+)" in the definitions in Table 1.

Abbreviation: SIJ = Sacroiliac Joint, FS fat Suppressed

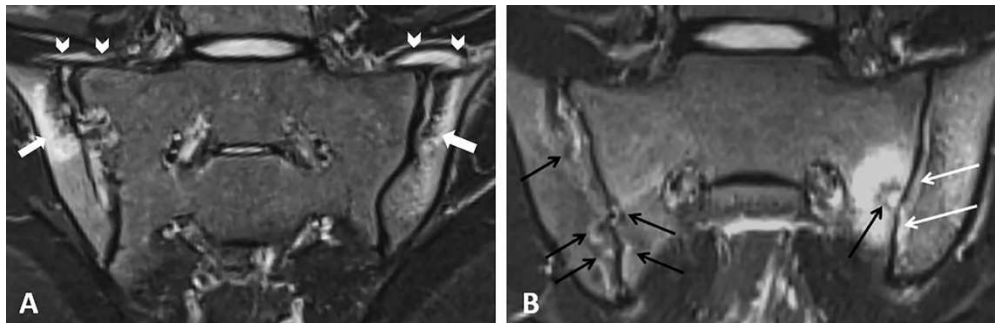


Figure-1: Coronal oblique T2-STIR MR images (A, B, through the sacroiliac Joints (SIJ) illustrating inflammatory components. A, SIJ in a 16-year-old girl with juvenile idiopathic arthritis (JIA) demonstrates bone marrow edema as subchondral marrow high signal intensity (arrows) along the iliac articular surfaces and capsulitis as a thickened and hyperintense antero-superior joint capsules (arrowheads), more prominent on the left side; B, SIJ in a 16-year-old boy with JIA shows joint space inflammation as an increased signal within the joint space of the cartilaginous portion of the left SI joint (white arrows) and erosion as a bony defect at the osteochondral interface (black arrows) bilaterally with increased marrow signal surrounding the left sided erosion.

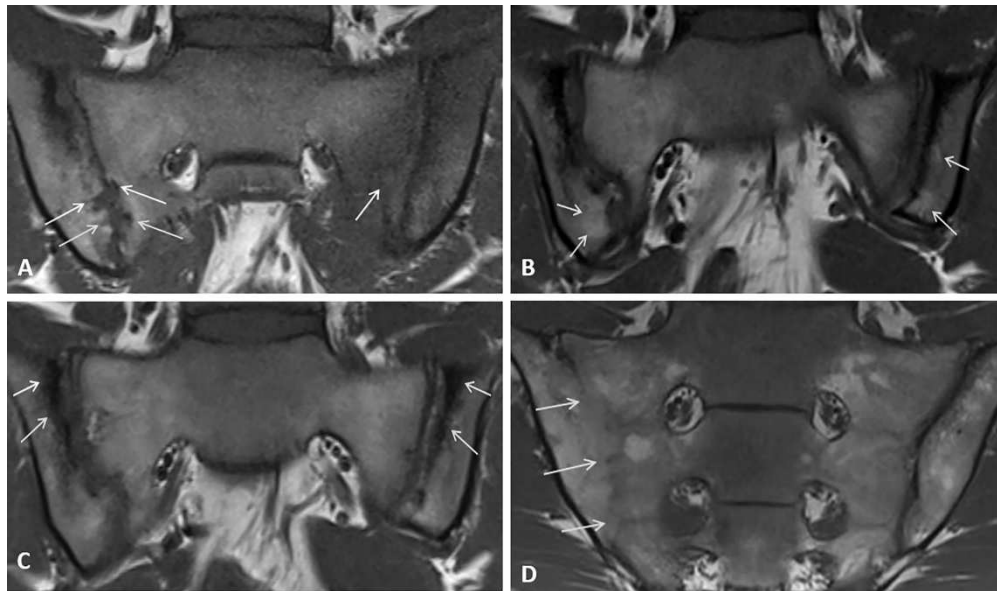


Figure 2. Coronal oblique T1-weighted MR images through the SIJ illustrating structural components (A, B, C, D). A, SIJ in a 16-year-old girl with JIA demonstrates erosion as a bony defect at the osteochondral interface (arrows) bilaterally, with the left sided sacral erosion surrounded by decreased bone marrow signal which fluid sensitive image (not shown) confirmed was due to bone marrow edema; B, SIJ in a 16-year-old girl with JIA shows subchondral fatty lesion as areas of homogeneous increased periarticular marrow signal intensity (arrows); C, SIJ in a 16-year-old girl with JIA depicts sclerosis as an area of very low subarticular bone marrow signal (arrows); D, SIJ in an 18-year-old boy with JIA shows ankylosis on the right side as continuous bone marrow signal that bridges the joint space and obliterates the articular surfaces of the SIJ (arrows).