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Diagnostyka obrazowa stawów krzyżowo-biodrowych u dzieci z klinicznym rozpoznaniem sacroiliitis

Rozprawa na stopień doktora nauk medycznych i nauk o zdrowiu w dyscyplinie nauki medyczne

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Spis treści

1. Wykaz stosowanych skrótów

ASAS – *The Assessment of Spondyloarthritis International Society*

CAS – *conjoint analysis survey* – ankieta analizy wspólnej

ERA – enthesitis-related arthritis

ILAR – *International League Against Rheumatism*

JAMRIS – *juvenile arthritis MRI scoring*

JAMRIS-SIJ – *juvenile arthritis MRI sacroiliac joint scoring*

JS – *juvenile sacroiliitis* – młodzieńcze zapalenie stawów krzyżowo-biodrowych

JSpA – *juvenile spondyloarthritis* – młodzieńcza spondyloartropatia

MIZS – młodzieńcze idiopatyczne zapalenie stawów

modNY – *modified New York criteria* – zmodyfikowane kryteria nowojorskie

MR – rezonans magnetyczny

MSpA – młodzieńcze spondyloartropatie

NIGRIR – Narodowy Instytut Geriatrii, Reumatologii i Rehabilitacji

NY – *New York criteria* – kryteria nowojorskie

RTG – zdjęcie rentgenowskie

SKB – stawy krzyżowo-biodrowe

SpA – spondyloartropatia

USG – ultrasonografia

2. Streszczenie w języku polskim

Młodzieńcze zapalenie stawów krzyżowo-biodrowych (*juvenile sacroiliitis*, JS) jest elementem obrazu chorobowego młodzieńczego idiopatycznego zapalenia stawów (MIZS), które stanowi najczęstszą chorobę zapalną stawów wieku rozwojowego (1).

Zgodnie z kryteriami klasyfikacyjnymi ILAR (*International League of Associations for Rheumatology*) młodzieńcze spondyloartropatie, tym samym JS, zostały włączone do 3 podtypów MIZS, tj. zapalenia stawów związanego z entezopatią (*enthesitis related arthritis*, ERA), łuszczycowego zapalenia stawów (*psoriatic arthritis*, PsA) oraz niezróżnicowanego zapalenie stawów (*undifferentiated arthritis*, UA). Rozpoznanie cech spondyloartropatii (SpA), w tym zapalenia stawów krzyżowo-biodrowych (SKB) i/lub kręgosłupa (*spondylitis*), ma istotne znaczenie w kontekście leczenia, ponieważ zmiany te nie reagują na leki pierwszego rzutu stosowane w leczeniu zapalenia stawów obwodowych, takie jak metotreksat (2).

Wcześniejsze badania wykazały, że u jednej trzeciej dzieci z młodzieńczą spondyloartropatią (*juvenile SpA*, JSpA) w ciągu kilku lat od diagnozy rozwija się sacroiliitis (1, 3, 4). W jednym z kolejnych badań aż u 80% pacjentów z podtypem ERA, u których występowały bóle pleców w okresie od 0 do 68 miesięcy od postawienia diagnozy, stwierdzono nieprawidłowy obraz SKB w badaniu MR (4). Zapalenie SKB w JSpA może również przebiegać bezobjawowo (2, 5). W retrospektywnym badaniu dzieci z ustaloną chorobą u jednej trzeciej pacjentów z nieprawidłowym obrazem SKB w MR nie stwierdzono w wywiadzie bólu pleców ani sztywności porannej, a badanie kliniczne było prawidłowe (1). Na podstawie tych badań ustalono, że dzieci z JSpA są narażone na ryzyko rozwoju sacroiliitis, zaś diagnoza oparta jedynie na badaniu klinicznym jest zawodna i powinna być wsparta badaniami obrazowymi.

U chorych dorosłych ze SpA, zgodnie z kryteriami ASAS (*The Assessment of Spondyloarthritis international Society*), zapalny ból pleców jest kryterium klinicznym stosowanym w celu rozpoznawania sacroiliitis (6). Na badania obrazowe SKB, tj. zdjęcia RTG i MR, kierowani są pacjenci z bólem pleców trwającym co najmniej 3 miesiące, który zmniejsza się po wysiłku fizycznym, ale nie po odpoczynku. Ból często pojawia się w nocy i słabnie po wstaniu z łóżka, ma podstępny początek. Występuje tkliwość palpacyjna okolicy SKB.

W przypadku pacjentów wieku rozwojowego przez wiele lat nie opracowano kryteriów diagnostycznych przeznaczonych dla tej grupy wiekowej, stąd w praktyce dzieci z sacroiliitis były kierowane na badania na podstawie objawu zapalnego bólu pleców występującego u dorosłych. Jednak u dzieci i młodzieży zapalny ból pleców występuje rzadziej niż u dorosłych (7, 8), wręcz jest nieobecny na początku choroby nawet u tych pacjentów, u których we wczesnym stadium wykryto cechy sacroiliitis w badaniu MR.

Kryteria rozpoznawania sacroiliitis w badaniu RTG i MR u dorosłych zostały opracowane i zwalidowane kilkanaście lat temu. Ich wykorzystanie w diagnostyce pacjentów pediatrycznych, według *Spondyloarthritis Research Consortium of Canada*, jest możliwe, jednak nie uwzględniają one zmian dojrzewania kośćca związanych z wiekiem (9).

Z tego powodu w 2018 roku międzynarodowa grupa ekspertów, w tym ośrodek własny, rozpoczęła współpracę naukową, której celem były opracowanie, a następnie walidacja kryteriów rozpoznawania sacroiliitis przeznaczonych dla pacjentów pediatrycznych z JSpA.

W ramach międzynarodowego projektu grupa OMERACT (*Outcome Measures in Rheumatology and Clinical Trials*) opracowała definicje i kryteria rozpoznawania w badaniu MR zmian tzw. zapalnych aktywnych i przewlekłych. Następnie opracowane kryteria stały się podstawą stworzonego przez grupę systemu oceny półilościowej zaawansowania choroby, tzw. JAMRIS-SIJ (10).

Celem pracy własnej było przedstawienie obrazu klinicznego i radiologicznego JSpA, z uwzględnieniem radiogramów i badania MR. Kolejny cel stanowiło omówienie spektrum zmian zapalnych w badaniu MR stawów krzyżowo-biodrowych oraz zmian przypadkowo stwierdzanych w trakcie tego badania w miednicy, w materiale pochodzącym z 3 ośrodków zagranicznych, w ramach międzynarodowej współpracy. Dodatkowo zaprezentowano wyniki wieloośrodkowego badania, z własnym udziałem, którego celem była walidacja skali JAMRIS-SIJ oceny sacroiliitis u dzieci i młodzieży.

W dwóch pierwszych pracach poglądowych powstałych w ramach międzynarodowej współpracy omówiono klasyfikację JSpA oraz metody diagnostyczne wykorzystywane w diagnostyce JSpA, tj. USG, MR oraz RTG. Przedstawiono w nich spektrum zmian zapalnych widocznych w badaniach obrazowych (tabele 1 i 2).

Podkreślono wiodącą rolę badania MR w porównaniu z RTG we wczesnej diagnostyce sacroiliitis. Zwrócono uwagę na nadrzędną rolę kryterium obrzęku szpiku kostnego, który jest wymagany w celu postawienia rozpoznania sacroiliitis.

Ponadto MR wykazuje wyższą czułość w ocenie zarówno zmian zapalnych, jak i destrukcyjnych niż badanie fizykalne czy radiogramy.

Radiografia konwencjonalna odgrywa dużą rolę w diagnostyce różnicowej, w wykluczaniu nowotworów, urazów lub specyficznych zapaleń i nadal pozostaje standardem w procesie diagnostycznym zmian zapalnych w SKB. We wczesnych stadiach sacroiliitis radiogramy są zazwyczaj negatywne lub przedstawiają wczesne etapy choroby w postaci zatarcia zarysów powierzchni stawowych. Jak wykazały porównawcze badania MR (11), specyfika budowy SKB w wieku rozwojowym odpowiada za wysoki odsetek błędnych rozpoznań saroiliitis w badaniu RTG (wyniki zarówno fałszywie ujemne, jak dodatnie).

W kolejnej publikacji, zatytułowanej *Juvenile spondyloarthritis and chronic recurrent multifocal osteomyelitis overlap syndrome in a 16 y.o. adolescent. A case report and literature review*, omówiono rzadki przypadek zespołu nakładania młodzieńczej spondyloartropatii i przewlekłego nawracającego wieloogniskowego zapalenia kości i szpiku (*chronic recurrent multifocal osteomyelitis*, CRMO) u 16-letniej dziewczynki diagnozowanej w naszym ośrodku oraz trudności diagnostyczne związane z rozpoznaniem tej choroby. Przykład ten ilustruje złożony proces rozpoznawania chorób reumatycznych u pacjentów wieku rozwojowego, szczególnie skomplikowany w przypadku współistnienia kilku jednostek u jednego pacjenta. Ścisła współpraca klinicystów i radiologów jest w takich przypadkach konieczna, jednak nawet wówczas nierzadko dochodzi do opóźnień diagnostycznych – dzieje się tak ze względu na brak jednoznacznych objawów oraz specyficznych markerów serologicznych, konieczność wykluczania kolejno innych artropatii i poszerzania diagnostyki o następne badania. Skutkuje to wyjściowo brakiem optymalnego leczenia, co prowadzi do progresji choroby.

Czwarta uwzględniona w cyklu praca oryginalna pt. *Common incidental findings on sacroiliac joint MRI in children clinically suspected of juvenile spondyloarthritis* powstała w ramach międzynarodowej współpracy pomiędzy ośrodkami polskim (ośrodek własny), belgijskim (Szpital Uniwersytecki w Gandawie) i kanadyjskim (Szpital Uniwersytetu Alberty).

W ramach retrospektywnego wieloośrodkowego badania stworzono repozytorium badań pochodzących z trzech ośrodków z lat 2012–2018. Zgromadzono 540 badań MR

stawów krzyżowo-biodrowych dzieci z klinicznym podejrzeniem JS. Celem analizy było określenie spektrum zmian zapalnych w SKB oraz zmian przypadkowo rozpoznawanych w miednicy w trakcie diagnostyki MR sacroiliitis.

W przeprowadzonym badaniu cechy sacroiliitis stwierdzono w MR u 106/540 (20%) dzieci. Co ciekawe, u dwukrotnie większej liczby chorych, tj. u 228 (42%) pacjentów, badanie MRI wykazało co najmniej jedną przypadkową zmianę/nieprawidłowość inną niż sacroiliitis – łącznie stwierdzono 271 nieprawidłowych „znalezisk". Najczęstsze zmiany występowały w kręgosłupie lędźwiowo-krzyżowym (158 pacjentów, 29%) i w stawach biodrowych (43 pacjentów, 8%). Najliczniejsze przypadki obejmowały: zmiany zwyrodnieniowe odcinka lędźwiowego kręgosłupa (94 pacjentów, 17%), prostą (kostną) torbiel (15 pacjentów, 2,8%), enthesitis u 16 pacjentów (3%), niespecyficzny ogniskowy BME w lokalizacji pozastawowej (nietypowy dla JSpA) u 10 pacjentów (1,9%), torbiele jajników u 7 pacjentek (1,3%), BME w przebiegu CRMO u 4 pacjentów (0,7%), patologie mięśni u 4 pacjentów (0,7%), zmiany ogniskowe o charakterze łagodnym u 3 pacjentów (0,6%), przebyte złamania u 3 pacjentów (0,6%), przebyte urazy awulsyjne kostnego wyrostka nasady u 2 pacjentów (0,4%) oraz guzy złośliwe u 2 pacjentów (0,4%).

Przeprowadzone badania wykazały, że u wielu pacjentów diagnozowanych pod kątem sacroiliitis w badaniu MR wykrywane są przypadkowo inne nieprawidłowości, których częstość przewyższa liczbę rozpoznawanych przypadków sacroiliitis, przy czym wiele wymaga pilnej interwencji.

Cykl prac zamyka kolejna publikacja oryginalna podsumowująca efekty wieloletniej międzynarodowej współpracy naszego ośrodka, której celem było opracowanie kryteriów oceny sacroiliitis u dzieci i młodzieży. Celem pracy zatytułowanej *Determination of Relative Weightings for the Component Pathologies of the OMERACT Juvenile Arthritis Magnetic Resonance Imaging Sacroiliac Joint Score* było dokonanie walidacji skali JAMRIS-SIJ na materiale 14 badań MR stawów krzyżowo-biodrowych, które zostały poddane wnikliwej analizie przez 17 międzynarodowych ekspertów. Ocenie podlegały zmiany zapalne aktywne (zapalenie szpiku kostnego (*osteitis*) – BME, zapalenie w nadżerce, wzmocnienie w szparze stawu, wysięk w stawie, zapalenie torebki stawowej, zapalenie więzadeł) oraz przewlekłe/destrukcyjne (sklerotyzacja, tłuszczowa przebudowa szpiku oraz metaplazja tłuszczowa w nadżerkach, nadżerki, ankyloza). Ocena polegała na przyporządkowaniu uwidocznionym zmianom wag (*weights*)/udziałów, istotnych pod kątem rozpoznania sacroiliitis.

Dwa najbardziej istotne pod kątem diagnostyki sacroiliitis elementy obrazu chorobowego w MR, tj. zapalenie szpiku kostnego (czyli osteitis, rozpoznawany w badaniu MR po dożylnym podaniu środka kontrastującego) i BME uzyskały równoważne wartości wag/udziałów w opinii eksperckiej: osteitis (24,7%) i BME (24,3%) Ich średnie wagi procentowe były wyższe w porównaniu z uzyskanymi dla pozostałych cech chorobowych, jak zapalenie w nadżerce (16,9%), wzmocnienie w jamie stawu (13,1%), wysięk w jamie stawu (9,1%), zapalenie torebki (7,3%) i zapalenie przyczepów (4,6%). Podobnie w domenie uszkodzeń ankyloza (41,3%) i nadżerka (25,1%) wykazały wyższe średnie wagi w porównaniu z metaplazją tłuszczową w nadżerce (13,9%), sklerotyzacją (10,7%) i metaplazją tłuszczową szpiku kostnego (9,1%) (tabela 1).

Przeprowadzone badanie potwierdziło przydatność skali JAMRIS-SIJ do diagnostyki JS, określenia aktywności choroby i oceny skuteczności leczenia.

Ponadto najwyższą zgodność oceny eksperckiej 14 badań MR (winiet JAMRIS-SIJ) obliczoną według CAS (*conjoint analysis survey* – ankieta analizy wspólnej) uzyskano w przypadku najmniej i najbardziej zaawansowanego sacroiliitis, podczas gdy dla mniej zaawansowanych przypadków ocena była znacznie zróżnicowana (rysunki 1A, B).

Nasze badanie potwierdziło przydatność skali do oceny SKB.

Na podstawie powyższych prac sformułowano następujące wnioski:

1. Młodzieńcze zapalenie stawów krzyżowo-biodrowych jest częstym problemem klinicznym, niejednokrotnie o niespecyficznej symptomatologii, wymagającym poszerzenia diagnostyki o badania obrazowe w celu uzyskania wczesnej diagnozy.
2. Badanie MR jest metodą o wyższej czułości niż badanie RTG w diagnostyce i monitorowaniu zmian zapalnych w stawach krzyżowo-biodrowych u dzieci z klinicznym rozpoznaniem sacroiliitis.
3. Zmiany zapalne w SKB są w badaniu MR stwierdzane u 20% dzieci i młodzieży z klinicznym rozpoznaniem sacroiliitis.
4. U istotnego odsetka dzieci (42%) z klinicznym podejrzeniem sacroiliitis w badaniu MR wykrywane są przypadkowe zmiany, których częstość przewyższa liczbę rozpoznawanych przypadków sacroiliitis (20%) i w wielu przypadkach wymaga interwencji.
5. Zaproponowana skala oceny zmian zapalnych SKB w MR (skala JAMRIS-SIJ), uwzględniająca kryteria sacroiliitis, przeznaczona dla pacjentów wieku

rozwojowego, jest użyteczna w diagnostyce sacroiliitis, w ocenie aktywności choroby i może być wykorzystana do monitorowania skuteczności leczenia.

3. Streszczenie w języku angielskim

Juvenile sacroiliitis (JS) is a component of the clinical picture of juvenile idiopathic arthritis (JIA), which is the most common inflammatory joint disease in childhood (1).

According to the ILAR (International League of Associations for Rheumatology) classification criteria, juvenile spondyloarthropathies, including JS, are included in three subtypes of JIA: Enthesitis Related Arthritis (ERA), Psoriatic Arthritis (PsA), and Undifferentiated Arthritis (UA). Recognizing features of spondyloarthropathy (SpA), including sacroiliitis (SI) and/or spinal involvement (spondylitis), is crucial in the context of treatment, as these conditions do not respond to first-line medications used for peripheral arthritis, such as methotrexate (2).

Previous studies have shown that one-third of children with juvenile spondyloarthropathy (Juvenile SpA – JSpA) develop sacroiliitis within a few years of diagnosis (1, 3, 4). In one subsequent study, abnormal sacroiliac joint (SIJ) findings on MRI were observed in up to 80% of patients with the ERA subtype who experienced back pain within 0 to 68 months after diagnosis (4). Sacroiliitis in JSpA can also be asymptomatic (2, 5). In a retrospective study of children with established disease, one-third of patients with abnormal SIJ findings on MRI reported no history of back pain or morning stiffness, and their clinical examination was normal (1). Based on these studies, it was concluded that children with JSpA are at risk of developing sacroiliitis, and diagnosis based solely on clinical examination is unreliable and should be supported by imaging studies.

In adult patients with SpA, according to the ASAS (The Assessment of Spondyloarthritis International Society) criteria, inflammatory back pain is a clinical criterion used to diagnose sacroiliitis (6). Imaging studies of the sacroiliac joints, such as X-rays and MRI, are recommended for patients with back pain lasting at least 3 months, which improves with physical activity but not with rest. The pain often occurs at night and decreases after getting out of bed, having an insidious onset. There is also tenderness upon palpation of the sacroiliac joint area.

For many years, no diagnostic criteria were developed specifically for the pediatric population, which is why, in practice, children with sacroiliitis were referred for testing based on the symptom of inflammatory back pain observed in adults. However,

inflammatory back pain occurs less frequently in children and adolescents than in adults (7, 8), and it may even be absent at the onset of the disease, even in those patients who show early features of sacroiliitis on MRI.

The criteria for diagnosing sacroiliitis on X-ray and MRI in adults were developed and validated over a decade ago. Their use in the diagnosis of pediatric patients, according to the Spondyloarthritis Research Consortium of Canada, is possible; however, they do not account for age-related skeletal maturation changes (9).

For this reason, in 2018, an international group of experts, including our own center, initiated a scientific collaboration aimed at developing and subsequently validating criteria for diagnosing sacroiliitis specifically tailored to pediatric patients with JSpA.

As part of this international project, the OMERACT group (Outcome Measures in Rheumatology and Clinical Trials) developed definitions and criteria for detecting active inflammatory and chronic changes on MRI. These criteria then formed the basis for the semi-quantitative disease assessment system created by the group, known as JAMRIS-SIJ (10).

The aim of this study was to present the clinical and radiological picture of JSpA, including radiographs and MRI examinations. Another objective was to discuss the spectrum of inflammatory changes observed on MRI of the sacroiliac joints, as well as incidental findings in the pelvis during these examinations, based on material from three foreign centers as part of an international collaboration. Additionally, the results of a multicenter study, in which our center participated, are presented, focusing on the validation of the JAMRIS-SIJ scale for assessing sacroiliitis in children and adolescents.

The first two review papers resulting from the international collaboration discuss the classification of JSpA and the diagnostic methods used in JSpA diagnosis, including ultrasound (US), MRI, and X-ray. They present the spectrum of inflammatory changes visible in imaging studies (Tables 1 and 2). The leading role of MRI compared to X-ray in the early diagnosis of sacroiliitis is emphasized. Particular attention is drawn to the primary role of bone marrow edema, which is required to diagnose sacroiliitis.

Moreover, MRI demonstrates higher sensitivity in assessing both inflammatory and destructive changes than physical examination or X-rays. Conventional radiography plays a significant role in differential diagnosis, excluding tumors, injuries, or specific inflammations, and it remains the standard in the diagnostic process for inflammatory changes in the sacroiliac joints. In the early stages of sacroiliitis, radiographs are typically

negative or show early signs of the disease, such as blurred joint surface outlines. As shown by comparative MRI studies (11), the specific anatomy of the sacroiliac joints during development accounts for the high rate of misdiagnosis of sacroiliitis on X-rays (both false negatives and positives).

Another publication titled "Juvenile spondyloarthritis and CRMO overlap syndrome in a 16-year-old adolescent" discusses a rare case of overlap syndrome involving juvenile spondyloarthropathy and Chronic Recurrent Multifocal Osteomyelitis (CRMO) in a 16-year-old girl diagnosed in our center, and the diagnostic challenges associated with recognizing this disease. This case illustrates the complex process of diagnosing rheumatic diseases in pediatric patients, particularly complicated when multiple conditions coexist in a single patient. Close collaboration between clinicians and radiologists is essential in such cases; however, even then, diagnostic delays are not uncommon due to the absence of clear symptoms, specific serological markers, and the need to sequentially exclude other arthropathies while expanding the diagnostic process with further tests. As a result, there is an initial lack of optimal treatment, leading to disease progression.

The fourth original study included in the cycle, titled "Common incidental findings on sacroiliac joint MRI in children clinically suspected of juvenile spondyloarthritis," was conducted as part of an international collaboration between Polish (our center), Belgian (Ghent University Hospital), and Canadian (University of Alberta Hospital) centers.

As part of a retrospective multicenter study, a repository of examinations from the three centers was created, covering the years 2012–2018. A total of 540 MRI scans of the sacroiliac joints of children with clinical suspicion of JS were collected. The aim of the analysis was to determine the spectrum of inflammatory changes in the sacroiliac joints and incidental findings in the pelvis during MRI diagnostics of sacroiliitis.

In the study, MRI features of sacroiliitis were identified in 106 out of 540 (20%) children. Interestingly, in twice as many patients, i.e., 228 (42%), the MRI revealed at least one incidental finding unrelated to sacroiliitis; a total of 271 abnormal findings were noted. The most common abnormalities were found in the lumbosacral spine (158 patients, 29%) and the hip joints (43 patients, 8%). The most frequent cases included: degenerative changes in the lumbar spine (94 patients – 17%), simple (bone) cysts (15 patients – 2.8%), enthesitis in 16 patients (3%), nonspecific focal BME in extra-articular locations (atypical for JSpA) in 10 patients (1.9%), ovarian cysts in 7 female

patients (1.3%), BME in the course of CRMO in 4 patients (0.7%), muscle pathologies in 4 patients (0.7%), benign focal lesions in 3 patients (0.6%), healed fractures in 3 patients (0.6%), prior avulsion injuries of bony apophyses in 2 patients (0.4%), and malignant tumors in 2 patients (0.4%).

The study showed that many patients being diagnosed for sacroiliitis have incidental findings on MRI, which occur more frequently than diagnosed cases of sacroiliitis, with many requiring urgent intervention.

The cycle of works concludes with another original publication summarizing the outcomes of years of international collaboration at our center, aimed at developing criteria for assessing sacroiliitis in children and adolescents. The goal of the study, titled "Determination of Relative Weightings for the Component Pathologies of the OMERACT Juvenile Arthritis Magnetic Resonance Imaging Sacroiliac Joint Score," was to validate the JAMRIS-SIJ scale using data from 14 MRI scans of sacroiliac joints, which were thoroughly analyzed by 17 international experts. The assessment focused on active inflammatory changes (BME, osteitis, erosion-associated inflammation, joint space enhancement, joint effusion, capsulitis, ligament inflammation) as well as chronic/destructive changes (sclerosis, fatty marrow replacement, fat metaplasia in erosions, erosions, ankylosis). The evaluation involved assigning weights to the identified changes, reflecting their significance in the diagnosis of sacroiliitis.

The two most significant elements for diagnosing sacroiliitis on MRI—osteitis (recognized in MRI after intravenous contrast administration) and bone marrow edema (BME)—were assigned equivalent weightings by expert opinion: osteitis (24.7%) and BME (24.3%). Their average percentage weightings were higher compared to those of other disease features, such as erosion-associated inflammation (16.9%), joint space enhancement (13.1%), joint effusion (9.1%), capsulitis (7.3%), and enthesitis (4.6%). Similarly, in the damage domain, ankylosis (41.3%) and erosions (25.1%) had higher average weightings compared to fat metaplasia in erosions (13.9%), sclerosis (10.7%), and bone marrow fat metaplasia (9.1%) (Table 1).

The study confirmed the utility of the JAMRIS-SIJ scale for diagnosing JSpA, assessing disease activity, and evaluating treatment effectiveness.

Moreover, the highest agreement in expert evaluation of the 14 MRI studies (JAMRIS-SIJ vignettes), calculated using CAS (conjoint analysis survey), was observed for the least and most advanced cases of sacroiliitis, while evaluations for less advanced cases showed significantly more variability (Figure 1A, B).

Our study confirmed the utility of the scale for assessing the sacroiliac joints.

Based on the above works, the following conclusions were drawn:

1. Juvenile sacroiliitis is a common clinical issue, often presenting with nonspecific symptoms, requiring the extension of diagnostics with imaging studies to achieve an early diagnosis.
2. MRI is a more sensitive method than X-ray in diagnosing and monitoring inflammatory changes in the sacroiliac joints of children with a clinical diagnosis of sacroiliitis.
3. Inflammatory changes in the sacroiliac joints are detected on MRI in 20% of children and adolescents with a clinical diagnosis of sacroiliitis.
4. A significant proportion of children (42%) with a clinical suspicion of sacroiliitis have incidental findings on MRI, which occur more frequently than diagnosed cases of sacroiliitis (20%) and, in many cases, require intervention.
5. The proposed scale for assessing inflammatory changes in the sacroiliac joints on MRI (JAMRIS-SIJ scale), which includes criteria for sacroiliitis tailored to pediatric patients, is useful for diagnosing sacroiliitis, assessing disease activity, and can be used to monitor treatment effectiveness.

4. Wstęp

Młodzieńcze zapalenie stawów krzyżowo-biodrowych (*juvenile sacroiliitis*, JS) jest elementem chorobowym tzw. młodzieńczych spondyloartropatii (JSpA), występujących u dzieci do 16 r.ż. i stanowiących do 1/5 przypadków spondyloartropatii (SpA) (11).

Według ILAR (*International League of Associations for Rheumatology*) JSpA nie stanowią oddzielnej jednostki, ale zaliczane są do 3 podtypów młodzieńczego idiopatycznego zapalenia stawów (MIZS), tj. zapalenia stawów związanego z entezopatią (*enthesitis-related arthritis*, ERA), łuszczycowego zapalenia stawów (*psoriatic arthritis*, PsA) oraz niezróżnicowanego zapalenia stawów (*undifferentiated arthritis*, UA).

Rozpoznanie cech SpA, tj. zapalenia stawów krzyżowo-biodrowych (sacroiliitis) i/lub kręgosłupa (spondylitis) ma istotne znaczenie w kontekście leczenia, ponieważ zmiany te nie reagują na leki pierwszego rzutu stosowane w leczeniu zapalenia stawów obwodowych, takie jak metotreksat (2).

Diagnostyka JS przez wiele lat pozostawała problematyczna z uwagi na brak specyficznych kryteriów klinicznych i markerów serologicznych, co prowadziło do postępu choroby i istotnych powikłań.

Zgodnie z kryteriami ASAS u chorych dorosłych ze SpA podstawowym kryterium klinicznym rozpoznawania sacroiliitis jest tzw. zapalny ból pleców. Jest on definiowany jako ból okolicy stawów krzyżowo-biodrowych (SKB) o podstępnym początku, trwający co najmniej 3 miesiące, nieustępujący po odpoczynku, zmniejszający się po wysiłku fizycznym, często pojawiający się w nocy i słabnący po przebudzeniu (6).

Pacjenci dorośli z bólem o takim charakterze są kierowaniu na badanie RTG stawów krzyżowo-biodrowych z podejrzeniem sacroiliitis. Zgodnie z kryteriami ASAS w przypadku negatywnego radiogramu albo sacroiliitis w RTG w stopniu 1 bądź jednostronnym stopniu 2 (zgodnie ze zmodyfikowanymi kryteriami nowojorskimi, modNY) u osób dorosłych wykonywane jest badanie MR SKB (6).

U dzieci i młodzieży z JSpA przez lata nie stworzono oddzielnego, przeznaczonego dla populacji wieku rozwojowego kryterium diagnostycznego i w celu kwalifikacji do badań obrazowych nadal stosowany jest zapalny ból krzyża, jak u osób dorosłych.

Nie dokonano także wnikliwej analizy wartości diagnostycznej kryteriów nowojorskich (NY) i modNY w badaniu RTG tej grupy wiekowej. Przez lata nie stworzono kryteriów ropoznawania sacroiliitis w badaniu MR przeznaczonych dla populacji wieku rozwojowego – mimo wprowadzenia i walidacji takowych dla chorych dorosłych.

Zmiany widoczne w badaniach RTG SKB u dzieci i młodzieży są takie same jak u pacjentów dorosłych.

W początkowym etapie zarysy stawów są nieostre, następnie, wraz z postępem choroby, obserwuje się płytkie nadżerki i podchrzęstne obszary sklerotyczne, przestrzeń stawowa ulega nieregularnemu poszerzeniu, zajęta przez coraz liczniejsze nadżerki. W końcowym etapie choroby obserwuje się segmentalne zwężenia przestrzeni stawowej z tworzeniem mostków kostnych. Ankyloza u dzieci jest stwierdzana bardzo rzadko.

Wśród zmian zapalnych w badaniu MR o typie sacroiliitis wyróżnia się tzw. zmiany aktywne i przewlekłe (strukturalne). Do pierwszej grupy zaliczane są: obrzęk szpiku kostnego (*bone marrow edema*, BME), wysięk w jamie stawu, zapalenie w jamie stawu, zapalenie torebki stawowej (*caspulitis*), zapalenie przyczepów więzadeł (*enthesitis*). Do zmian przewlekłych należą: podchrzęstna sklerotyzacja, nadżerki, przebudowa tłuszczowa w nadżerce (*backfill*), tłuszczowa przebudowa szpiku kostnego, mostki kostne, ankyloza.

W porównaniu z badaniem RTG MR cechuje wyższa czułość w diagnozowaniu sacroiliitis (9–11). MR pozwala na rozpoznanie wczesnych zmian zapalnych niewidocznych w RTG. Ostatnie prace porównujące obie modalności wykazują ponadto, że w MR dobrze widoczne są również zmiany przewlekłe (7), w związku z czym istnieje duże prawdopodobieństwo, że w przyszłości MR zastąpi także w tym zakresie badanie RTG.

W porównaniu z dorosłymi JSpA są trudne do rozpoznania. Po pierwsze, u dzieci rzadko choroba zaczyna się od zajęcia SKB czy kręgosłupa i w początkowych latach choroba zazwyczaj obejmuje stawy kończyn dolnych (12). Po drugie, spełnienie kryterium zapalnego bólu krzyża u dzieci i młodzieży jest problematyczne, gdyż w tej grupie wiekowej pacjentów objaw ten rzadko występuje w początkowym okresie choroby albo nie jest zgłaszany przez dzieci (2, 5). Niektóre publikacje wykazują przydatność MR w wykrywaniu początkowych etapów sacroiliitis, które są bezobjawowe w badaniu klinicznym i nie są widoczne w RTG (13). Ponadto radiogramy SKB u dzieci i młodzieży cechuje duża liczba błędnych wyników zawansowania sacroiliitis wg kryteriów NY. To

powoduje, że jedynym w pełni wartościowym badaniem obrazowym SKB jest RM (5, 11, 14). Takie postępowanie diagnostyczne ma olbrzymie znaczenie w rozpoznawaniu zwłaszcza wczesnych zmian zapalnych SKB, gdyż bezpośrednio przekłada się na bezzwłoczne wprowadzenie skutecznych form terapii, a tym samym poprawia prognozę.

W przeciwieństwie do powszechnie stosowanych w praktyce, zwalidowanych kryteriów oceny MRI stawów krzyżowo-biodrowych u dorosłych nie opracowano jednak kryteriów oceny MR dla pacjentów wieku rozwojowego z sacroiliitis. W diagnostyce obrazowej przez lata kierowano się takimi samymi parametrami jak u chorych dorosłych. Według *Spondyloarthritis Research Consortium of Canada* kryteria zmian aktywnych i przewlekłych są możliwe do wykorzystania w obrazowaniu dzieci i młodzieży, ale nie uwzględniają zmian w kośćcu związanych z procesem jego dojrzewania (9, 10).

Z tego powodu w 2018 roku międzynarodowa grupa ekspertów, w tym ośrodek własny, rozpoczęła współpracę naukową, której celem były opracowanie, a następnie walidacja kryteriów rozpoznawania sacroiliitis przeznaczonych dla pacjentów pediatrycznych z JSpA. W ramach międzynarodowego projektu grupa OMERACT (*Outcome Measures in Rheumatology and Clinical Trials*) opracowała definicje i kryteria rozpoznawania w badaniu MR zmian zapalnych tzw. aktywnych i przewlekłych. Następnie opracowane kryteria stały się podstawą stworzonego przez grupę systemu oceny półilościowej zaawansowania choroby, tzw. JAMRIS-SIJ (10).

5. Założenia i cel pracy

Zapalenie SKB w przebiegu JSpA pozostaje istotnym klinicznie problemem ze względu na późne występowanie objawów przedmiotowych, powiązane z tym problemy diagnostyczne i opóźnione rozpoznanie, a poprzez to pogorszenie prognozy stanu zdrowia. Obecnie w wielu przypadkach, dzięki lekom modyfikującym przebieg choroby, w tym lekom biologicznym, możliwe jest znaczne spowolnienie choroby oraz zmniejszenie ryzyka wystąpienia zmian destrukcyjnych i zaburzeń rozwojowych (14, 15).

Wprowadzenie metod obrazowania SKB, zwłaszcza we wczesnym etapie choroby badania MR, pozwala na wczesne rozpoznanie choroby i jej skuteczne monitorowanie.

Celem pracy własnej było przedstawienie obrazu klinicznego i radiologicznego JSpA, z uwzględnieniem radiogramów i badania MR. Kolejnym celem było omówienie spektrum zmian zapalnych w badaniu MR stawów krzyżowo-biodrowych oraz zmian przypadkowo stwierdzanych w trakcie tego badania w miednicy, w materiale pochodzącym z 3 ośrodków zagranicznych, w ramach międzynarodowej współpracy. Dodatkowo zaprezentowano wyniki wieloośrodkowego badania, z własnym udziałem, którego celem była walidacja skali JAMRIS-SIJ oceny sacroiliitis u dzieci i młodzieży.

6. Materiał i metody

6.1. Materiał

Retrospektywnej analizie poddano wyniki badań MR i RTG stawów krzyżowo-biodrowych wykonanych w latach 2013–2015 u pacjentów Kliniki i Polikliniki Reumatologii Wieku Rozwojowego Narodowego Instytutu Geriatrii, Reumatologii i Rehabilitacji w Warszawie.

180 badań MR z wyjściowej liczby 217, ilustrujących poszczególne typy zmian zapalnych w MR o charakterze sacroiliitis, włączono do międzynarodowego repozytorium.

Łącznie zgromadzono w nim 540 badań MR stawów krzyżowo-biodrowych wykonanych w latach 2013–2018 u pacjentów w wieku 4–18 lat z klinicznym podejrzeniem sacroiliitis, pochodzących z trzech ośrodków: polskiego (Narodowy Instytut Geriatrii, Reumatologii i Rehabilitacji w Warszawie), belgijskiego (Szpital Uniwersytecki w Gandawie), Kanadyjskiego (Szpital Uniwersytetu Alberty).

Badanie zostało przeprowadzone zgodnie z deklaracją helsińską i zatwierdzone przez lokalną komisję bioetyczną (nr KBT-2/1/2018 z dn. 22.02.2018 r.)

Rodzice/opiekunowie prawni wszystkich pacjentów wyrazili świadomą zgodę na udział dziecka w badaniu.

6.2. Metody

Rezonans magnetyczny

Wszyscy pacjenci mieli oznaczone stężenie kreatyniny we krwi oraz wyliczony wskaźnik eGFR.

Badania MR wykonywano na aparacie o mocy 1,5 T (Avanto, Siemens Medical, Erlangen, Niemcy). Stawy krzyżowo-biodrowe były obrazowane za pomocą cewki elastycznej na ciało (Siemens Medical, Erlangen, Niemcy).

Protokół MR SKB obejmował projekcje:

– czołową skośną (wzdłuż długiej osi kości krzyżowej, równolegle do tylnej powierzchni trzonu kręgu S2) w sekwencjach T1-zależnej turbo spin echo (TSE);
– T1z z saturacją tkanki tłuszczowej (*fat sat*, FS);

– T2z z FS (*short tau inversion recovery sequence*, STIR);
– poprzeczną skośną w sekwencji PD (*proton density*) FS;
– strzałkową w sekwencji T2z TSE.

Z ośrodka belgijskiego uzyskano dodatkowo sekwencję czołową skośną T1z FS ze wzmocnieniem kontrastowym po dożylnym (IV) podaniu kontrastu z gadolinium – DTPA (Gd) (T1/Gd) (Dotarem, 0,1 mmol/kg masy ciała).

Na uzyskanych obrazach ocenianie były cechy obecności zmian zapalnych aktywnych i przewlekłych (tabela 1). Zgodnie z kryteriami ASAS wymaganym warunkiem rozpoznania sacroiliitis jest stwierdzenie BME w typowej przystawowej lokalizacji, w warstwie podchrzęstnej kości krzyżowej lub biodrowej (16,17). BME, zgodnie z kryterium, musi być widoczny albo na jednej warstwie w co najmniej dwóch różnych kwadrantach stawowych, albo na co najmniej dwóch równoległych warstwach w jednej lokalizacji (16, 17). Pozostałe aktywne zmiany bez obecności BME nie pozwalają na postawienie rozpoznania sacroiliitis (16, 17).

Tabela 1. Aktywne i przewlekłe zmiany zapalne w przebiegu zapalenia stawów krzyżowo-biodrowych, stwierdzane w badaniu MR według kryteriów ASAS

Aktywne zmiany zapalne	**Przewlekłe zmiany zapalne**
Obrzęk szpiku kostnego	Podchrzęstna sklerotyzacja
Zapalenie w jamie stawu	Nadżerki
Wysięk w jamie stawu	Tłuszczowa przebudowa szpiku kostnego
Zapalenie torebki stawowej	Tłuszczowa przebudowa w nadżerce (*backfill*)
Zapalenie przyczepu więzadeł	Mostki kostne, ankyloza

Wyniki badania MR skorelowano z podstawowymi danymi klinicznymi, przede wszystkim informacjami o ostatecznym rozpoznaniu, które przestawiono w publikacji nr 4 należącej do cyklu przedłożonych prac, zatytułowanej *Common incidental findings on sacroiliac joint MRI in children clinically suspected of juvenile spondyloarthritis*.

W następnej publikacji zawartej w cyklu, pt. *Determination of Relative Weightings for the Component Pathologies of the OMERACT Juvenile Arthritis Magnetic Resonance Imaging Sacroiliac Joint Score*, badania własne zostały wykorzystane do kolejnej analizy przy współudziale innych 16 międzynarodowych ekspertów.

Jej cel stanowiła walidacja systemu półilościowej analizy zaawansowania zmian o charakterze sacroiliitis w przebiegu JS – skali JAMRIS-SIJ (9), która powstała z potrzeby standaryzacji interpretacji obrazów SKB w badaniach MR. W ramach tego badania przeprowadzono adaptacyjną analizę wielokryterialną (*multicriteria decision analysis*, MCDA) za pomocą aplikacji internetowej 1000minds, aby określić względne wagi (*weights*) elementów w domenach zapalenia i uszkodzenia wg skali JAMRIS-SIJ. Eksperci w dziedzinie obrazowania i reumatologii niezależnie wypełnili ankietę analizy wspólnej (*conjoint analysis survey*, CAS) w celu określenia wartości punktowej kryteriów zapalnych zawartych w skali JAMRIS-SIJ. Każde pytanie ankiety CAS polegało na porównaniu dwóch hipotetycznych profili pacjentów, które były podobne, z wyjątkiem dwóch elementów, i na wybraniu elementu wskazującego bardziej zaawansowane stadium zapalenia lub uszkodzenia (ryc. A1, A2 w publikacji). Dodatkowo eksperci uszeregowali 14 winiet pacjentów JAMRIS-SIJ zawierających tylko ocenę bądź ocenę wraz z obrazem, bez wiedzy odnośnie do wag pochodzących z CAS.

RTG

Radiogramy wykonywane były aparatem firmy Quantum. Każdy pacjent miał wykonane badanie miednicy w projekcji przód–tył oraz odcinka lędźwiowego kręgosłupa w projekcji bocznej. Do badania wymagane było przygotowanie: 48 godzin przed badaniem – dieta ubogoresztkowa, 24 godzin przed badaniem – dieta płynna: woda niegazowana, przecedzony bulion, galaretki owocowe, słaba herbata bez cukru oraz przyjmowanie Espumisanu 3 razy dziennie po 2 kapsułki. W dniu badania należało pozostać na czczo.

Podstawą oceny radiogramów były kryteria NY z 1966 r. z uwzględnieniem zmodyfikowanych kryteriów nowojorskich z 1984 r. modNY dla zesztywniającego zapalenia stawów kręgosłupa. Zapalenie stawów krzyżowo-biodrowych jest rozpoznawane w przypadku uwidocznienia zmian zapalnych w stopniu co najmniej drugim obustronnie lub trzecim jednostronnie (16).

Tabela 2. Kryteria nowojorskie zapalenia stawów krzyżowo-biodrowych

Stopień 0	bez zmian (stawy krzyżowo-biodrowe prawidłowe)
Stopień 1	podejrzenie zmian (zatarte zarysy szpar stawowych)
Stopień 2	minimalne zmiany (pojedyncze nadżerki i przystawowa sklerotyzacja)
Stopień 3	zaawansowane zmiany (wyraźna przystawowa sklerotyzacja, liczne nadżerki z poszerzeniem szpary stawowej, pojedyncze mostki kostne)
Stopień 4	całkowita ankyloza

Badania własne zostały uzupełnione trzema artykułami przeglądowymi opublikowanymi w recenzowanych czasopismach w ramach międzynarodowej współpracy, dotyczącymi klasyfikacji klinicznych i diagnostyki obrazowej JSpA.

7. Wyniki

Wyniki badań przedstawiono w cyklu prac opublikowanych w recenzowanych czasopismach:

1. **Imaging of Juvenile Spondyloarthritis. Part I: Classifications and Radiographs.**
   Sudoł-Szopińska I, Gietka P, Znajdek M, Matuszewska G, Bogucevska M, Damjanovska-Krstikj L, Ivanoski S.
   J Ultrason. 2017 Sep;17(70):167–175. doi: 10.15557/JoU.2017.0025. Epub 2017 Sep 29. PMID: 29075521; PMCID: PMC5647611.
   Punktacja MNiSW: 10 pkt

2. **Imaging of Juvenile Spondyloarthritis. Part II: Ultrasonography and Magnetic Resonance Imaging.**
   Sudoł-Szopińska I, Znajdek M, Gietka P, Vasilevska-Nikodinovska V, Patrovic L, Salapura V.
   J Ultrason. 2017 Sep;17(70):176–181. doi: 10.15557/JoU.2017.0026. Epub 2017 Sep 29. PMID: 29075522; PMCID: PMC5647612.
   Punktacja MNiSW: 10 pkt

3. **Juvenile spondyloarthritis and chronic recurrent multifocal osteomyelitisoverlap syndrome in a 16 y.o. adolescent. A case report and literature review.**
   Znajdek M, Gazda A, Gietka P, Wysmołek M, Sudoł-Szopińska I.
   J Ultrason. 2019;19(77):152–157. doi: 10.15557/JoU.2019.0022. Epub 2019 Jun 28. PMID: 31355588; PMCID: PMC6750310.
   Punktacja MNiSW: 20 pkt

4. **Common incidental findings on sacroiliac joint MRI in children clinically suspected of juvenile spondyloarthritis.**
   Schiettecatte E, Jaremko JL, Sudoł-Szopińska I, Znajdek M, Mandegaran R, Swami V, Jans L, Herregods N.
   Eur J Radiol Open. 2020 Mar 4;7:100225. doi: 10.1016/j.ejro.2020.100225. PMID: 32154331; PMCID: PMC7058907.
   Punktacja MNiSW: 70 pkt

5. **Determination of Relative Weightings for the Component Pathologies of the OMERACT Juvenile Arthritis Magnetic Resonance Imaging Sacroiliac Joint Score.**

   Otobo TM, Tolend M, Meyers AB, Sudol-Szopinska I, Joshi S, Stimec J, Herregods N, Jaremko JL, Tse SML, Haroon N, Moineddin R, Tzaribachev N, Appenzeller S, Znajdek M, Perez M, Ligha AE, Jans L, Inarejos Clemente EJ, Weiss P, Papakonstantinou O, Kirkhus E, van Rossum MAJ, Rumsey DG, Carrino J, Akikusa JD, Conaghan PG, Doria AS. J Clin Med. 2023 Apr 6;12(7):2729. doi: 10.3390/jcm12072729. PMID: 37048812; PMCID: PMC10095587.
   Punktacja MNiSW: 140 pkt, IF 4,964

W pierwszej z cyklu publikacji wprowadzających w tematykę pracy, zatytułowanej *Imaging of Juvenile Spondyloarthritis. Part I: Classifications and Radiographs*, przedstawiono klasyfikpA oraz obraz radiograficzny JS.

JSpA stanowią ok. 10–20% przypadków (SpA). Według ILAR należą, jak wspomniano powyżej, do obrazu klinicznego MIZS (1).

Kryterium rozpoznania JSpA jest obecność zapalenia stawów i przyczepów ścięgien albo zapalenia stawów lub zapalenie przyczepów ścięgien oraz obecność co najmniej dwóch poniższych kryteriów. Są to:

1. bolesność SKB lub zapalny ból krzyża;
2. obecność antygenu HLA-B27;
3. wywiad rodzinny wskazujący na co najmniej jednego krewnego I lub II stopnia z chorobą związaną z obecnością antygenu HLA-B27;
4. zapalenie przedniego odcinka błony naczyniowej oka;
5. wystąpienie zapalenia stawów u chłopca po ukończeniu 6. roku życia.

Ponadto warunkiem koniecznym do postawienia diagnozy jest wykluczenie łuszczycy u chorego lub krewnego I lub II stopnia, a także obecność układowego zapalenia stawów.

Najczęstsze objawy JSpA to zapalenie przyczepów ścięgnistych oraz kliniczne cechy zapalenia stawów typu oligo- i polyarthritis z przewagą zajęcia stawów kończyn dolnych (najczęściej staw kolanowy, biodrowy, skokowy, śródstopno-paliczkowy i międzypaliczkowy palucha) (12).

U około 30–40% dzieci choroba postępuje, dochodzi do zajęcia SKB, a u części także do zajęcia kręgosłupa, które – inaczej niż u dorosłych – zazwyczaj nie są objęte procesem zapalnym w początkowym etapie choroby (15–17).

Współczesny proces diagnostyki obrazowej osiowych postaci SpA u osób dorosłych opiera się na radiografii konwencjonalnej i MR, zgodnie z kryteriami z ASAS z 2009 roku, stosowanymi u pacjentów z tzw. przewlekłym lub zapalnym bólem pleców (krzyża) (9).

U pacjentów w wieku rozwojowym, podobnie jak u dorosłych, wiarygodna diagnoza sacroiliitis na podstawie zdjęcia RTG jest możliwa dopiero po kilku miesiącach lub nawet latach od początku choroby. Wczesne etapy sacroiliitis nie są widoczne na radiogramach albo ich diagnoza jest obarczona dużym odsetkiem pomyłek. Podobna sytuacja dotyczy zmian zapalnych w kręgosłupie, które we wczesnym etapie nie są widoczne na radiogramach i zwykle rozwijają się później niż sacroiliitis (14). Mimo tych ograniczeń radiografia szkieletu osiowego i stawów obwodowych jest nadal w wielu ośrodkach podstawą diagnozy JSpA.

W badaniu radiograficznym w przypadku sacroiliitis:

– mogą być zajęte zarówno części chrzęstne, jak i część więzadłowa stawu;
– część biodrowa SKB jest zajęta wcześniej, prawdopodobnie z powodu czynników mechanicznych i anatomicznych;
– początkowo zarysy powierzchni stawowych są nieostre (utrata linearnego brzegu kości korowej), następnie widoczne są płytkie nadżerki i podchrzęstne obszary sklerotyczne;
– wraz ze zwiększeniem liczby nadżerek powierzchnia kostna staje się wyraźnie nierówna, szpara stawowa ulega poszerzeniu;
– kolejnym etapem choroby jest odcinkowe zwężenie przestrzeni stawowej z tworzeniem się mostków kostnych.

Ankyloza u dzieci występuje bardzo rzadko (głównie u młodych dorosłych). Zazwyczaj rozpoznawany jest stopień 1, 2 lub 3 sacroiliitis według kryteriów nowojorskich (NY) (17, 18).

W drugiej publikacji włączonej do cyklu prac, pt. *Imaging of Juvenile Spondyloarthritis. Part II: Ultrasonography and Magnetic Resonance Imaging*, omówiono wykorzystanie ultrasonografii (USG) oraz badania MR w diagnostyce JS.

Badanie MR jest obecnie szeroko stosowaną metodą w celu wczesnej diagnostyki JS, choć, jak wspomniano wcześniej, dopiero w 2021 r. opracowano kryteria MR rozpoznawania sacroiliitis u dzieci.

Zmiany widoczne w MR podzielono na tzw. aktywne i przewlekłe (strukturalne) (9). Zgodnie z JAMRIS-SIJ do zmian zapalnych tzw. aktywnych zaliczane są:

– obrzęk szpiku kostnego (*bone marrow edema*, BME);
– zapalenie w jamie stawu;
– wysięk;
– zapalenie torebki stawowej (*capsulitis*);
– zapalenie przyczepów więzadeł (*enthesitis*).

Do zmian tzw. przewlekłych należą:

– podchrzęstna sklerotyzacja;
– nadżerki;
– metaplazja tłuszczowa w nadżerce (*backfill*);
– tłuszczowa przebudowa (metaplazja) szpiku kostnego;
– mostki kostne, ankyloza.

W porównaniu z badaniem RTG badanie MR cechuje wyższa czułość w diagnozowaniu sacroiliitis (5, 11, 14). MR pozwala na rozpoznanie wczesnych zmian zapalnych niewidocznych w RTG. Ostatnie prace porównujące obie modalności wykazują ponadto, że w MR dobrze widoczne są zmiany przewlekłe (6), w związku z czym istnieje duże prawdopodobieństwo, że w przyszłości MR zastąpi także w tym zakresie badanie RTG.

W artykule podkreślono ponadto istotną rolę badania USG w diagnostyce zapalenia stawów obwodowych i entez, które cechują jSpA. Natomiast nie jest to metoda pozwalająca na diagnostykę sacroiliitis.

W kolejnej publikacji, *Juvenile spondyloarthritis and chronic recurrent multifocal osteomyelitisoverlap syndrome in a 16 y.o. adolescent. A case report and literature review*, omówiono rzadki przypadek zespołu nakładania młodzieńczej spondyloartropatii i przewlekłego nawracającego wieloogniskowego zapalenia kości i szpiku (*chronic recurrent multifocal osteomyelitis*, CRMO) u 16-letniej dziewczynki diagnozowanej w naszym ośrodku i trudności diagnostyczne związane z rozpoznaniem tej choroby.

Przykład ten ilustruje złożony proces rozpoznawania chorób reumatycznych u pacjentów wieku rozwojowego, szczególnie skomplikowany w przypadku współistnienia kilku jednostek u jednego pacjenta. Ścisła współpraca klinicystów

i radiologów jest w takich przypadkach konieczna, jednak nawet wówczas nierzadko dochodzi do opóźnień diagnostycznych (w omawianym przypadku 4 lata) – dzieje się tak z uwagi na brak jednoznacznych objawów oraz specyficznych markerów serologicznych, konieczność wykluczania kolejno innych artropatii i poszerzania diagnostyki o kolejne badania. Skutkuje to wyjściowo brakiem optymalnego leczenia, co prowadzi do progresji choroby. U naszej chorej rozpoznanie ustalono w badaniu MR na podstawie obecności mnogich obszarów BME, ognisk litycznych oraz zmian sklerotycznych w charakterystycznych dla obu jednostek chorobowych lokalizacjach, które korelowały z objawami klinicznymi: bólami kostno-stawowymi oraz obrzękami. Ponadto badania laboratoryjne wykazały miernie podwyższony poziom CRP oraz obecność antygenu HLA-B27. W początkowym etapie choroby wykonywano badania RTG i MR, następnie wyłącznie w MR, pod kątem monitorowania skuteczności leczenia i aktywności choroby.

Czwarta uwzględniona w cyklu praca oryginalna, pt. *Common incidental findings on sacroiliac joint MRI in children clinically suspected of juvenile spondyloarthritis*, powstała w ramach międzynarodowej współpracy pomiędzy ośrodkami polskim (ośrodek własny), belgijskim (Szpital Uniwersytecki w Gandawie) i kanadyjskim (Szpital Uniwersytetu Alberty).

W ramach retrospektywnego wieloośrodkowego badania stworzono repozytorium badań pochodzących z trzech ośrodków z lat 2012–2018. Zgromadzono w nim 540 badań MR stawów krzyżowo-biodrowych dzieci z klinicznym podejrzeniem JS, po 180 badań z każdego ośrodka. Materiał obejmował 267 (51%) badań MR SKB chłopców i 264 (49%) badania dziewczynek, ze średnią wieku, odpowiednio, 14,8 roku oraz 14,4 roku (zakres 0,9–23,1). W ośrodku belgijskim (BEL) mediana wieku pacjentów wynosiła 13,5 roku, średnia wieku 13,4 roku, zakres 4,3–23. Mediana wieku pacjentów z ośrodka w Kanadzie (CAN) wynosiła 15,5 roku, średnia wieku 14,8 roku, zakres 0,9–20,6. W grupie pacjentów własnych (POL) mediana wieku pacjentów wynosiła 15,3 roku, średnia wieku 14,8 roku, zakres 4,8–18,4.

Celem analizy było określenie spektrum zmian zapalnych w SKB oraz zmian przypadkowo rozpoznawanych w miednicy w trakcie diagnostyki MR sacroiliitis.

W przeprowadzonym badaniu cechy sacroiliitis stwierdzono w MR u 106/540 (20%) dzieci. Co ciekawe, u dwukrotnie większej liczby chorych, tj. u 228 (42%) pacjentów, badanie MRI wykazało co najmniej jedną przypadkową zmianę/nieprawidłowość inną niż sacroiliitis. Łącznie stwierdzono 271 nieprawidłowych „znalezisk". Najczęstsze zmiany występowały w kręgosłupie lędźwiowo-krzyżowym

(158 pacjentów, 29%) i w stawach biodrowych (43 pacjentów, 8%). Najliczniejsze przypadki obejmowały: zmiany zwyrodnieniowe odcinka lędźwiowego kręgosłupa (94 pacjentów, 17%), prostą (kostną) torbiel (15 pacjentów, 2,8%), enthesitis u 16 pacjentów (3%), niespecyficzny ogniskowy BME w lokalizacji pozastawowej (nietypowy dla JSpA) u 10 pacjentów (1,9%), torbiele jajników u 7 pacjentek (1,3%), BME w przebiegu CRMO u 4 pacjentów (0,7%), patologie mięśni u 4 pacjentów (0,7%), zmiany ogniskowe o charakterze łagodnym u 3 pacjentów (0,6%), przebyte złamania u 3 pacjentów (0,6%), przebyte urazy awulsyjne kostnego wyrostka nasady u 2 pacjentów (0,4%) oraz guzy złośliwe u 2 pacjentów (0,4%). Co istotne, u 7,5% pacjentów stwierdzono w MR zapalenie stawu biodrowego i entezopatie, co u pacjentów z podejrzenie JSpA może być ściśle powiązane z chorobą podstawową, zwłaszcza że JS częściej przebiega z objawami zapalenia stawów obwodowych i entezopatii, podczas gdy sacroiliitis i spondylitis z reguły rozwijają się w okresie późniejszym (11, 12, 16, 17).

Przeprowadzone badanie wykazało, że u wielu pacjentów diagnozowanych pod kątem sacroiliitis w badaniu MR wykrywane są przypadkowo inne nieprawidłowości, których częstość przewyższa liczbę rozpoznawanych przypadków sacroiliitis, przy czym wiele wymaga pilnej interwencji.

Ostatnią w cyklu zgłoszonych prac jest publikacja oryginalna podsumowująca efekty wieloletniej międzynarodowej współpracy naszego ośrodka, której celem było opracowanie kryteriów oceny sacroiliitis u dzieci i młodzieży (10). Celem pracy zatytułowanej *Determination of Relative Weightings for the Component Pathologies of the OMERACT Juvenile Arthritis Magnetic Resonance Imaging Sacroiliac Joint Score* było dokonanie walidacji skali JAMRIS-SIJ na materiale 14 badań MR stawów krzyżowo-biodrowych, które zostały poddane wnikliwej analizie przez 17 międzynarodowych ekspertów. Ocenie podlegały zmiany zapalne aktywne (zapalenie szpiku kostnego (*osteitis*), BME, zapalenie w nadżerce, wzmocnienie w szparze stawu, wysięk w stawie, zapalenie torebki stawowej, zapalenie więzadeł) oraz przewlekłe/destrukcyjne (sklerotyzacja, tłuszczowa przebudowa szpiku, metaplazja tłuszczowa w nadżerkach, nadżerki, ankyloza). Ocena polegała na przyporządkowaniu uwidocznionym zmianom wag(*weights*)/udziałów, istotnych pod kątem rozpoznania sacroiliitis.

Dwa najbardziej istotne pod względem diagnostyki sacroiliitis elementy obrazu chorobowego w MR, tj. zapalenie szpiku kostnego (tzn. *osteitis*, rozpoznawany w badaniu MR po dożylnym podaniu środka kontrastującego) i BME uzyskały

równoważne wartości wag w opinii eksperckiej: *osteitis* (24,7%) i BME (24,3%). Ich średnie wagi procentowe były wyższe w porównaniu z uzyskanymi dla pozostałych cech chorobowych, jak zapalenie w nadżerce (16,9%), wzmocnienie w jamie stawu (13,1%), wysięk w jamie stawu (9,1%), zapalenie torebki (7,3%) i zapalenie przyczepów (4,6%). Podobnie w domenie uszkodzeń ankyloza (41,3%) i nadżerka (25,1%) wykazały wyższe średnie wagi w porównaniu z metaplazją tłuszczową w nadżerce (13,9%), sklerotyzacją (10,7%) i metaplazją tłuszczową szpiku kostnego (9,1%) (tabela 1).

Podczas gdy ankyloza jest zaawansowanym, nieodwracalnym powikłaniem zapalenia, BME i nadżerka zostały uznane za preferowane elementy obrazu chorobowego, które należy monitorować w MR, oceniając skuteczność leczenia JSpA. Obecność BME jest wskaźnikiem aktywności choroby, dowodem umożliwiającym rozpoczęcie terapii. Nadżerka z kolei została uznana za negatywny czynnik prognostyczny, który wymaga stosowania bardziej agresywnej terapii w JSpA, takiej jak biologiczne środki lecznicze (19).

Ponadto współczynnik korelacji Spearmana dla kolejności winiet ważonych CAS i nieważonych ocen JAMRIS-SIJ dla wszystkich ekspertów wyniósł 0,79 dla domeny aktywnego zapalenia i 0,80 dla uszkodzeń. Korelacje między winietami obrazów ekspertów w dziedzinie obrazowania a wynikami CAS wynosiły 0,75 dla zapalenia i 0,90 dla uszkodzeń. Analiza wielokryterialna zidentyfikowała różnice we względnych wagach między elementami pomiarowymi JAMRIS-SIJ. Najwyższą zgodność oceny eksperckiej 14 badań MR (winiet JAMRIS-SIJ), obliczoną według CAS, uzyskano w przypadku najmniej i najbardziej zaawansowanego sacroiliitis, podczas gdy dla mniej zaawansowanych przypadków ocena była znacznie zróżnicowania (ryc. 1A, B).

Uzyskane różnice wag elementów pomiarowych w JAMRIS-SIJ były podobne jak w przypadku systemu oceny MRI stawów skroniowo-żuchwowych w MIZS (20).

Przeprowadzone badanie udowodniło przydatność skali JAMRIS-SIJ, tym samym badania MR do diagnostyki JS, określania aktywności choroby i oceny skuteczności leczenia (21). Badanie potwierdziło, że w celu obiektywnej oceny aktywności JS i monitorowania skuteczności terapii można wykorzystać wieloskładnikowy wynik JAMRIS-SIJ bez ważenia każdego składnika. Jednak pożądane jest również wygenerowanie pojedynczego złożonego wyniku jako biomarkera. Takie podejście, tj. ważenie, czyli przyporządkowanie wartości punktowych poszczególnych elementów pomiarowych pod względem ich znaczenia klinicznego, wpływa na optymalizację ostatecznego wyniku, który uwzględnia czułość i specyficzność poszczególnych zmian

w kontekście diagnostyki JS, poprawiając trafność konstrukcyjną złożonego wyniku domeny poprzez zwiększenie ważenia zmian, które są bardziej specyficzne i/lub czułe na JIA.

8. Wnioski

1. Młodzieńcze zapalenie stawów krzyżowo-biodrowych jest częstym problemem klinicznym, niejednokrotnie o niespecyficznej symptomatologii, wymagającym poszerzenia diagnostyki o badania obrazowe w celu uzyskania wczesnej diagnozy.
2. Badanie MR jest metodą o wyższej czułości niż badanie RTG w diagnostyce i monitorowaniu zmian zapalnych w stawach krzyżowo-biodrowych u dzieci z klinicznym rozpoznaniem sacroiliitis.
3. Zmiany zapalne w SKB są w badaniu MR stwierdzane u 20% dzieci i młodzieży z klinicznym rozpoznaniem sacroiliitis.
4. U istotnego odsetka dzieci (42%) z klinicznym podejrzeniem sacroiliitis w badaniu MR wykrywane są przypadkowe zmiany, których częstość przewyższa liczbę rozpoznawanych przypadków sacroiliitis (20%) i w wielu przypadkach wymaga interwencji.
5. Zaproponowana skala oceny zmian zapalnych SKB w MR (skala JAMRIS-SIJ), uwzględniająca kryteria sacroiliitis, przeznaczona dla pacjentów wieku rozwojowego, jest użyteczna w diagnostyce sacroiliitis, w ocenie aktywności choroby i może być wykorzystana do monitorowania skuteczności leczenia.

9. Przedstawienie opublikowanych prac

1. **Imaging of Juvenile Spondyloarthritis. Part I: Classifications and Radiographs.**
   Sudoł-Szopińska I, Gietka P, Znajdek M, Matuszewska G, Bogucevska M, Damjanovska-Krstikj L, Ivanoski S.
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Imaging of juvenile spondyloarthritis. Part I: Classifications and radiographs

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Keywords
juvenile spondyloarthritis, enthesitis-related arthritis, juvenile psoriatic arthritis, reactive arthritis, juvenile ankylosing spondylitis

Abstract

Juvenile spondyloarthropathies are manifested mainly by symptoms of peripheral arthritis and enthesitis. By contrast with adults, children rarely present with sacroiliitis and spondylitis. Imaging and laboratory tests allow early diagnosis and treatment. Conventional radiographs visualize late inflammatory lesions and post-inflammatory complications. Early diagnosis is possible with the use of ultrasonography and magnetic resonance imaging. The first part of the article presents classifications of juvenile spondyloarthropathies and discusses their radiographic presentation. Typical radiographic features of individual types of juvenile spondyloarthritis are listed (including ankylosing spondylitis, juvenile psoriatic arthritis, reactive arthritis and arthritis in the course of inflammatory bowel diseases). The second part will describe changes visible on ultrasonography and magnetic resonance imaging. In patients with juvenile spondyloarthropathies, these examinations are conducted to diagnose inflammatory lesions in peripheral joints, tendon sheaths, tendons and bursae. Moreover, magnetic resonance imaging also visualizes early inflammatory changes in the axial skeleton and subchondral bone marrow edema, which is considered an early sign of inflammation.

Introduction

Juvenile-onset spondyloarthropathies (JSpAs) account for 15–20% of all forms of arthritis occurring in the developmental age[1]. They belong to rheumatic diseases with first symptoms, in the form of peripheral arthritis and enthesitis of non-symmetrical localization as well as axial skeleton inflammation, appearing prior to the age of 16. Apart from musculoskeletal symptoms, the disease may also affect the eyes, bowels, skin as well as (although very rarely) heart and lungs[1,2].

The etiopathogenesis of JSpA has not been fully explained. The development of the disease depends on genetic and infectious factors. The presence of HLA–B27 antigen, with its most common subtype HLA-B27*05, is characteristic of JSpA[1]. The IgM rheumatoid factor (IgM-RF) and antinuclear antibodies (ANA) are not detected in the serum[1]. TNFα cytokine is said to play an important role in the etiopathogenesis. It takes part in neutrophil and lymphocyte activation and upregulation of adhesion molecules, stimulates production of other proinflammatory cytokines and promotes the production of matrix metalloproteinases. All these effects have an impact on bone and cartilage resorption[2]. As in adults, increased intestinal permeability is underlined also in JSpA. It enables transition of enterobacterial antigens that induce arthritis[4]. In the initial phase of the disease, inflammatory infiltrates and vascular changes prevail in the synovium. Later, extensive fibrosis of the joint capsule is observed. The changes within the sacroiliac joints, i.e. inflammatory infiltrates in the subchondral bone tissue, synovitis with subsequent destructive lesions (erosions) of the articular surfaces or syndesmosis inflammation, are identical to those observed in spondyloarthropathies in adult patients. The inflammatory reaction may be observed in only one sacroiliac joint, particularly in the initial stage of the disease, and only later in the other. Inflammation can also involve joints of the spine.

Clinical classifications

Juvenile spondyloarthropathies can be divided into undifferentiated and differentiated forms (Tab. 1).

	Undifferentiated forms
1.	Seronegative enthesopathy and arthropathy syndrome (SEA)
2.	Enthesitis-related arthritis (ERA)
	Differentiated forms
1.	Juvenile ankylosing spondylitis (JAS)
2.	Psoriatic arthritis (PsA)
3.	Reactive arthritis (ReA)
4.	Arthritis associated with inflammatory bowel diseases (IBD)

Tab. 1. *Classification of juvenile spondyloarthropathies*[1]

JSpAs are difficult to diagnose and differentiate particularly from juvenile idiopathic arthritis (JIA). Apart from undifferentiated forms (seronegative ones – absence of rheumatoid factor), which are sometimes initially included in the group of JIA, the symptoms of JSpAs develop gradually in many patients[2]. By contrast with adults with spondyloarthropathies[6,7], the disease in children rarely starts with involvement of the sacroiliac joints or spine. Moreover, children rarely meet the modified New York criteria (for radiographs), used in diagnosing SpA in adults[7].

Currently, there are several classifications and diagnostic criteria for JSpA, including those used in adult patients and validated for children (Amor, ESSG, ASAS criteria for peripheral spondyloarthropathy) as well as criteria prepared specifically for JSpA (SEA, Garmisch-Partenkirchen, ILAR)[2,3,8].

According to ILAR (International League of Associations for Rheumatology), JSpAs are classified as one of JIA entities, called ERA (enthesitis-related arthritis) (Tab. 2). However, this definition excludes cases of reactive arthritis, enteropathy-related arthritis, juvenile ankylosing spodylitis and juvenile psoriatic arthritis[1,2,9].

	JIA category
1.	Systemic arthritis
2.	Oligoarthritis (persistent or extended)
3.	Polyarthritis (RF negative)
4.	Polyarthritis (RF positive)
5.	Psoriatic arthritis
6.	Enthesitis-related arthritis (ERA)
7.	Undifferentiated arthritis

Tab. 2. *International League of Associations for Rheumatology (ILAR) classification of juvenile idiopathic arthritis*

According to the ESSG (European Spondyloarthropathy Study Group), JSpAs are a separate group of diseases, divided into entities as in adult patients. In the initial stage of the disease, most of JSpA cases are classified as undifferentiated, so-called seronegative enthesopathy and arthritis syndrome (SEA). Differentiated forms encompass four entities (Tab. 3). A classification criterion is, according to ESSG, the presence of so-called inflammatory back pain (as in adults) (Tab. 4), but identification of this symptom in children is frequently problematic[1,2,3,9].

JSpA can be diagnosed when the ESSG criteria, listed in Tab. 4, are met. Subsequently, one of the aforementioned forms of JSpA is specified, as shown in Tab. 3.

	Undifferentiated forms
1.	Seronegative enthesopathy and arthritis syndrome (SEA)
	Differentiated forms
1.	Juvenile ankylosing spondylitis (JAS)
2.	Reactive arthritis (formerly including Reiter's syndrome)
3.	Arthritis associated with inflammatory bowel diseases (IBD)
4.	Juvenile psoriatic arthritis (JPsA)[2,9]

Tab. 3. *Juvenile spondyloarthropaties divided into differentiated and undifferentiated forms according to ESSG*

Inflammatory sacral pain or asymmetrical synovitis in the lower extremities plus at least one of the following:	
1.	Positive family history
2.	Psoriasis
3.	Inflammatory bowel disease
4.	Urethritis, cervicitis or acute diarrhea occurring within one month before onset of arthritis
5.	Pain alternating between the right and left buttock
6.	Enthesopathy*
7.	Sacroiliitis**
Exceptions: none	

* Enthesopathy – past or present pain in an enthesis on physical examination.

** Sacroiliitis that meets so-called modified New York criteria[9,10,11].

Tab. 4. *ESSG criteria for the classification of spondyloarthropathies*[2,11]

Seronegative enthesopathy and arthritis syndrome (SEA) was first described in 1982 by Jacobs et al., who found signs of enthesitis in 75% of children with positive HLA-B27 in the serum[1,12]. Other authors demonstrated that this syndrome can reflect initial pauciarticular (oligoarticular) form of reactive arthritis or the onset of childhood arthropathies associated with HLA–B27 antigen. Moreover, Burgos-Vargas et al.[13], reported that 75% of children with an initial diagnosis of SEA developed JAS within 5 years. The diagnosis of SEA in the articles quoted above was based on a clinical examination. At present, such data must be verified in imaging, i.e. by ultrasonography (US) and magnetic resonance imaging (MRI). Coates et al.[14] admitted that clinical assessment of enthesitis (edema and pain at the site of an enthesis subsiding upon mobilization) does not display a sufficient correlation with a US and MR image. Our own observations and prospective studies based on the calcaneal tuberosity in adults[15] did not confirm that US features visible in patients with clinically suspected enthesitis of the Achilles tendon and plantar fascia enable confirmation of the clinical diagnosis of enthesitis. We did not find any signs of increased vascularization of the entheses. Instead there were scars at various levels of organization, delaminated tears, shallow irregularities or erosions and cysts in the bony component of the entheses. In adults, they are usually a sign of chronic microinjuries and degeneration. The spectrum of changes in children has not been published thus far.

Moreover, statistical data on the number of children with a changed diagnosis in the course of the disease are not known either[16]. According to some reports, the verification of the diagnosis from JIA to JSpA takes place in 0–4% to even 36% of patients with chronic peripheral arthritis[5,16]. This results from the fact that most patients with JSpA initially suffer from peripheral arthritis, which is impossible to distinguish from JIA[16]. Such an inflammation is persistent and non-destructive (*persistens non-destructive*)[16]. According to Rosenberg and Petty's hypothesis concerning enthesopathic arthropathy, ERA (i.e. JSpA according to ILAR) and enthesitis in particular, may be a prodromal manifestation of seronegative spondyloarthropathies[17]. This hypothesis is not confirmed by all reports: according to various authors[18], JSpA (or more precisely JAS) was diagnosed in 9% to 92% of cases within 5 years in patients with enthesitis at the onset of the disease.

Factors of poor prognosis

The predictors of JSpA progression are: involvement of the tarsal joints, presence of HLA-B27 antigen, absence of HLA-DPB1*02, involvement of the hip joint in the first 6 months of the disease and the onset after the age of 8[12]. Flato et al. analyzed data of children registered during the first visit and their records after 10 years from the onset. They demonstrated that risk factors of progression and disability were persistently active disease and polyarticular course 5 years after the first visit ($p<0.05$)[8]. The predictors of erosions (articular destruction) were: elevated erythrocyte sedimentation rate (ESR) persisting for a long time, delayed decision to see a doctor and delayed treatment with so-called disease-modifying antirheumatic drugs (DMARDs)[8]. The analysis revealed that early diagnosis and treatment are significant in disease preventing progression and its complications[18].

Difficulties in early diagnosis

As has been mentioned above, an early diagnosis of JSpA is difficult and frequently delayed by several years (average 8.3 years) due to a different picture in the initial stage of the disease than in ankylosing spondylitis (AS) in adults[13,19,18]. In children, peripheral joints are usually involved whereas axial skeleton involvement prevails in adults[5,19]. Sacroiliitis and spodylitis can be observed in children usually 5–10 years after the onset[5,19]. Typically, joints of the lower extremities are involved. Changes in the upper limbs are rarely observed; in such cases, humeral joint is usually inflamed, and slight joints of the hand are spared[19].

Tarsitis, diagnosed in 1/3 of patients at the initial stage of the disease, is a unique sign of JSpA[13]. Moreover, enthesitis, which is identified in a clinical examination in 60–80% of patients[13], is typical of JSpA. According to clinical data, inflammation usually involves the patellar ligament, Achilles tendon and plantar fascia.

Burgos-Vargas et al.[20] compared the clinical picture of JAS (onset <16 years of age) and AS (onset in adulthood). The involvement of peripheral joints was observed in nearly 90% of children and in merely 37.5% of adults with AS. Enthesopathies were present in $^2/_3$ of children and only in $^1/_3$ of adults. The tarsal joints and feet were involved significantly more frequently in children. All children developed peripheral arthropathies as the disease progressed, and 78.7% developed enthesopathies. It adults, the respective values were: 55% and 47.5%[20].

Another cause of diagnostic pitfalls is a similar clinical picture of JSpA and JIA. In both cases, there are features of

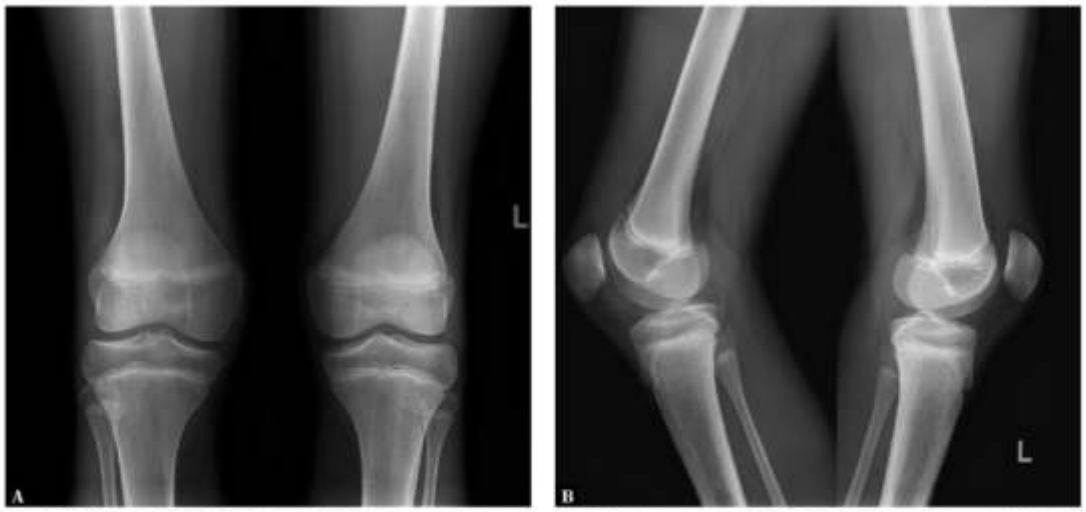

Fig. 1. *AP* **(A)** *and lateral* **(B)** *radiographs of the knee joints in a 16-year-old boy: increased density of periarticular soft tissue with lesions prevailing on the right side and hypertrophied epiphyses of the right knee joint*

peripheral arthritis, tenosynovitis, enthesitis or SEA. The disease is usually classified as one of JIA forms, most often as type 2 (pauciarticular juvenile rheumatoid arthritis, JRA) [18]. Spondylitis and sacroiliitis as well as progression of SEA to AS are observed in most children 5–10 years after the onset[18]. Compared with adults, the axial skeleton is rarely involved in the first year after the onset[18]. In JSpA, the disease rarely progresses to the radiographic forms of bilateral sacroiliitis that fulfil the New York criteria for adults[17].

Based on these observations, 2 types of JAS onset have been defined: 1) the aforementioned SEA syndrome – the involvement of peripheral joints and entheses with progression to AS several years after the onset, and 2) a rarer form resembling adult AS in which the axial skeleton becomes involved shortly after the onset[19].

Burgos-Vargas et al.[3] identified features of the disease that enable the differentiation of early JAS from early JIA in the first year after the onset. They are: pauciarthritis/oligoarthritis, enthesitis in the lower extremities, tarsitis, presence of HLA-B27 antigen and rare involvement of the joints of the upper extremity (which, in turn, is typical of JIA)[3]. The inflammation of the knee, ankle and interphalangeal joints was observed in both forms with a similar frequency. In the material of Burgos-Vargas et al., the hip joint became involved several years after the onset whereas other authors report its involvement in the early stage of JAS[3].

Imaging of juvenile spondyloarthritis

The contemporary diagnostic process of axial spondyloarthropathies (sacroiliitis and spondylitis) in adults is based on an plain radiography and MRI, in accordance with the ASAS criteria (*Assessment of Ankylosis Spondylitis*) from 2009[6,10,21]. Imaging is conducted in patients with so-called chronic or inflammatory back (spinal) pain[6,10,21].

As has already been mentioned, the identification of this sign in children and adolescents is difficult since it rarely occurs in this age group in the initial stage of the disease or is not reported by children[5,22]. This probably refers to the youngest patients since large population-based studies among adolescents have demonstrated that nearly a half of them experience severe back pain. The frequency of this ailment increases with age and is associated with the sedentary lifestyle and a low level of physical activity. SpA is diagnosed in over 40% of children and adolescents that report to the doctor, which is a greater percentage than in adults in whom mechanical back pain is usually diagnosed[23].

Another reason for diagnostic problems in children and adolescents with suspected SpA is a difficulty in interpreting radiographs, which are often negative in early stages of the disease due to a greater quantity of cartilage than in adults. As in adults, a certain diagnosis of sacroiliitis based on radiography is possible after several months or even years after the onset. Similarly, early inflammatory lesions in the spine are invisible on radiography and usually develop later than sacroiliitis[24].

If, however, radiographic changes in the sacroiliac joints are visible (so-called radiographic form), the consecutive grades of sacroiliitis (according to New York criteria) are not distinct from one another, which results in an uncertain diagnosis of the grade of the disease. Moreover, interpretation of radiographs depends on additional factors: the quality of a radiograph, technique in which it is taken, experience of a radiologist and individual variability in the shape of the sacroiliac joints[25].

As in adult patients with SpA, early stages of sacroiliitis are localized in the subchondral bone tissue, which is visible only on MRI. According to the ASAS criteria, MRI is conducted in adults if radiography is negative, grade 1 sacroiliitis is diagnosed or grade 2 is identified unilaterally[10]. There are no such criteria for children and adolescents with SpA. By contrast with adults with spondyloarthropathies, single existing reports concerning patients with JSpA indicate low specificity of inflammatory back pain. Moreover, there are no critical papers on the diagnostic value of radiography of the sacroiliac joins or publications confirming the usefulness of MRI[22,28].

Still, radiography of the axial skeleton and peripheral joints is the basis for JSpA diagnosis in children. In peripheral spondyloarthropathies, pediatricians base their assessment on a clinical examination of joints and entheses for arthritis and enthesitis. There are no criteria or standards that would include US or MRI in diagnostic schemes of early inflammatory changes; such criteria are already in use with respect to adult patients[6,10,23].

Below, we present radiographic pictures of individual entities belonging to the group of juvenile spondyloarthropathies, according to the ESSG classification[27]. Subsequently, in the second part of that paper, we will discuss the usefulness of US and MRI in the diagnosis of early inflammatory changes in the course of JSpA.

Plain radiography

Juvenile ankylosing spondylitis (JAS)

Juvenile ankylosing spondylitis (JAS) usually begins with acute, subacute or primarily chronic inflammation in a single joint, typically in the lower extremity (knee, ankle or hip joint). Also, inflammation of the first metatarsophalangeal joint and the first interphalangeal joint is typical of the initial stage of the disease. One or both sternoclavicular articulations can be involved. In merely 10–20% of cases, the disease begins with inflammatory back pain.

Radiographic changes are observed in a late stage of the disease when cartilaginous and bony components of peripheral joints or joints of the axial skeleton are already being destroyed. In the axial skeleton, one can observe features of sacroiliitis, which can initially be unilateral. By contrast with AS in adults, children do not usually develop complete ankylosis of the sacroiliac joints (grade IV of sacroiliitis) or the spine. Squaring of the vertebral bodies and syndesmophyte formation are rare. Destructive changes in the body–disk–body complex (spondylodiscitis) are sporadic, and the cervical spine involvement is exceptionally rare.

Peripheral joints (Fig. 1):
- Usually, lower extremity joints are involved, such as: knee, hip, ankle, the first toe; sometimes joints of the upper extremities.
- Changes are usually unilateral.
- Osteoporosis or cysts are visible.
- Erosions are identified extremely rarely; destruction is not extensive.

Entheses (Fig. 2):
Enthesopathic lesions of tendons, aponeuroses and capsuloligamentous complexes are visible as ossifications of various shapes (band-like, linear, cloud-like) and erosions in the bony component of an enthesis. Typical lesions are seen in the entheses of the calcaneal tuberosity.

Sacroiliac joints (SIJs) (Fig. 3):
- Both the cartilaginous (symphysis and synchondrosis types) and syndesmotic parts of the joint can be involved.
- The iliac part of the SIJs becomes involved earlier, probably due to mechanical and anatomic factors.
- Initially, articular margins are blurred (loss of the linear margin of the cortical bone); there are shallow erosions and areas of subchondral sclerosis.
- With increasing number of erosions, the bone surface becomes markedly serrated and the joint space unevenly dilated. Subsequently, segmental narrowing of the joint space with bony bridge formation is observed. Ankylosis in children is very rare (mainly in young adults). Usually, grade I, II or III of sacroiliitis (according to the New York Criteria) is diagnosed[7].

Spine (Fig. 4):
- Lesions in the cervical spine, in the form of vertebral body destruction with subsequent osseous regeneration in the later stage of the disease, may also appear and be the only change within the spine.
- Squaring of the vertebral bodies and syndesmophyte formation are very rare and can develop many years after the onset.
- Sporadically, other lesions, typical of adult AS, may develop: ankylosis of sacroiliac and lumbosacral ligaments, ankylosis of the costovertebral articulations and intervertebral joints, spondylodiscitis and lesions in the atlantoaxial joint.
- Lesions typical of adult patients with AS, such as ankylosis on several levels of the spine and the formation of a "bamboo spine" do not develop.

Moreover, the clinical picture includes eye inflammation, sometimes being the first sign of JAS.

Juvenile psoriatic arthritis (JPsA)

The radiographic image in children is not different from that in adults. However, sacroiliitis and spondylitis are not as common in children. Moreover, the full spectrum of radiographic lesions typical of JPA is rarely observed. Boys more frequently develop sacroiliitis (usually asymmetrical) and spondylitis (C1/C2 subluxation and syndesmophytes are rare). In girls, peripheral arthritis prevails.

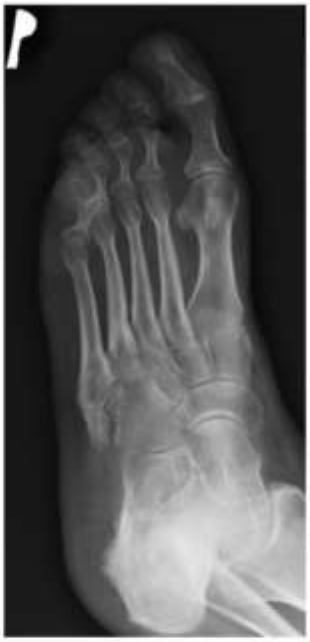

Fig. 2. *Oblique radiograph of the right foot in an 18-year-old boy: enthesopathic changes in the plantar fascia attachment to the calcaneus*

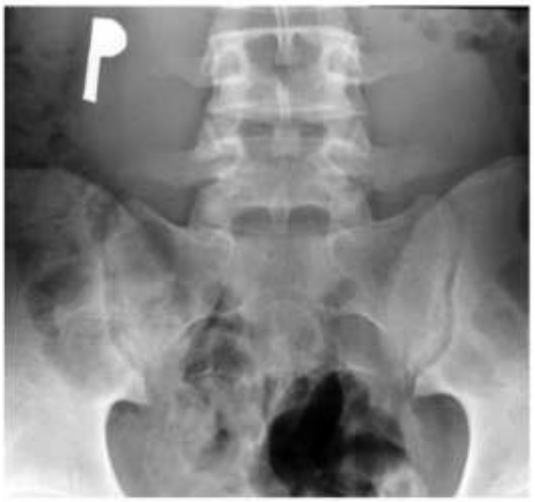

Fig. 3. *AP radiographs of the sacroiliac joints in an 18-year-old girl diagnosed with sacroiliitis in the early period: unclear outline of the sacroiliac joints with changes prevailing on the right side and subchondral bone sclerosis in the right sacroiliac joint*

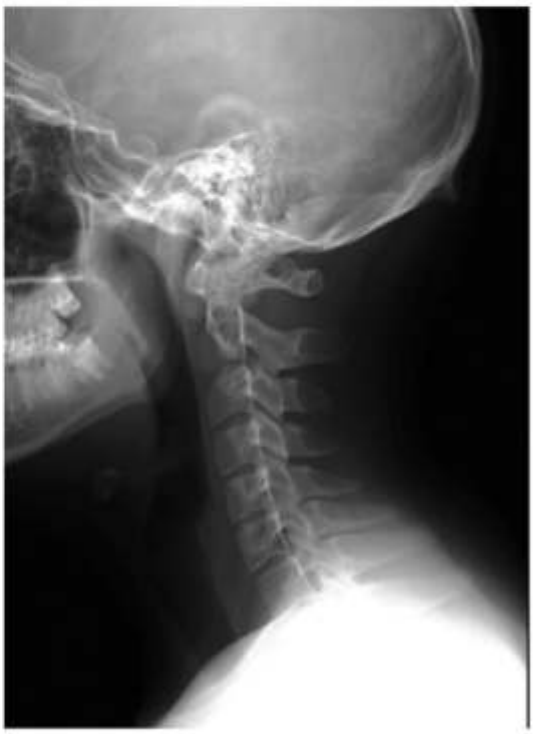

Fig. 4. *Lateral radiograph of the cervical spine in a 16-year-old patient with AS: loss of cervical lordosis and the concave line of anterior parts of the cervical vertebral bodies*

Entheses:

- Enthesopathic lesions are frequently the only sign for a long time.
- Enthesopathic lesions of tendons, aponeuroses and capsuloligamentous complexes are visible as ossifications of various shapes (band-like, linear, cloud-like) and erosions in the bony component of an enthesis (typically in the region of the calcaneal tuberosity).

Peripheral joints (Fig. 5):

- The image is initially normal, or periarticular osteoporosis is present.
- The disease usually begins with inflammation in a single joint (typically the knee) or several articulations (knee, ankle, hip, foot). The further course is in most patients polyarthritic with asymmetrical lesions involving joints of the upper and lower extremities.
- Periosteal thickening (periostitis) on the phalanges, metacarpal and metatarsal shafts is typical.
- Acroosteolysis of the distal phalanges is characteristic.
- Sometimes, osteolysis and ankylosis are observed in the same hand and foot.
- Inflammation of distal interphalangeal joints in the hands and feet with simultaneous destruction (geodes, erosions) and proliferative lesions are typical.
- Joint space narrowing.
- The image of so-called "sausage digits" in the course of tenosynovitis of flexor digitorum tendons or inflamma-

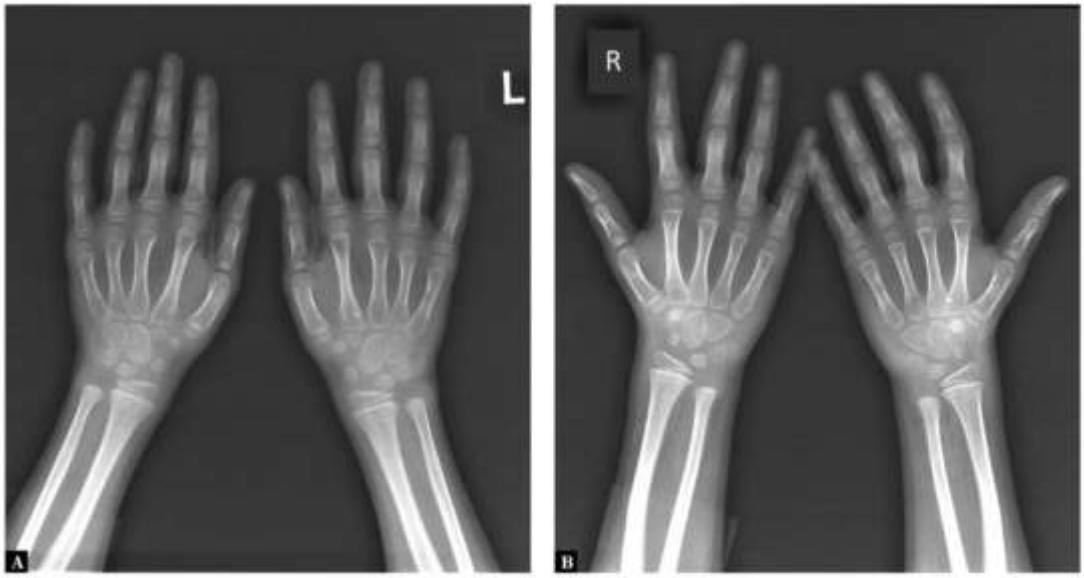

Fig. 5. *AP* **(A)** *and oblique* **(B)** *radiograph of the hands in a 6-year-old girl: periarticular osteoporosis of the hands, periosteal buildup/thickening along the 2nd and 3rd distal phalanges of both hands*

tion of soft tissues of a digit, or as a result of synovitis of the proximal and distal interphalangeal joints.
- Inflammatory changes are more symmetrical than in JIA.

Reactive arthritis (ReA)

This form of the disease is rare in children. It is characterized by enthesopathies of the calcaneal tuberosity.

Peripheral joints are usually asymmetrically involved. Similarly to JPsA, this concerns several or numerous large joints of the lower extremity (often the knee and ankle, rarely the hip joint). Sometimes, small joints of the foot are involved as well (sausage toes).

Sacroiliitis, usually symmetrical and bilateral (rarely unilateral), is observed. The lesions in the SIJ are similar to those in JAS.

Peripheral joints:
- Thickening and increased density of periarticular soft tissue – identical to JAS.
- Periarticular osteoporosis appears during an acute attack; in chronic inflammation, it can be invisible or poorly marked.
- Erosions are initially marginal and subsequently subchondral; joint space narrowing.

Entheses:
- Compared to adults with ReA, enthesopathies occur more rarely.

Spondyloarthritis in the course of colitis ulcerosa and Crohn disease (enteropathic JSpA)

JSpA is found in approximately 10% of children with inflammatory bowel diseases, more often in those with Crohn's disease than ulcerative colitis. Arthritis may pre-

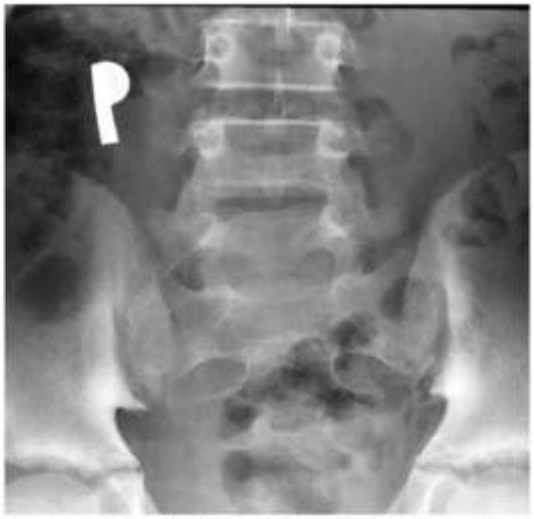

Fig. 6. *AP radiograph of the sacroiliac joints in an 18-year-old patient with Crohn disease: uneven and obscure lines of the right sacroiliac joint*

cede bowel disease, but usually develops in the course of enteropathy (Fig. 6).

There are two forms of this JSpA: a peripheral form with peripheral arthritis and a rarer axial form with sacroiliitis and spondylitis.

Peripheral joints:
- In the peripheral form, large joints of the lower extremity are usually involved (typically the knee and ankle). The wrist, hand and glenohumeral joints are involved more rarely, sometimes asymmetrically.
- Thickening and increased density of periarticular soft tissue.
- Periarticular osteoporosis.
- Usually, there are no features of bone destruction.

Entheses:
Typically, enthesopathic lesions of the Achilles tendon and plantar aponeurosis up to the calcaneal tuberosity.

Axial skeleton:
- Involvement of the spine and sacroiliac joints is rare in children; these changes develop in adulthood.
- The radiological picture resembles JAS. The sacroiliac joints are usually involved symmetrically, the involvement of the spine with squaring of the vertebral bodies and syndesmophyte formation is less common.

Conclusion

Plain radiography still remains a standard in the diagnostic process of early inflammatory changes in the course of JSpAs. Its role is, among others, to rule out malignancies, trauma or specific inflammations of bones and joints. In early stages of JSpAs, radiographs are usually negative or reveal features of osteoporosis, increased radiodensity and extended shadow of soft tissues or hypertrophic epiphyses. Depending on the clinical suspicion, the next examination is ultrasonography or magnetic resonance imaging in order to diagnose early inflammatory lesions in peripheral joints, tendon sheaths, bursae or entheses, or abnormalities in the course of axial spondyloarthropathies. Changes seen in these examinations will be discussed in the second part of the publication.

Conflict of interest

Authors do not report any financial or personal connections with other persons or organizations, which might negatively affect the contents of this publication and/or claim authorship rights to this publication.

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2. **Imaging of Juvenile Spondyloarthritis. Part II: Ultrasonography and Magnetic Resonance Imaging.**
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Imaging of juvenile spondyloarthritis. Part II: Ultrasonography and magnetic resonance imaging

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Keywords
juvenile spondyloarthropathies, ultrasonography, magnetic resonance imaging

Abstract

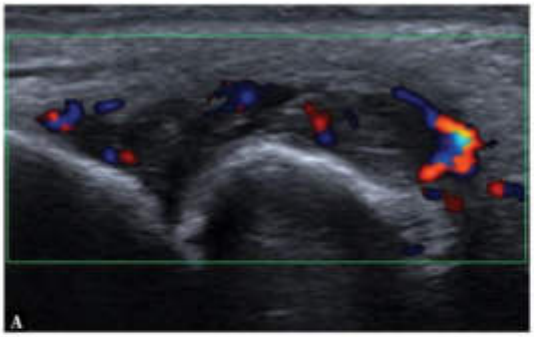
Juvenile spondyloarthropathies are mainly manifested by symptoms of peripheral arthritis and enthesitis. Early involvement of sacroiliac joints and spine is exceptionally rare in children; this usually happens in adulthood. Conventional radiographs visualize late inflammatory lesions. Early diagnosis is possible with the use of ultrasonography and magnetic resonance imaging. The first part of the article presented classifications and radiographic presentation of juvenile spondyloarthropathies. This part discusses changes seen on ultrasonography and magnetic resonance imaging. In patients with juvenile spondyloarthropathies, these examinations are conducted to diagnose inflammatory lesions in peripheral joints, tendon sheaths, tendons and bursae. Moreover, magnetic resonance also shows subchondral bone marrow edema, which is considered an early sign of inflammation. Ultrasonography and magnetic resonance imaging do not show specific lesions for any rheumatic disease. Nevertheless, they are conducted for early diagnosis, treatment monitoring and identifying complications. This article presents a spectrum of inflammatory changes and discusses the diagnostic value of ultrasonography and magnetic resonance imaging.

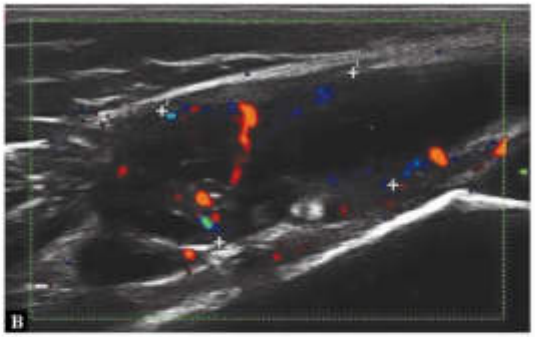
Ultrasonography

The range of features visible on ultrasonography is not different from those seen in adult patients with rheumatic diseases[11]. A US examination is conducted for initial diagnosis and monitoring of treatment efficacy.

Peripheral joints

The first sign of peripheral arthritis, tenosynovitis and bursitis is the thickening of the synovial membrane resulting from synoviocyte hyperplasia and edema of the synovial subintima. It is followed by its increased vascularization and effusion that accompanies synovitis (Fig. 1). At this stage, ultrasonography enables assessment of the spectrum of inflammatory changes, their location and





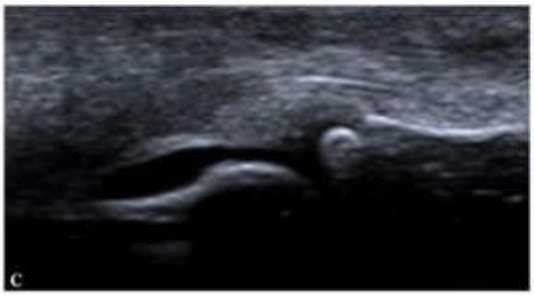
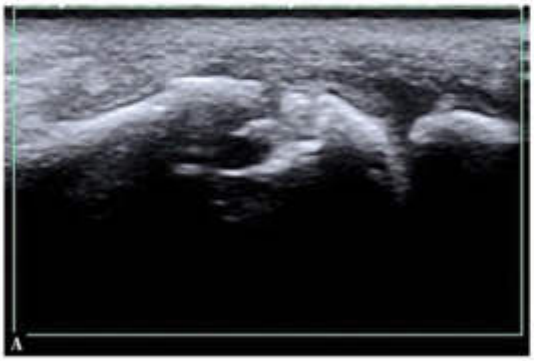


Fig. 1. *Effusion, thickening and enhanced blood flow in the synovium of:* **A.** *2th MCP joint in the right hand of a 17-year-old girl with JSpA;* **B.** *knee joint in a 10-year-old girl with JSpA;* **C.** *effusions, no synovial pathology in the MCP 3 joint of the left hand in a 11-year-old girl*

advancement. Moreover, based on a US examination, a child can be selected for a decompression procedure or deemed ineligible if US shows bands of fibrosis, thickened synovium or that the joint cavity is filled with multiple textured elements.

As the disease develops, erosions form. Initially, they can be seen at the border of the articular surface covered with cartilage and the site of joint capsule attachment (so-called *bare area*). They are called marginal erosions (Fig. 2, 3). When the articular cartilage is destroyed, subchondral erosions appear. By contrast with radiography, ultrasonography can identify the first stages of articular cartilage destruction, in the form of its increased echogenicity, as well as deeper and deeper defects caused by pannus invasion. Inflammatory cysts (also called geodes) reflect the presence of inflammatory infiltrates in the subchondral bone tissue (Fig. 2).

In chronic conditions, the synovial membrane becomes hypertrophic until it assumes forms of various shapes; in this case, so-called rice bodies develop as a result of fragmentation of the hypertrophic synovium. Enhanced synovial vascularization reduces or subsides completely in the case of a positive response to treatment. Persisting intensive synovial vascularization can be an indication for surgical or radioisotope synovectomy, the latter should be conducted under US guidance[23].



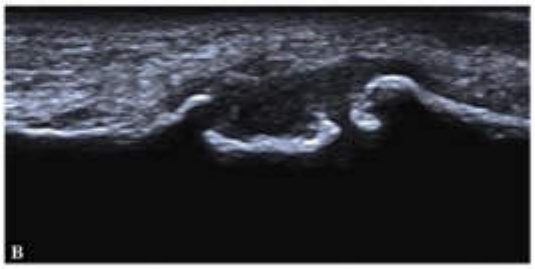


Fig. 2. *US:* **A.** *small marginal erosion and large geode in the head of the 5th metacarpal bone in the right hand of a 16-year-old boy;* **B.** *large erosion in the 2nd MTP joint in the right foot of a 14-year-old-boy with JSpA*

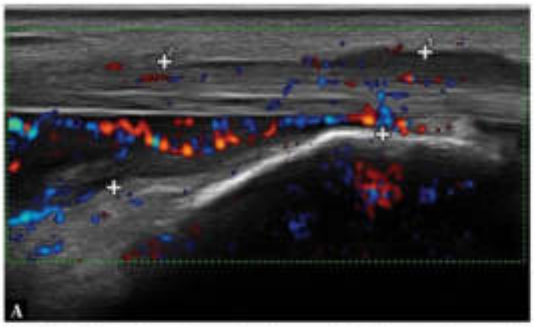


Fig. 3. *Thickened and intensively vascularized synovium of the tibialis posterior tendon sheath in a 16-year-old girl with JSpA*

Tendon sheaths

Tenosynovitis (tenovaginitis) is manifested by thickened synovium and its increased vascularization, usually with accompanying effusion (Fig. 3). Tendinitis (also tendonitis) is a complication of tenosynovitis. A tendon that is weakened by inflammation may undergo damage, including complete tear.

Bursae

In the case of bursitis, the following signs can be observed: synovial thickening, hypervascularization and effusion (Fig. 4). A bursa that is filled with fluid and hypertrophic synovium can rupture (usually Baker's cyst). Persisting bursitis (of e.g. Achilles tendon or deep infrapatellar bursa) may involve the adjacent tendon, leading to its damage and causing erosions in the bony wall of the bursa. The administration of a steroid drug into an inflamed bursa complicated with tendinitis may lead to tendon damage.

Intraarticular and extraarticular fat tissue

It has been demonstrated in adults with rheumatoid arthritis that fat tissue is another site (next to the synovium and subchondral bone tissue) for inflammatory infiltrates, the cells of which participate in the joint destruction process[35]. No such studies have been conducted for juvenile spondyloarthropathies or juvenile idiopathic arthritis. Nevertheless, a US scan shows edema and hypervascularization of the intra- and extraarticular fat tissue even more frequently in children than in adults (author's own unpublished observations), which suggests that identical pathological processes are involved[36] (Fig. 5).

Enthesopathies

In a US examination, pathological entheses are thickened (edema) and hypoechoic. Moreover, one can observe delaminations, areas of degeneration and vessels of the inflammatory-repair process. The bone layer may present erosions and cysts. In adult patients, pathological lesions in entheses cannot be discriminated from far more common microinjuries or degenerative changes, frequently seen also in healthy individuals, since they produce identical US images. In children, however, the probability of injuries or enthesis degeneration is low and therefore an abnormal image, particularly hypervascularization, in combination with other clinical data can be interpreted as enthesitis (Fig. 6). This issue requires further studies particularly because SEA or ERA are, according to clinical data, crucial JSpA entities (see part 1 of the publication).

Magnetic resonance imaging

In addition to identical to US ability to visualize features of synovitis, tenosynovitis, bursitis, enthesopathies and fat tissue pathologies, magnetic resonance imaging (MRI) enables assessment of[5,6] (Fig. 7):

- bone marrow edema, which is a pre-erosional condition and a sign of inflammation;
- articular cartilage in its entire range;
- changes in the spine and spinal cord;
- activity of the involved synovium and subchondral bone tissue in a contrast-enhanced examination.

MRI is more sensitive in assessment of inflammatory and destructive changes in JIA and JSpA than physical examination, radiographs or US. MRI protocols enable

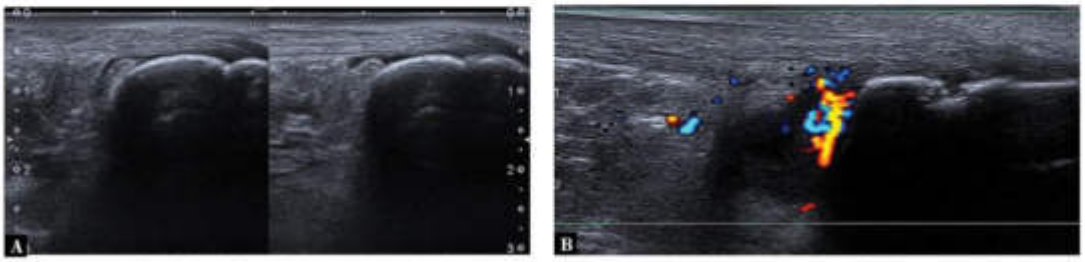


Fig. 4. *Bursitis of the left Achilles tendon:* **A.** *Bilateral slight effusion in the Achilles tendon bursae in a 13-year-old girl, no synovial pathology, rounded fat fold of the left bursa – chronic inflammatory changes;* **B.** *thickened and intensively vascularized synovium of the Achilles tendon bursa in a 15-year-old girl, erosion in the bony wall of the bursa*

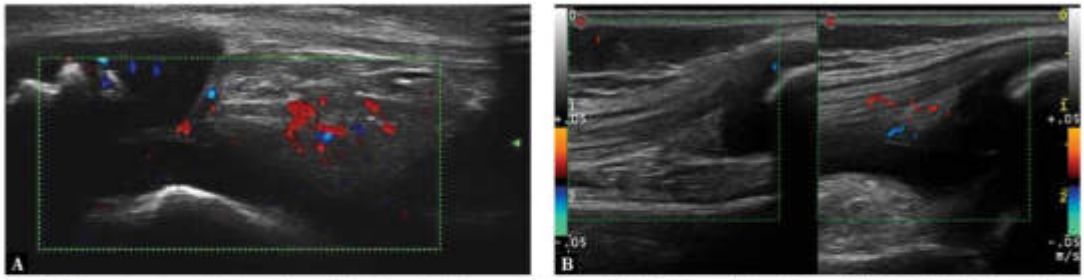


Fig. 5. *Edema, features of enhanced vascularization of the intraarticular fat: A. Hoffa's fat pad in a 10-year-old girl with JSpA; B. fat tissue of the left quadriceps femoris tendon / suprapatellar fat pad (normal in the right joint)*

examinations without the need of administering an anesthetic and sedative agents even in young children[7–12]. However, the available literature contains few papers devoted to MRI in children with JSpA. Bollow et al.[10] scanned sacroiliac joints (SIJs) of 100 children with suspected JSpA and in 30 controls. Active inflammatory changes were detected in 42.9% of children with JSpA while radiographs were normal. In the entire group of 130 children, active and chronic inflammatory lesions were detected in 41% of children whereas chronic changes were visualized only in patients with clinically suspected JSpA. Chronic inflammatory changes were detected on MRI more frequently than on radiographs (14.3% vs 6.7%), which is consistent with our studies conducted in adults[11]. Children with suspected JSpA, in whom active lesions were detected in MRI, also had considerably higher levels of C-reactive protein (p=0.01) and significantly longer medical history (p=0.01) compared to children without features of sacroiliitis in MRI: 63.2 ± 44.1 months vs 28.2 ± 29.7 months. The onset of symptoms in the first group took place at the age of 8.5± 3 years, and in the group of children without sacroiliitis in MRI at the age of 11.0 ± 3.2 years[10].

Another publication[12] demonstrated higher sensitivity of MRI compared with radiography in diagnosing sacroiliitis. Apart from the features of sacroiliitis, MRI also showed signs of enthesitis in the pelvis (pubic symphysis 91%, greater or lesser trochanter 55%, hip joint 45%, iliac crest 27%, ischial tuberosity 27%).

Herregods et al.[13] conducted MRI examinations of the sacroiliac joints in 80 children with clinically suspected JSpAs. Sacroiliitis was not detected in most patients. Bone marrow edema (BME) was found in 16 of 80 children (20%), high signal in the articular cavity in 18 of 80 children (22.5%) and sacroiliac capsulitis in 6 children (7.5%). The authors found that MRI performed before contrast enhancement was consistent with contrast-enhanced examination in detecting BME and capsulitis. A high signal in the sacroiliac joint cavity was present in 22.5% of patients, including contrast enhancement in 83%. The authors did not find any significant benefits of contrast-enhanced MRI and claimed that, as in adults, STIR/TIRM (*short tau inversion recovery/turbo inversion recovery magnitude*) sequences were sufficient to make a diagnosis. JSpA was not ultimately confirmed in patients with a high signal in the joint cavity with no other features of sacroiliitis. Different conclusions were drawn by Lin et al.[14] They stated that, by contrast with adults, capsulitis in children can be an independent factor of inflammation, without accompanying BME.

Rachlis et al.[15] demonstrated that whole body MRI is superior to pelvic MRI in assessing inflammatory and enthesopathic changes in the hip, sacroiliac and spinal joints. The authors did not confirm the features of enthesitis suspected in a clinical examination.

Conclusion

Plain radiography, with its role to rule out malignancies, trauma or specific inflammations, still remains a standard in the diagnostic process of early inflammatory changes in the course of JSpA. In early stages of JSpA, radiography is usually negative or reveals features of osteoporosis, increased density and extended soft tissue shadow, followed by erosions and cysts. Typically, lower extremity joints are involved (see part 1 of the article). The next ex-

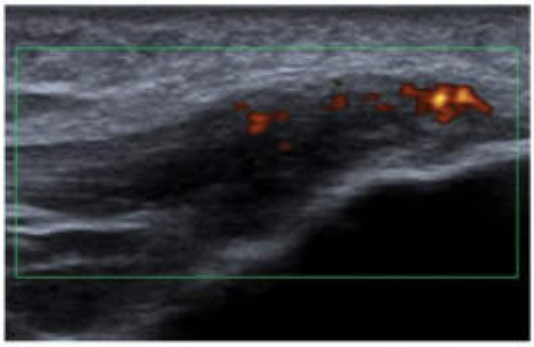


Fig. 6. *Enthesitis-like changes of the tibial enthesis of the patellar tendon in a 15-year-old HLA-B27+ boy: swollen enthesis with lower echogenicity and hypervascularization*

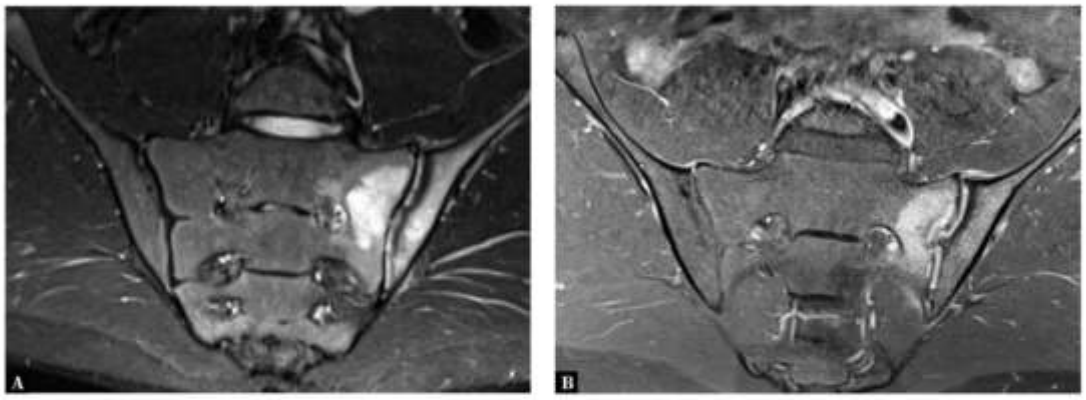


Fig. 7. *MRI of the sacroiliac joints in a 12-year-old boy with suspected sacroiliitis. Coronal oblique planes.* **A.** *T2-weighted TIRM,* **B.** *T1-weighted FS CM (contrast medium): bilateral bone marrow edema, more marked in the left joint, thickened contrast-enhancing synovium*

amination is usually ultrasonography. Its aim is to show early inflammatory lesions in peripheral joints, tendon sheaths, bursae and entheses. Additionally, MRI presents bone marrow edema in the sacroiliac joints in the course of sacroiliitis and as well as atlanto-occipital pathologies. Bollow et al.[10] compared a population of HLA-B27-positive children and adults with peripheral arthritis in terms of the co-occurrence of sacroiliitis. It was detected in 70–80% of adults, and in merely 35% of children[10]. Despite the fact that the SIJs are rarely involved in early JSpAs, children and adolescents with a suspected disease should be referred to an MRI examination for early identification of inflammatory changes and swift implementation of treatment that will prevent the progression of inflammation in the axial spine. It is possible that the detection of the signs of sacroiliitis in MRI at an early stage of the disease is another unfavorable prognostic factor indicating a severe course of the disease and possible transformation into AS in adulthood[10].

There is a need not only for further research on this issue, but also for an update of JSpA diagnostic algorithms. Another suggestion of JSpA clinical criteria[16] is a step towards this goal since they include MRI is the diagnostic process of sacroiliitis. Jaremko et al.[17] compared radiographs and MRI of the sacroiliac joints and demonstrated superiority of MRI.

Conflict of interest

Authors do not report any financial or personal connections with other persons or organizations, which might negatively affect the contents of this publication and/or claim authorship rights to this publication.

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3. **Juvenile spondyloarthritis and chronic recurrent multifocal osteomyelitisoverlap syndrome in a 16 y.o. adolescent. A case report and literature review.**

   Znajdek M, Gazda A, Gietka P, Wysmołek M, Sudoł-Szopińska I.

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Juvenile spondyloarthritis and chronic recurrent multifocal osteomyelitis overlap syndrome in a 16-year-old adolescent. A case report and literature review

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Keywords
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Abstract

The authors present a very rare case of juvenile spondyloarthritis and chronic recurrent multifocal osteomyelitis overlap syndrome in a 16-year-old girl and discuss diagnostic difficulties associated with this case. Juvenile spondyloarthropathies are a type of rheumatic diseases characterized by non-symmetrical peripheral arthritis and enthesitis as well as by spondylitis. Chronic recurrent multifocal osteomyelitis is a rare, possibly autoimmune disease found primarily in children and adolescents. The disease is characterized by bone marrow inflammation and the presence of lytic and sclerotic lesions. Diagnostic imaging plays a key role in the identification of both diseases. The primary modality is X-ray; however, currently, magnetic resonance imaging and ultrasound are increasingly important. A correct early diagnosis allows one to start appropriate treatment to reduce the consequences of these diseases.

Case report

A 16-year-old patient with juvenile spondyloarthritis and chronic recurrent multifocal osteomyelitis (CRMO) overlap syndrome was admitted to our department for follow-up examinations. She had been hospitalized at the department a few times before.

The patient had a history of joint and back pain and pain in the left buttock and the left thigh when walking since 2011. Physical examination revealed abnormal gait with sparing of the left leg and signs of peripheral arthritis. On ultrasound, peripheral arthritis, including in the left ankle (Fig. 1), left knee, the first metatarsophalangeal joint of the left foot and the right sternoclavicular joint was confirmed. On X-ray of the spine, rotoscoliosis of the thoracic and lumbar spine was found. Laboratory tests revealed moderately elevated inflammatory markers and the presence of the HLA-B27 antigen.

In December 2012, whole-body MRI revealed bone marrow edema in C7, Th5 and Th6 vertebral bodies, Th6 endplate damage, reduction of Th6 body height and bone marrow edema in the sternoclavicular joint, in the left sacroiliac joint, in the diaphyses of both ilia, in the right navicular bone (Fig. 2) with associated edema of soft tissues and of the left lateral malleolus.

On chest X-ray, the following abnormalities were found: pleuro-diaphragmatic adhesions in the left dome of the diaphragm, significant right thoracic scoliosis, irregular contours and subchondral sclerosis of the edge of the sternal end of the right clavicle (Fig. 3). On X-ray of sacroiliac joints bilateral grade 2 inflammation was found.

At the time, the diagnosis of enthesitis-related juvenile idiopathic arthritis (ERA-JIA) was made, i.e. a form of juvenile idiopathic arthritis (JIA) which also belongs to the category of juvenile spondyloarthropathies (diseases in which peripheral arthritis is combined with spondylitis).

Non-steroid anti-inflammatory drug and sulfasalazine therapy was administered (November–December 2012) and pain was reduced. However, due to the patient's parents' failure to report to the department with their child, consecutive stages of treatment were discontinued. In addition, due to a positive result of a tuberculin test, the girl was hospitalized three times (in 2012, 2013 and 2016) at a respiratory disease and tuberculosis treatment center. Latent tuberculosis was diagnosed.

Further in the disease process (2013–2015) the patient had periods of active peripheral arthritis, sacroiliitis and spondylitis.

Further MRI examinations (2015, 2016) revealed a significant progression of the lesions: vertebral body fractures, bone marrow edema in multiple additional locations: in the right iliac bone body, the right iliac acetabulum, the right pubic bone, the left femoral neck and greater trochanter, the head of the right fibula and the first metatarsal bone of the right foot, massive bone marrow edema in both sacroiliac joints (Fig. 4) and soft-tissue edema at the level of the affected joints.

On MRI, chronic recurrent multifocal osteomyelitis (CRMO) associated with JIA was diagnosed, i.e. an overlap syndrome was present.

On ultrasound of the right foot the following abnormalities were noted: a thickened, intensively vascularized synovial membrane in the first metatarsophalangeal joint, a large erosion filled with vascularized synovial membrane on the medial surface of the first metatarsal bone head (Fig. 5), a small effusion under the fifth metatarsal bone head and a thickened synovial membrane of the bursa (submetatarsal bursitis). On left knee ultrasound effusion in the joint cavity was revealed.

Combined Metex + adalimumab therapy was applied and clinical symptoms resolved and inflammation markers returned to normal.

Since April 2017 the parents did not report with the child to the department again and they discontinued the treatment.

In September 2017 the girl was readmitted to the department due to pain recurrence, particularly in the

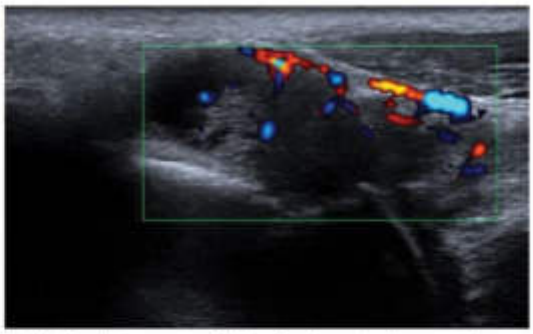

Fig. 1. *Developing erosion filled with a hypertrophic synovial membrane with increased vascularization and effusion on ultrasound*

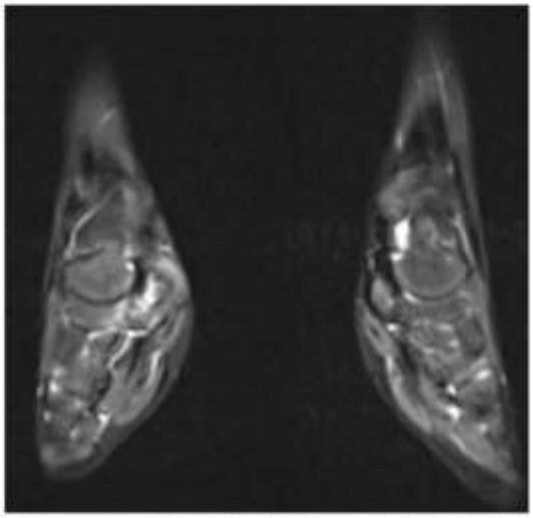

Fig. 2. *Bone marrow edema in the right navicular bone on whole-body MRI, the high signal intensity on the left is consistent with visualized vessels*

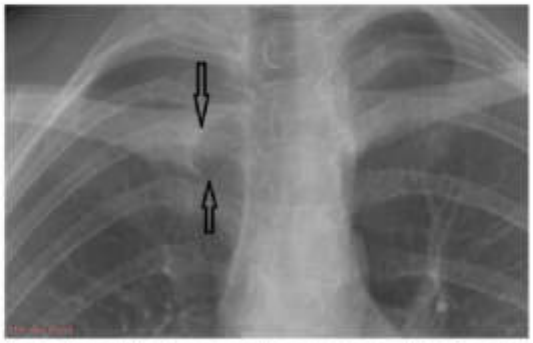

Fig. 3. *Areas of bone loss, irregular contours surrounded by a sclerotic margin in the lower central part of the sternal end of the right clavicle*

left leg. Diagnostic imaging revealed further progression of the lesions, including multilevel vertebral body fractures and syndesmophytes in the lumbar spine on X-ray (Fig. 6).

Discussion

Juvenile spondyloarthropathies and CRMO are rare childhood disorders and their identification is often very difficult. This paper presents an even rarer case of an overlap syndrome involving the coexistence of juvenile spondyloarthropathy and CRMO. A dramatic course of the disease is described which is primarily due to the non-compliance of the sick child's parents.

According to the International League of Associations for Rheumatology (ILAR), juvenile spondyloarthropathies (JSpA) belong to the subtype of JIA called enthesitis-related arthritis (ERA)[1–3]. However, the European Spondyloarthropathy Study Group (ESSG) treats JSpA as a separate group of conditions divided further into a few entities, as in adults. In our department the ILAR definition of the disease has been adopted.

ERA accounts for approximately 5–10% of all forms of JIA. The criteria for the diagnosis of this condition include the presence of arthritis and enthesitis or arthritis or enthesitis alone and the presence of at least two characteristics below:

- sacroiliac tenderness or inflammation-related sacral pain;
- the presence of the HLA-B27 antigen;
- family history of at least one first- or second degree relative with a disease associated with the presence of the HLA-B27 antigen;
- anterior uveitis; arthritis in a boy after 8 years of age.

In addition, excluding psoriasis in the patient or a first- or second degree relative and finding the presence of systemic arthritis are a prerequisite for the diagnosis.

The most common manifestations are enthesitis and clinical signs of oligo- and polyarthritis, predominantly in the joints of the legs (most commonly the knee, the hip, the ankle, the metatarsophalangeal joint and interphalangeal joint of the hallux)[4–6]. In approximately 30–40% of children the disease progresses and the spinal and sacroiliac joints become involved, which, unlike in adults, are usually not affected by inflammation at the initial stage of the disease (spondylitis, sacroiliitis)[5, 6]. The case presented in our study shows the involvement of multiple joints and a significant disease progression.

The primary method of ERA (JSpA) diagnosis is radiographs[7, 9, 10] of the peripheral and spinal joints. The limitation of radiographs is their ability to detect only advanced inflammatory and destructive lesions. Early stages of the disease are diagnosed using MRI and ultrasound.

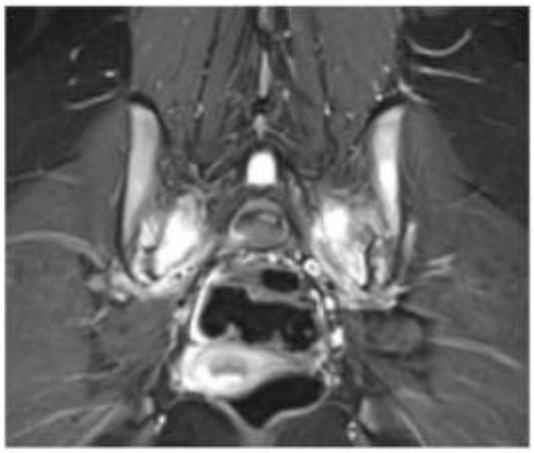

Fig. 4. *Bone marrow edema in both sacroiliac joints on whole-body MRI*

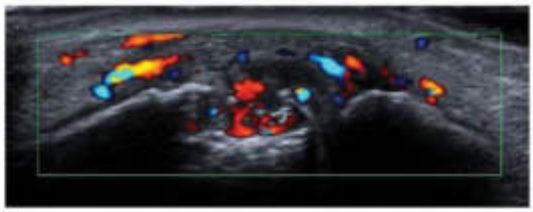

Fig. 5. *Large erosion filled with vascularized synovial membrane on the medial surface of the head of the first metatarsal bone*

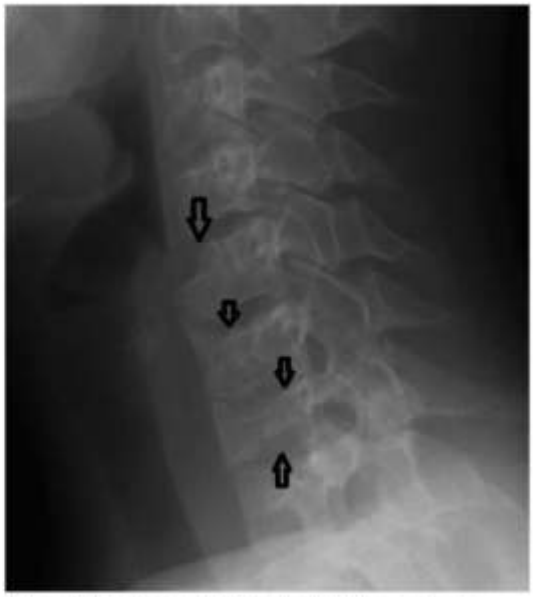

Fig. 6. *Multilevel vertebral body fractures in the cervical spine*

X-ray

Sacroiliitis can be unilateral at the initial stage of the disease. The stage of the disease is assessed in the same way as in adults on the basis of the New York criteria (Tab. 1)[8,7,11]. The end stage of the disease is the fusion of the iliac and sacral bones (ankylosis), which is, however, extremely rarely observed in children.

In addition, radiographs show enthesopathic lesions (ossifications and erosions in the osseous part of the enthesis) and lesions in peripheral joints (manifesting as soft tissue shadow widening, osteoporosis, cysts and, less commonly, erosions). In children, unlike in adults, vertebral rigidity (bamboo spine sign) does not occur. Square vertebral bodies and syndesmophytes, which were found in our patient, are evident only after many years of disease[18]. There is characteristic, although very rarely diagnosed, vertebral body destruction with osseous reconstruction, usually in the cervical spine. We report it in the present case.

Ultrasound

Peripheral joints, synovial bursae, tendons, tendon sheaths and entheses are subject to evaluation[10,12]. At the initial stage of the disease, the thickening of the synovial membrane and, subsequently, its increased vascularization and effusion are observed. Further lesions include geodes and erosions of the articular surfaces of bones as well as damage to the hyaline cartilage, often beginning with an increased echogenicity, which is probably a sign of biochemical disturbances in the cartilage. The appropriate response to treatment is the disappearance of increased vascularization in the synovial membrane and the lack of disease progression and signs of destruction.

Inflammatory lesions in the entheses manifest as thickening and decreased echogenicity, disturbed filamentous echostructure, often increased vascularization and lesions in the osseous part of the enthesis (irregularities, erosions, geodes)[13].

Magnetic resonance imaging

Apart from lesions evident on ultrasound, MRI also makes it possible to assess[10,14] edema in the bone marrow (the earliest sign of inflammation), in the spine and in the spinal cord, articular cartilage in its entirety as well as the level of activity of a synovial membrane affected with inflammation and subchondral bone tissue following the administration of a contrast agent. Magnetic resonance imaging is considered to be a more sensitive procedure to evaluate inflammatory and destructive lesions associated with JSpA and JIA than physical examination, ultrasound scan or X-ray[15,2].

CRMO

Chronic recurrent multifocal osteomyelitis (CRMO) is a rare form of osteitis of a possible autoimmune origin, found mainly in children and young adults, primarily in females. Localized bone and joint pain, often occurring at night, joint edema and tenderness are characteristic of the disease. General symptoms of inflammation such as fever, weakness and weight loss can occur and laboratory signs such as slightly elevated ESR, CRP, leukocytosis and the TNF-α cytokine can be present. The course of the disease is usually recurrent with periods of exacerbations and remissions, less commonly chronic[16–18]. The most common locations of abnormalities include the epiphyses and metaphyses of long bones (the femur, the tibia, the fibula), the clavicle, the thoracic wall, vertebral bodies, the mandible and pelvic bones. There can be single or multiple inflammatory foci, which are often distributed symmetrically. The disease starts with bone marrow inflammation which is readily visible on MRI before lytic and sclerotic lesions develop that will be evident on radiography[19–23]. Approximately 25% of patients develop skin lesions: pustulosis of the palms and feet, generalized pustulosis, psoriasis and acne[24,25].

Currently, the Bristol diagnostic criteria of 2016 are applied[26]:

1. the presence of typical clinical findings (bone pain ± localized swelling, without local or systemic features of inflammation or infection);
2. typical radiological findings: X-ray (lytic and sclerotic lesions, new bone formation), MRI (bone marrow edema ± lytic areas, periosteal reaction).

With the following conditions being met:

1. lesions in more than one bone (or a single lesion in the clavicle), moderately increased CRP (< 30 g/l);
2. if the disease is unifocal (in a location other than the clavicle) or CRP is > 30 g/l: bone biopsy showing inflammatory changes (plasma cells, osteoclasts, fibrosis, sclerosis) with no bacterial growth while not on antibiotic therapy.

Tab. 1. *The New York diagnostic criteria for sacroiliitis*

Grade 0	No abnormalities (normal sacroiliac joints)
Grade 1	Suspected abnormalities (blurred joint margins)
Grade 2	Minimal abnormalities (single erosions and juxta-articular sclerosis)
Grade 3	Advanced abnormalities (distinct juxta-articular sclerosis, multiple erosions with widening of the joint space, possible partial ankylosis)
Grade 4	Complete ankylosis

In our patient, the diagnosis was made using MRI based on the presence of multiple sites of bone marrow edema, lytic areas and sclerotic lesions in locations typical for both JIA and CRMO. The abnormalities found correlated with clinical symptoms: bone and muscle pain and edema. Moreover, laboratory tests revealed a moderately increased CRP level and the presence of the HLA-B27 antigen.

The case discussed in this study shows that the differential diagnosis of JSpA should not only take into account the presence of CRMO, which was indicated by Robertson *et al.*[27], among others, but also the coexistence of JSpA and CRMO. The case of the 16-year-old girl with an overlap syndrome presented in this study, which was diagnosed after a few years of delay, is not an isolated one: there are cases reported in medical literature in which both conditions were not diagnosed at the same time[28–31]. However, in the cases described in the literature CRMO was diagnosed first and then JIA was identified[28–32], while our case is the first one in which JIA was diagnosed before CRMO.

In our patient, a more than 4-year delay in the diagnosis of the overlap syndrome was due to a non-specific clinical and radiological presentation, the need to exclude other diseases, the lack of close disease monitoring and treatment discontinuation, which led to spinal fractures.

Summary

The diagnosis of rheumatic arthritis in children is often difficult and overlapping syndromes are particularly difficult to identify. It is essential for clinicians and radiologists to cooperate closely, however, even if they do, the diagnosis is still often delayed due to the lack of specific symptoms and the need to exclude other arthropathies one by one and perform further diagnostic procedures. Consequently, the patient does not receive optimal treatment until later in the disease, which results in progression. A lack of improvement may also discourage parents from continuing the treatment, which happened in the present case. These difficulties lead to disease progression and advanced lesions.

Conflict of interest

The authors do not report any financial or personal affiliations to persons or organizations that could negatively affect the content of or claim to have rights to this publication.

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4. **Common incidental findings on sacroiliac joint MRI in children clinically suspected of juvenile spondyloarthritis.**
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Common incidental findings on sacroiliac joint MRI in children clinically suspected of juvenile spondyloarthritis

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ABSTRACT

Purpose: To determine the prevalence of incidental findings on sacroiliac (SI) joint MRI in children clinically suspected of Juvenile Spondyloarthritis (JSpA).

Methods: In this retrospective multi-center study of 540 children clinically suspected of JSpA who underwent MRI of SI joints from February 2012 to May 2018, the prevalence of sacroiliitis and other incidental findings was recorded.

Results: In 106/540 (20 %) children MRI features of sacroiliitis were present. In 228 (42 %) patients MRI showed at least one incidental finding other than sacroiliitis. A total of 271 abnormal findings were reported. The most frequent incidental findings were at lumbosacral spine (158 patients, 29 %) and hip (43 patients, 8 %). The most common incidental finding was axial degenerative changes, seen in 94 patients (17 %). Other less frequent pathologies were: simple (bone) cyst in 15 (2,8 %) patients; enthesitis/tendinitis in 16 (3 %) patients; non-specific focal bone marrow edema (BME) away from SI joints in 10 (1,9 %) patients; ovarian cysts in 7 (1,3 %) patients; BME in the course of chronic recurrent multifocal osteomyelitis (CRMO) in 4 (0,7 %) patients; muscle pathology in 4 (0,7%) patients; benign tumors in 3 (0,6 %) patients; (old) fractures in 3 (0,6 %) patients; bony apophyseal avulsion in 2 (0,4 %) patients and malignant tumors in 2 (0,4 %) patients.

Conclusion: Incidental findings are common on MRI of the SI joints in children clinically suspected of JSpA, particularly at the lumbar spine and hips. They are seen even more frequently than sacroiliitis and can be relevant, as some will have clinical significance or require treatment.

1. Introduction

JSpA represents an important subgroup of chronic arthritis in children [1]. It is defined as a group of seronegative rheumatologic disorders with initial complaints emerging before 16 years of age [2–4]. There is a strong association to human leukocyte antigen (HLA-B27) [5].

New medical treatment options have recently become available to treat inflammation, delay progression of the disease and prevent irreversible damage [6–11]. MRI of the SI joints is increasingly being obtained [11,12], since MRI can depict inflammatory lesions long before radiographic changes become evident [12–15]. MRI of the SI joints may show active as well as structural lesions in sacroiliitis [11].

Most scan protocols of SI joints include part of the lower lumbar spine, hips, pelvis and the muscles and bones of the pelvic girdle. MRI of the SI joints may demonstrate incidental findings in these areas, not associated with JSpA, which might have clinical significance and need to be reported.

The aim of this study was to determine the prevalence of incidental findings demonstrated on MRI of the SI joints in children clinically suspected of JSpA.

Abbreviations: AVN, avascular necrosis; BME, bone marrow edema; CRMO, chronic recurrent multifocal osteomyelitis; FOV, field of view; Gd, gadolinium DTPA; HLA-B27, human leukocyte antigen B27; IV, intravenous; JSpA, juvenile spondyloarthritis; MRI, magnetic resonance imaging; TE, echo time; TR, repetition time; TSE, turbo spin echo; SI, sacroiliac; ST, slice thickness; STIR, short tau inversion recovery

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2. Materials and methods

This retrospective multicentric study was approved by the institutional ethics committee in all 3 institutions. Informed consent was obtained.

2.1. Study group

All consecutive MRI of the SI joints from February 2012 to May 2018 in children clinically suspected of JSpA.

All MRI scans were collected from three different hospitals (Ghent University Hospital (Belgium); University of Alberta Hospital (Canada); National Institute of Geriatrics (Poland)).

In total 540 pediatric patients were included, 267 (51 %) boys and 264 (49 %) girls with a median age of 14,8 and a mean age of 14,4 (range 0,9–23,1). 180 consecutive patients were included in every single institution. In the Belgian institution (BEL) median age of the patients was 13,5; mean age 13,4; range 4,3–23,1. In the Canadian institution (CAN) median age of the patients was 15,5; mean age 14,8; range 0,9–20,6. In the Polish institution (POL) median age of the patients was 15,3; mean age 14,8; range 4,8–18,4.

2.2. MRI

In Belgium MRI was performed on a 1.5 T MRI unit (Avanto, Siemens Medical, Erlangen, Germany). The SI joints were imaged in a body flexed array coil (Siemens Medical, Erlangen, Germany). Sequence protocol included: semicoronal (along long axis of the sacral bone perpendicular to the S2 vertebral body) T1-weighted turbo spin echo (TSE) (slice thickness (ST): 3 mm; repetition time/echo time (TR/TE): 595/20 ms); semicoronal short tau inversion recovery (STIR) (ST: 3 mm;TR/TE/TI: 5030/67/150 ms); axial STIR related to the pelvis (ST:5 mm; TR/TE/TI: 7540/67/150 ms;). Field of view (FOV) 400 mm × 400 mm from L5 to the lesser trochanter. Contrast-enhanced pulse sequences were also obtained: semicoronal (ST: 3 mm; TR/TE: 558/20 ms) and axial fat saturated T1-weighted TSE (ST: 5 mm; TR/TE: 558/9,8 ms) 120 s after intravenous (IV) administration of Gadolinium – DTPA (Gd) contrast (T1/Gd) (Dotarem, 0.1 mmol/kg body weight).

In Canada MRI was performed on one of several Siemens 1.5 T MRI units with a body array coil. Sequences included semicoronal T1-weighted TSE (ST 4 mm, typical TR/TE 476/13 ms) and STIR (ST 4 mm, typical TR/TE/TI 4170/50/150 ms), with FOV typically 250 × 250 mm). No post-gadolinium imaging.

In Poland MRI was performed on a 1.5 T MRI unit (Avanto, Siemens Medical, Erlangen, Germany). The SI joints were imaged in a body flexed array coil (Siemens Medical, Erlangen, Germany). Sequence protocol included: Sagittal T2 TSE localizer (TR/TE: 4960/77; FOV 300 layers 26); semicoronal T1 TSE (TR/TE: 644/10; FOV 260 layers 25); semicoronal T1 TSE FS (TR/TE: 600/10; FOV 260 layers 25); semicoronal T2 TSE (TR/TE: 4960/90; FOV 260 layers 25); semicoronal T2 TSE TIRM (TR/TE: 4600/40; FOV 260 layers 25); Semicoronal PD TSE (TR/TE 3630/34; FOV 270 Layers up to 33). No post-gadolinium imaging.

2.3. Image review

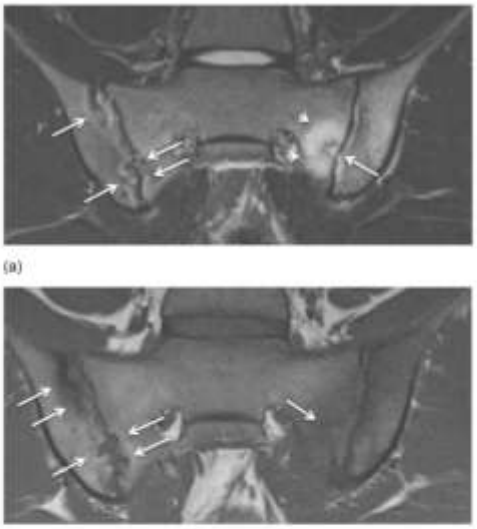
The images were collected from three different hospitals (BEL) (CAN) (POL).

The MRI images were reviewed in consensus for the presence of sacroiliitis or other incidental findings in the three different institutions ((ES) (NH) (LJ) in the Belgian institution; (RM) (JJ) in the Canadian institution; (IS) (MZ) in the Polish institution).

A template was provided for the three institutions and contained: date of examination, date of birth, gender, presence of sacroiliitis, presence of JSpA and a list of incidental findings. Other (rare) incidental findings could be manually added to the list.

Table 1
List of the incidental findings demonstrated on MRI of the SI joints.

Disease	
Lumbosacral spine	Degenerative disc of the lower lumbar - lumbosacral spine
	Facet joint arthrosis/arthritis
	Edema pedicle/ spondylolyse with BME
	Lumbosacral transitional variant, with or without BME
	Spina bifida occulta
	Schmorl nodules
Hip joint	Hip fluid (no evidence of synovial proliferation)
	Hip arthritis (evidence of synovial proliferation)
	Hip AVN
	Degenerative hip
Simple cyst	Tarlov cyst
	Ganglion cyst
	Subchondral cyst
	Bone cyst
BME	Focal bone marrow edema (CRMO/sacroiliitis excluded): aspecific, Posttraumatic or mechanical CRMO
Tumor	Benign tumor
	Malignant tumor
Enthesitis/tendinitis	Enthesitis/tendinitis gluteus muscle
	Enthesitis other (not SIJ/not gluteus muscle)
Muscle pathology	Muscle tear
	Myositis
	Muscle strain
Fracture	Old or new
Bony apophyseal avulsion	
Ovarian cyst	
Other	



(a)

(b)

Fig. 1. Sacroiliitis in a 17-year-old boy. (a) Semicoronal STIR MR image shows erosions on both SI joints (arrows) with extensive surrounding BME at the sacral side of the left SI joint (short arrows). (b) Semicoronal T1-weighted MR image shows erosions on both SI joints and subchondral sclerosis at the iliac side of the right SI joint.

The presence of active lesions of sacroiliitis was recorded and included capsulitis, joint space enhancement, inflammation at the site of erosion, enthesitis and joint space fluid [16]. The presence of structural lesions of sacroiliitis was also recorded and included sclerosis, fat

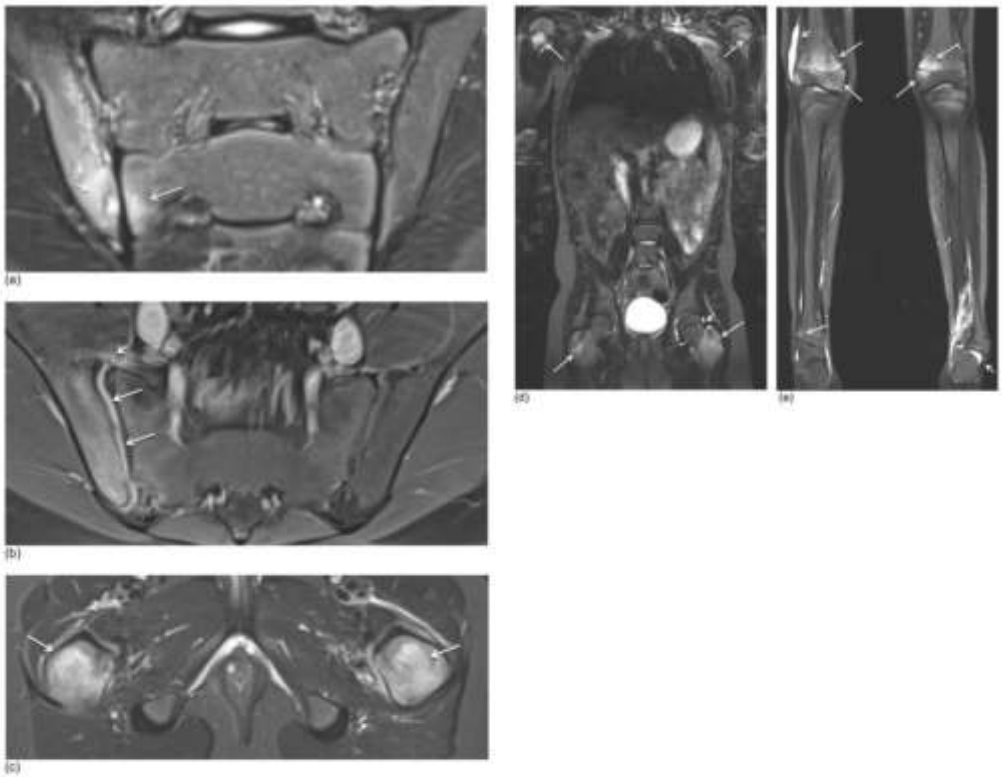


Fig. 2. Sacroiliitis (active and structural lesions) and CRMO in a 13-year-old boy. (a) Semicoronal STIR MR image shows an active erosion with extensive BME at the iliac side of the right SI joint (short arrow) and moderate BME at the sacral side of the right SI joint (arrow). (b) Axial fat saturated T1-weighted MR image after IV Gd shows synovitis with extensive synovial enhancement (arrows) and capsulitis (short arrow). (c) Axial STIR MR image shows diffuse BME in the proximal femur on both sides (arrows). (d-e) Whole body MRI was performed and confirmed the diagnosis of CRMO with arthritis of multiple joints (short arrow) and diffuse epiphyseal and metaphyseal BME (arrows) on coronal STIR MR images.

Table 2
The prevalence of sacroiliitis in the three institutions (N = number of patients).

Institution	Total N	N	%
Belgium	180	40	22
Canada	180	29	16
Poland	180	37	20
Total sacroiliitis	540	106	20

Table 3
The prevalence of lumbosacral spine disease demonstrated on MRI of the SI joints (N = number of patients).

Disease	N	%
Degenerative disc of the lower lumbar - lumbosacral spine	87	161
Lumbosacral transitional variant, no BME	22	4,1
Schmorl nodules	17	3,1
Edema pedicle/ spondylolyse with BME	12	2,2
Facet joint arthrosis/arthritis	7	1,3
Spina bifida occulta	7	1,3
Lumbosacral transitional variant, with BME	6	1,1
Total of lumbosacral spine disease	158	29,2

lesion, erosion, ankylosis and non-bridging bone bud [16]. A global diagnostic impression of sacroiliitis (sacroiliitis yes/no) was recorded. We also looked for incidental findings apart from the SI joint itself (Table 1).

2.4. Statistical analysis

Statistical analysis was performed using software package SPSS 20.0 for Windows (SPSS, Chicago, IL, USA). Basic descriptive statistics were performed where appropriate.

3. Results

In 106 (20 %) of 540 patients MRI features of sacroiliitis were present (Fig. 1–2) (Table 2).

In 228 (42 %) of all patients MRI showed an incidental finding (one or more, sacroiliitis not included) and a total of 262 abnormal findings were reported. In 312 (58 %) of all patients there were no incidental findings.

The prevalence of the incidental findings (sacroiliitis not included) seen in MRI of the SI joints is presented in Table 3–6 (Fig. 3–5).

Of all the incidental findings, axial degenerative changes were the most common. In 87 (16,1 %) patients there was disc degeneration and in 7 (1,3 %) patients there was facet joint degeneration (Fig. 6) (Table 3). Another frequent incidental finding was hip pathology

Table 4
The prevalence of hip disease demonstrated on MRI of the SI joints (N = number of patients).

Disease	N	%
Hip fluid (no evidence of synovial proliferation)	24	4,4
Hip arthritis (evidence of synovial proliferation)	17	3,1
Hip avascular necrosis (AVN)	1	0,2
Degenerative hip	1	0,2
Total of hip disease	43	7,9

Table 5
The prevalence of less frequent incidental findings demonstrated on MRI of the SI joints (N = number of patients).

Disease	N	%
Simple (bone) cyst	15	2,8
Focal BME (CRMO/sacroiliitis excluded)	10	1,9
Enthesitis/tendinitis gluteus muscle	8	1,5
Enthesitis other (not SIJ/not gluteus muscle)	8	1,5
Ovarian cyst	7	1,3
CRMO	4	0,7
Muscle pathology	4	0,7
Other	4	0,7
Benign tumor	3	0,6
Fracture	3	0,6
Malignant tumor	2	0,4
Bony apophyseal avulsion	2	0,4
Total	70	13,1

(Fig. 7) with hip joint effusion as the most frequent finding in 24 (4,4 %) patients (Table 4).

There were 3 cases of benign tumor: hemangioma, osteoid osteoma and a non-specific bony lesion of the right iliac wing with benign morphology (no further differentiation possible). There were 2 cases of malignant tumors: Hodgkin lymphoma (Fig. 8) and a large bone tumor of the sacrum (referred to an oncology centre). There were 4 unique cases listed as 'other' in Tables 1, 5 and 6 (together 0,7 %): pilonidal cyst (Fig. 9), scoliosis, hypertrophic nerve roots and sequelae of previous infective sacroiliitis.

4. Discussion

There is more to see on MRI of the SI joints in children than the SI joints alone. Our study demonstrated that MRI of the SI joints showed twice as many incidental findings (42 %) than sacroiliitis itself (20 %).

Incidental findings such as these can be important in daily radiology, since their detection may prevent unnecessary or alternative further imaging or require prompt further therapy [11]. In our study lumbosacral spine disease, especially axial degenerative changes, was the most frequent incidental finding. Tumor, infection and fracture were less frequently seen. This may be in part due to the distinct clinical presentation and the low incidence of the latter entities in children. However, given that these non-rheumatological diseases often are unexpected, accurate diagnosis is mandatory for timely and tailored treatment [11].

The incidental findings in our study are also seen in the normal population. Lumbosacral transitional anomaly can be present in 4–30 % of the general population [17] (in our study 5,2 %). By the age of 30 years, 40 % have lumbar intervertebral disc degeneration in general [18], in our study already 14,4 % of pediatric patients show degenerative disc disease.

Spina bifida occulta has an overall prevalence of 12,4 % in the general population [19]. In our study only 1,3% of patients had spina bifida occulta, which may be underestimated due to technical factors, including the lower spatial resolution of MRI than radiographs and the MRI field of view which in many scans only included a limited part of the posterior elements of the lumbosacral spine used in the protocol of SI joints.

The overall prevalence of Schmorl nodules in general population has been reported to be around 3,8 % [20], similar to the 3,1 % rate we found in our study.

Our study shows only limited correspondence between clinical findings and radiological findings. Only 20 % of patients proved to have sacroiliitis on MRI. In some patients, MRI might have been performed to rule out sacroiliitis rather than to confirm it, but this is hazardous since only about half of pediatric patients presenting with inflammatory back

Table 6
The prevalence of the incidental findings demonstrated on MRI of the SI joints in the different institutions (N = number of patients).

	Total N	Total %	BEL N	BEL %	CAN N	CAN %	POL N	POL %
Degenerative disc of the lower lumbar spine	87	16,1	12	6,7	40	22,2	35	19,4
Hip fluid (no evidence of synovial proliferation)	24	4,4	8	4,4	16	8,9	0	0
Lumbosacral transitional variant, no BME	22	4,1	11	6,1	8	4,4	3	1,7
Schmorl nodules	17	3,1	2	1,1	1	0,6	14	7,8
Arthritis hip (evidence of synovial proliferation)	17	3,1	12	6,7	4	2,2	1	0,6
Simple (bone) cyst	15	2,8	7	3,9	1	0,6	7	3,9
Edema pedicle/ spondylolyse with BME	12	2,2	2	1,1	10	5,6	0	0
BME, non-specific (CRMO excluded)	10	1,9	3	1,7	4	2,2	3	1,7
Enthesitis/tendinitis gluteus muscle	8	1,5	8	4,4	0	0	0	0
Enthesitis other (not SIJ/not gluteus muscle)	8	1,5	6	3,3	2	1,1	0	0
Facet joint arthrosis/arthritis	7	1,3	1	0,6	5	2,8	1	0,6
Spina bifida occulta	7	1,3	2	1,1	3	1,7	2	1,1
Ovarian cyst	7	1,3	0	0	4	2,2	3	1,7
Lumbosacral transitional variant, with BME	6	1,1	2	1,1	4	2,2	0	0
Muscle pathology/ edema	4	0,7	1	0,6	3	1,7	0	0
CRMO	4	0,7	3	1,7	0	0	1	0,6
Other	4	0,7	0	0	4	2,2	0	0
Benign tumor	3	0,6	1	0,6	2	1,1	0	0
Fracture	3	0,6	0	0	3	1,7	0	0
Bony apophyseal avulsion	2	0,4	2	1,1	0	0	0	0
Malignant tumor	2	0,4	1	0,6	0	0	1	0,6
Degenerative hip	1	0,2	0	0	1	0,6	0	0
AVN hip	1	0,2	0	0	1	0,6	0	0
Total pathology	271		84		116		71	
Total patients with incidental findings	228	42	72	40	96	53	60	33

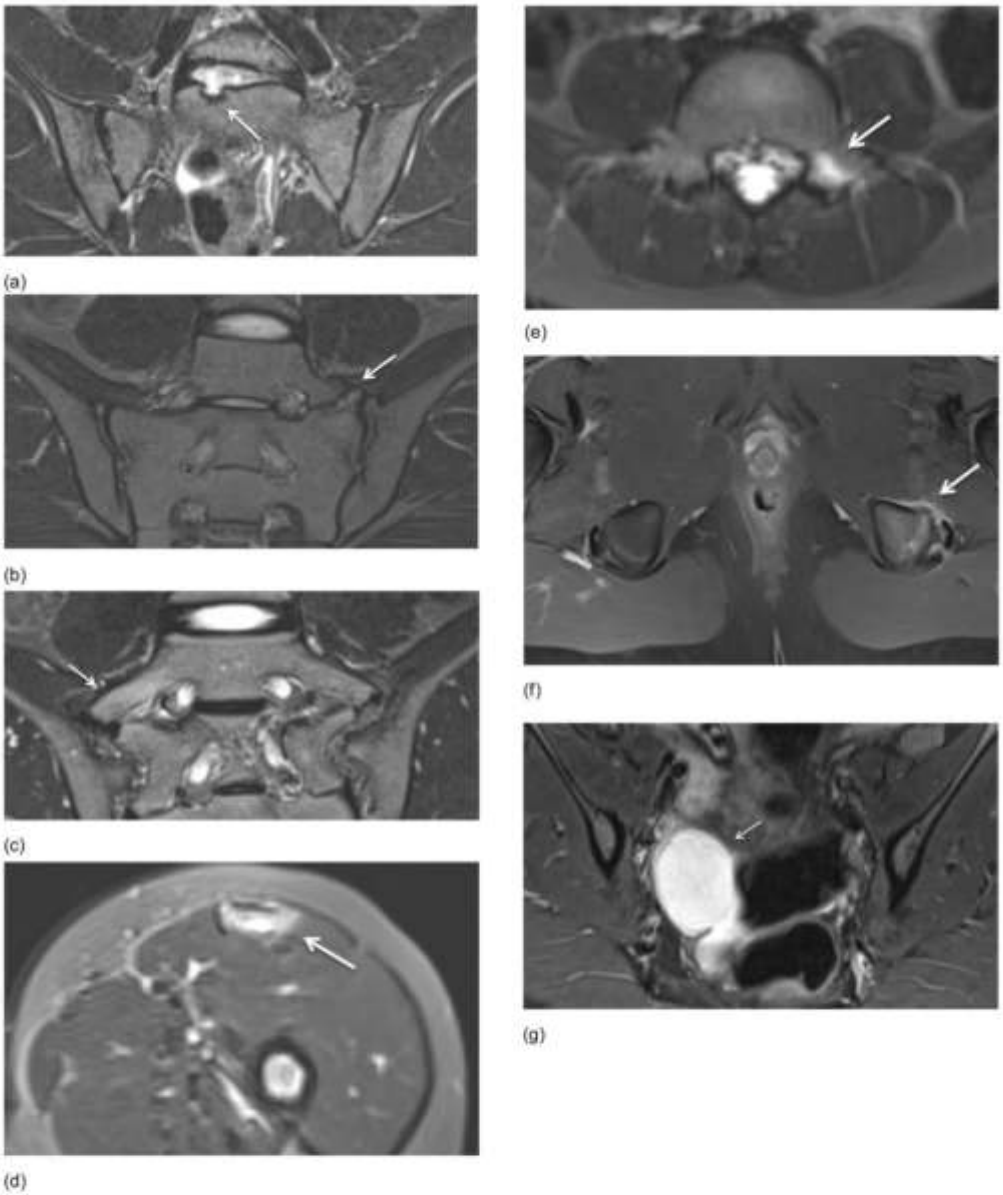


Fig. 3. Incidental findings seen on MRI of SI joints in different patients. (a) Semicoronal STIR MR image of a Schmorl nodules (arrow) in a 12-year-old boy. (b) Semicoronal STIR MR image of a lumbosacral transitional variant on the left side without BME (arrow) in a 15-year old girl. (c) Semicoronal STIR MR image of a lumbosacral transitional variant on the right side with discrete BME (arrow) in a 13-year-old. (d) Axial STIR MR image of a muscle tear with hyperintense signal changes of the rectus femoris muscle (arrow) seen on the most inferior image in a 9-year-old boy. (e) Axial STIR MR image shows bone marrow edema of the pedicle on the left side (arrow) suspicious for spondylolysis in a 7-year-old boy. (f) Axial fat saturated T1-weighted MR image after IV Gd of an bony apophyseal avulsion with soft tissue edema and enhacement on the left side (arrow) in a 14-year-old boy. (g) Semicoronal STIR MR image shows an ovarian cyst (arrow) in a 14-year-old girl.

pain who ultimately are diagnosed with spondyloarthritis have any MRI abnormalities [12]. A thorough history and physical exam is important and may be helpful for correct diagnosis [11,21,22].

The presence of hip arthritis and enthesitis, characterized as incidental findings here, in patients suspected of JSpA may in fact be closely linked to the primary disease, considering that patients with JSpA more often present with peripheral arthritis and enthesitis, while symptoms involving the spine and SI joints often occur later [12,23].

There were some limitations to our study. First, all patients were imaged due to symptoms, giving us no normal control group. Second,

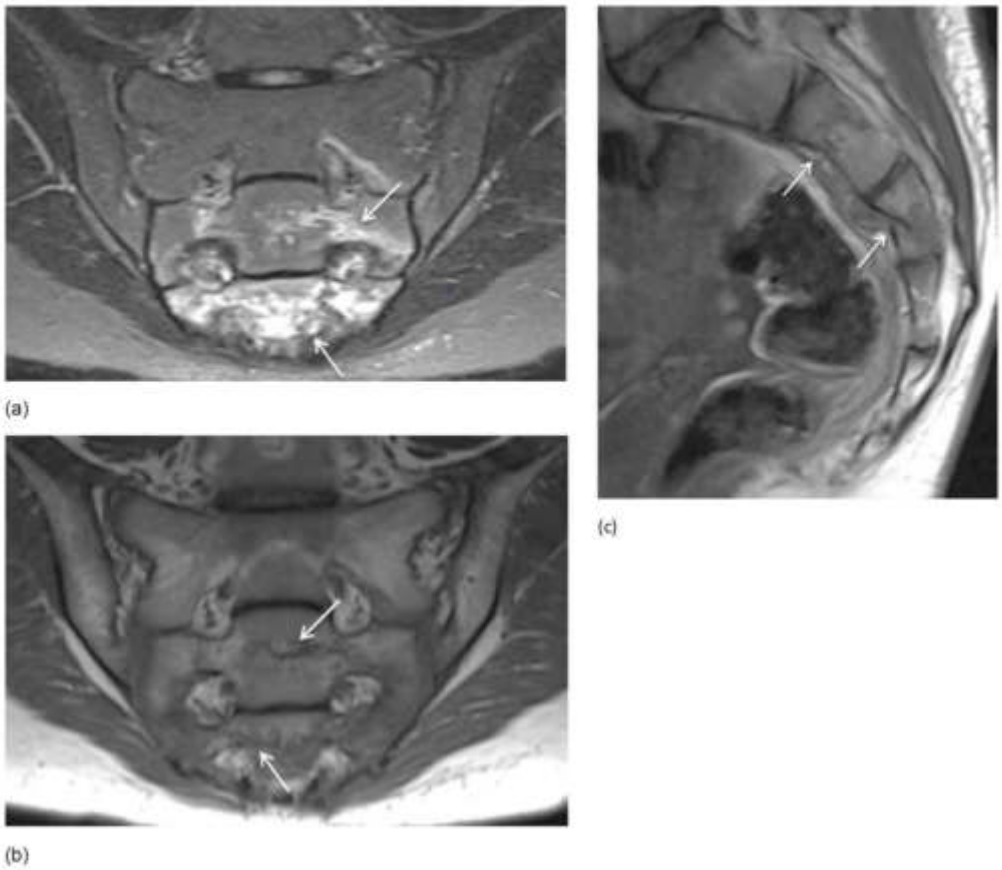


Fig. 4. (a-b) Semicoronal STIR and T1 MR image in a 13-year-old girl with sacral fractures shows BME of S2-S3 on STIR (arrows) and transverse fracture lines on T1 (arrows). (c) Additional sagittal T1 was performed and shows disruption of the anterior cortex of S2 and S3 with mild anterior compression on S3 (arrows).

our patient population came from three different hospitals, from different countries, with different MRI protocols and were reviewed by different radiologists. To some extent this is a strength of the study since it demonstrates that incidental findings are consistently seen across a wide range of MRI protocols and observers. However, some differences between the three institutions were substantial (Table 6). There was a notable difference in reporting of degenerative disc disease of the lumbosacral spine, edema pedicle/spondylolyse with BME, hip fluid/arthritis, simple (bone) cyst and enthesitis/tendinitis. Likely the main reason for this is that the Canadian and Polish institutions use a much narrower field of view, in which the hip and groin are mostly not shown, limiting assessment for hip fluid/arthritis and enthesitis/tendinitis. The sagittal localizer used in the Polish institution also facilitates detection of degenerative disc disease at that site. Degenerative disc disease may be less at the Belgian institution since their median age is a bit lower.

Our findings suggest, not surprisingly, that the larger the MRI field of view, the more incidental findings may be seen. Obtaining axial STIR images and a large FOV from L5 to the lesser trochanter when performing MRI of the SI joints can be helpful in a more comprehensive evaluation of inflammatory type back pain. If only semicoronal sequences of the SI joint and narrow field of view axial sequences are obtained, other findings that may be clinically relevant such as hip joint disease and enthesitis may remain undetected [11]. However, a trade-off with wide FOV imaging is decreased resolution at the SI joints, which may limit confidence when the primary question is whether sacroiliitis is present.

Another difference in MRI protocol was use of intravenous contrast. In Belgium Gd was administered to all patients routinely, while in Canada and Poland, no Gd was administered (except for one patient in the Polish institution who had a large sacral bone tumor). This might help account for different prevalence of hip arthritis seen.

5. Conclusion

In conclusion, incidental findings are common on MRI of the SI joints in children clinically suspected of JSpA. They are seen even more frequently than sacroiliitis and can be relevant to symptoms. Reporting

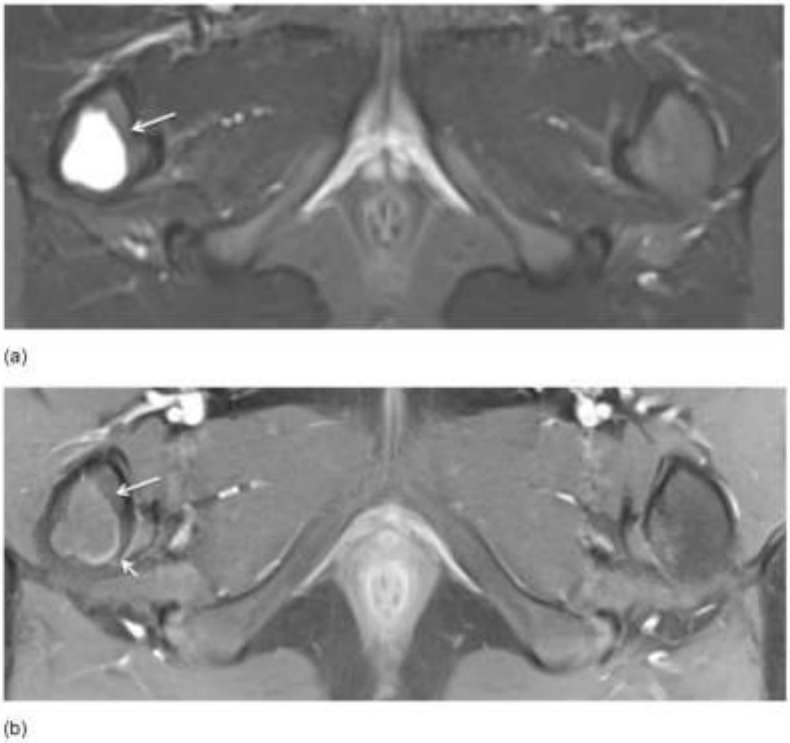


Fig. 5. (a-b) Axial STIR and axial fat saturated T1-weighted MR image after IV Gd in a 9-year-old boy. Simple bone cyst was seen as a well-demarcated metaphyeal STIR hyperintense lesion (arrow) and T1 hypo-intense lesion (arrow) with minimal rim enhancement (short arrow) in the right femur.

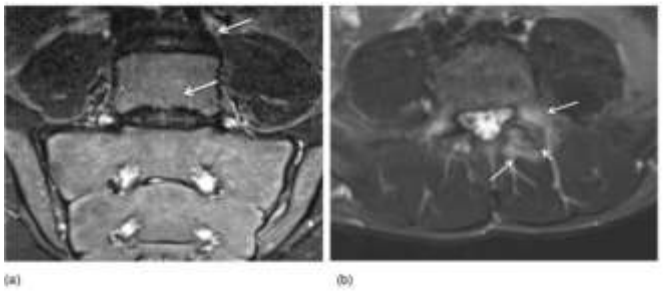
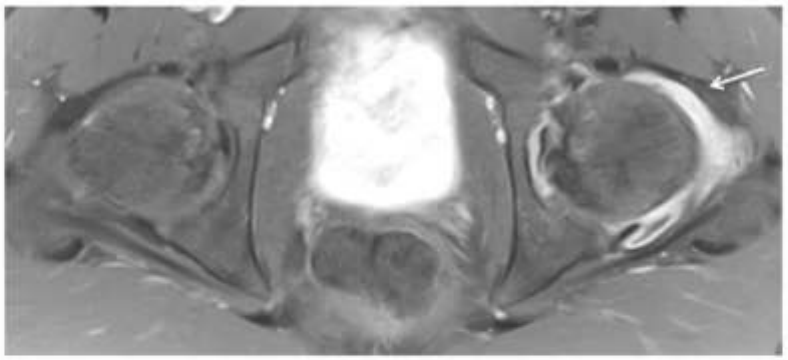


Fig. 6. Degenerative changes of the lower lumbar spine. Semicoronal STIR MR images and axial STIR MR image (a) Disc degeneration in a 14-year-old girl shows disc space narrowing, loss of T2 signal within the nucleus pulposus and endplate changes (arrows). (b) Facet arthritis in a 14-year-old girl with surrounding soft tissue inflammation (arrows) with (secondary) degenerative changes with joint space narrowing, hypertrophy of the joint (short arrow) and fluid in the joint (not showed on this image).

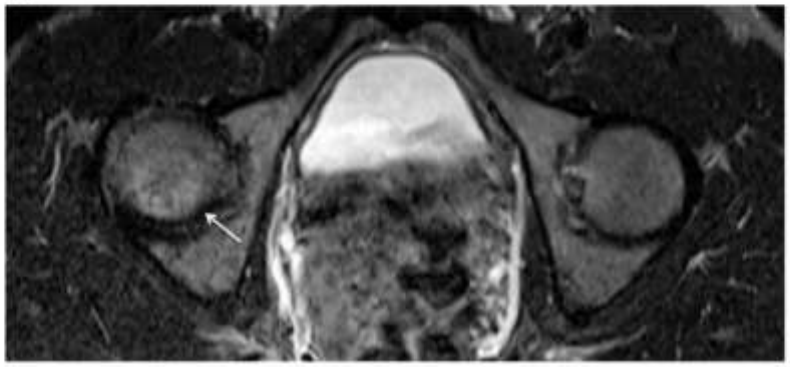
of these findings is important, as some will have clinical significance or require treatment. Axial degenerative changes and hip disease were the most common findings. Whether the MRI field of view should be designed to capture these findings is an open question.

CRediT authorship contribution statement

E. Schiettecatte: Conceptualization, Methodology, Validation, Formal analysis, Investigation, Resources, Data curation, Writing - original draft, Visualization, Supervision, Project administration. **J.L. Jaremko:** Validation, Formal analysis, Investigation, Resources, Data curation, Writing - review & editing, Visualization, Project administration. **I. Sudoł-Szopińska:** Validation, Formal analysis, Investigation, Resources, Data curation, Writing - review & editing, Visualization, Project administration. **M. Znajdek:** Formal analysis, Investigation, Resources, Data curation, Writing - review & editing, Visualization. **R. Mandegaran:** Formal analysis, Investigation, Resources, Data curation, Writing - review & editing, Visualization. **V. Swami:** Formal analysis, Investigation, Resources, Data curation, Writing - review & editing, Visualization. **L. Jans:** Conceptualization, Methodology, Validation,



(a)



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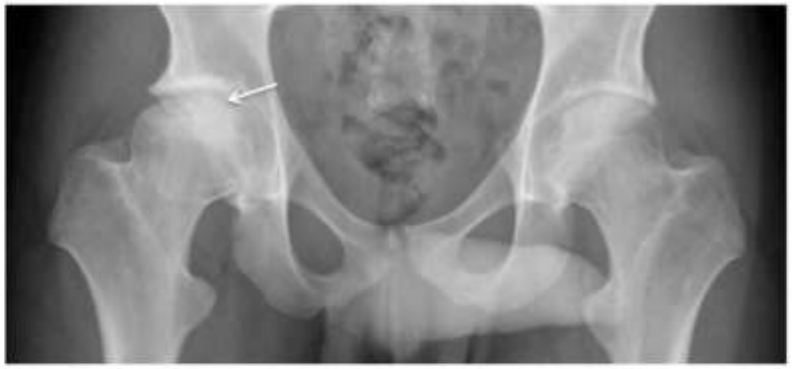

(c)

Fig. 7. Hip joint disease. Axial fat saturated T1-weighted MR image after IV Gd and axial STIR MR images. (a) Hip arthritis in a 13-year-old boy shows a joint effusion in the left hip joint with synovial enhancement (arrow) (b) Avascular necrosis (AVN) in a 17-year-old-boy demonstrates discrete T2 hyperintense signal changes in the femoral head on the right side (arrow), AVN was suspected and confirmed. (c) Radiography of the pelvis in the same patient one year later also confirmed the diagnosis of AVN. There is a subchondral fracture, subchondral sclerosis and flattening of the femoral head on the right side (arrow).

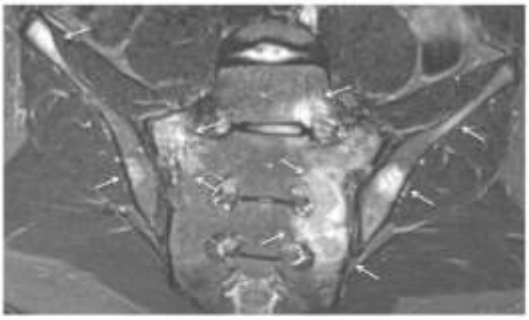

Fig. 8. Semicoronal STIR MR images in a 13-year-old boy. Diffuse areas of bone marrow edema (arrows) are present. This patient was ultimately diagnosed with Hodgkin lymphoma.

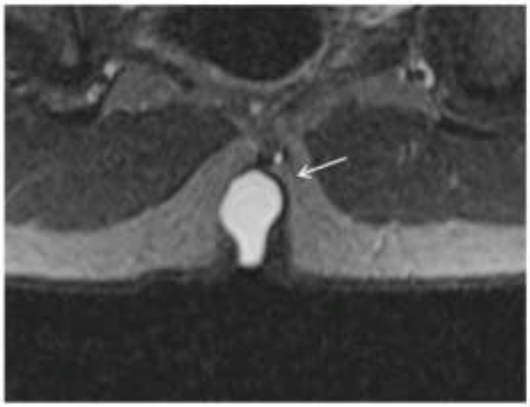

Fig. 9. Semicoronal STIR MR image shows a pilonidal cyst (arrow) in a 14-year-old boy in the superior part of the intergluteal cleft.

Formal analysis, Investigation, Data curation, Writing - review & editing, Visualization, Supervision, Project administration. **N. Herregods:** Conceptualization, Methodology, Validation, Formal analysis, Investigation, Resources, Data curation, Writing - review & editing, Visualization, Supervision, Project administration.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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5. **Determination of Relative Weightings for the Component Pathologies of the OMERACT Juvenile Arthritis Magnetic Resonance Imaging Sacroiliac Joint Score.**

Otobo TM, Tolend M, Meyers AB, Sudol-Szopinska I, Joshi S, Stimec J, Herregods N, Jaremko JL, Tse SML, Haroon N, Moineddin R, Tzaribachev N, Appenzeller S, Znajdek M, Perez M, Ligha AE, Jans L, Inarejos Clemente EJ, Weiss P, Papakonstantinou O, Kirkhus E, van Rossum MAJ, Rumsey DG, Carrino J, Akikusa JD, Conaghan PG, Doria AS. J Clin Med. 2023 Apr 6;12(7):2729. doi: 10.3390/jcm12072729. PMID: 37048812; PMCID: PMC10095587.

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Determination of Relative Weightings for Sacroiliac Joint Pathologies in the OMERACT Juvenile Arthritis Magnetic Resonance Imaging Sacroiliac Joint Score

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Abstract: This study aims to determine the relative weights (point value) of items of the juvenile idiopathic arthritis magnetic resonance imaging-sacroiliac joint scoring system (JAMRIS-SIJ). An adaptive multicriteria decision analysis was performed using the 1000Minds web application to determine the relative weights of the items in the JAMRIS-SIJ inflammation and damage domains. Experts in imaging and rheumatology independently completed a conjoint analysis survey (CAS) to determine the point value of the measurement items of the JAMRIS-SIJ. Each CAS survey question asked the expert to compare two hypothetical patient profiles, which were otherwise similar but different at two items at a time, and to select which item showed a more severe stage of inflammation or osteochondral damage. In addition, experts ranked 14 JAMRIS-SIJ grade only or image + grade patient vignettes while blinded to the CAS-derived weights. The validity of the weighted JAMRIS-SIJ was tested by comparing the expert CAS-weighted score and the image + grade ranking method. Seventeen experts completed the CAS (11 radiologists and 6 rheumatologists). Considering the point value for inflammation domain items, osteitis (24.7%) and bone marrow edema (24.3%) had higher group-averaged percentage weights compared to inflammation in erosion cavity (16.9%),

joint space enhancement (13.1%), joint space fluid (9.1%), capsulitis (7.3%), and enthesitis (4.6%). Similarly, concerning the damage domain, ankylosis (41.3%) and erosion (25.1%) showed higher group-averaged weights compared to backfill (13.9%), sclerosis (10.7%), and fat metaplasia lesion (9.1%). The Spearman correlation coefficients of the CAS-weighted vignette order and unweighted JAMRIS-SIJ grade only order vignettes for all experts were 0.79 for inflammation and 0.80 for damage. The correlations of image vignettes among imaging experts to CAS were 0.75 for inflammation and 0.90 for damage. The multicriteria decision analysis identified differences in relative weights among the JAMRIS-SIJ measurement items. The determination of the relative weights provided expert-driven score scaling and face validity for the JAMRIS-SIJ, enabling the future evaluation of its longitudinal construct validity.

Keywords: OMERACT; JAMRIS-SIJ; juvenile idiopathic arthritis; MRI; outcome measure; face validity; 1000Minds; conjoint analysis

1. Introduction

Juvenile idiopathic arthritis (JIA) is a chronic arthritis of unknown etiology occurring before the age of 16 years. Sacroiliac joint (SIJ) pathology can most commonly be seen in the JIA subtype known as enthesitis-related arthritis (ERA). This can cause lower back, buttock pain, and stiffness in affected individuals [1]. JIA can significantly affect the psychosocial development and wellbeing of children with a substantial financial burden to health systems [2,3]. Commonly used assessment methods for JIA disease activity, such as clinical examination, patient-reported outcomes (PROs), and serological biomarkers, have variable reliability and validity [4]. Moreover, the anatomical location of the SIJ poses significant limitations for accurate clinical examination [5]. Early detection of SIJ inflammation in JIA is essential for therapeutic intervention to prevent disease progression and irreversible joint damage [6]. Radiography has been used for SIJ imaging in JIA, but it is not sensitive in detecting early inflammatory joint lesions [7,8]. Magnetic resonance imaging (MRI) is capable of detecting early SIJ pathologies, which is helpful for disease monitoring and treatment decision making in JIA [6,7]. However, there is a need for the standardization of SIJ MRI interpretation, and this need underpins the iterative development of the outcome measure in rheumatology (OMERACT) juvenile idiopathic arthritis MRI SIJ scoring system (JAMRIS-SIJ) as a standardized objective outcome measurement tool for the assessment of JIA treatment effectiveness in clinical trials [9].

The JAMRIS-SIJ is a multi-component outcome tool that semi-quantitatively measures inflammation and damage in the SIJ [9]. The component items (SIJ MRI pathologies) are distinct and have relative importance in measuring SIJ inflammation and damage. Each item contributes to part of the measurement construct, and in conjunction, the items form the entire construct. This conceptual framework between the measurement items and construct is a formative model [10]. Although the individual item scores can be meaningful when reported separately, it is also desirable to be able to aggregate the items in a domain to form a single composite score. This requires estimating the point value of the respective components for a formative model. Determining the relative weightings of the measurement components will provide a standardized and objective approach in deriving a composite domain score. In the absence of a feasible external criterion for SIJ inflammation and damage, multicriteria decision analysis (MCDA) (conjoint analysis) was utilized to elicit expert judgment to determine the relative weights of the measurement items [11]. A conjoint analysis survey elicited expert preferences for the relative importance of measurement items to define the relative weightings of the JAMRIS-SIJ [12,13].

This study aims to determine the relative weightings of the JAMRIS-SIJ measurement components as part of the face validity assessment of the OMERACT JAMRIS-SIJ.

2. Materials and Methods

We performed a partial profile conjoint analysis using a decision-making software application called 1000Minds to objectively elicit the opinion of imaging and rheumatology experts to determine the relative weights of the JAMRIS-SIJ. Afterwards, experts performed an independent ordinal ranking of 14 cases of JAMRIS-SIJ grade-only and image + grade-based vignettes, to test the face and convergent validity of the conjoint analysis derived-weighted JAMRIS-SIJ.

2.1. Conjoint Analysis Survey

The conjoint analysis survey (CAS) allowed seventeen experts comprising eleven radiologists (65%) and six rheumatologists (35%) to provide their preferences anonymously for each measurement item in the JAMRIS-SIJ to measure SIJ inflammation and damage in JIA. Over 80% of experts who completed the CAS had between 11–30 years of experience in imaging and rheumatology practice (Table S1). Experts were prompted to compare the measurement items (Figures A1 and A2) conjointly, making trade-offs among the items according to their opinion of item importance using a CAS web application called 1000Minds [13].

The 1000Minds software utilized the 'potentially all pairwise ranking of possible alternative' (PAPRIKA) method to compute the relative weightings. In this method, the expert was required to pairwise rank potentially all pairs of possible alternatives of the JAMRIS-SIJ measurement items for each patient scenario. In each patient comparison scenario, a pair of hypothetical patients is presented to the expert, with each patient characterized by differing grades in two of the inflammation (Figure A1) or damage (Figure A2) domains of the JAMRIS-SIJ items. This hypothetical comparison scenario assumes all other JAMRIS-SIJ measurement items are equal for both patients. The pair of JAMRIS-SIJ measurement items presented to the expert for comparison (undominated pairs) constitute a partial profile of the JAMRIS-SIJ, as it is a partial set of the eight or five items of the two domains.

To complete the pairwise partial-profile comparison, the experts were instructed to choose the patient scenario which was greater in the level of inflammation or damage in the SIJ or rate them as equal. These comparison questions continue until the ranking of all possible alternative item combinations are determined adaptively based on the responses from the expert. The number of explicitly compared undominated pairs is reduced by the PAPRIKA method, which identifies and eliminates all pairs implicitly ranked as corollaries of the explicitly ranked pairs, using the transitivity property of additive multicriteria decision analysis [13].

To ensure the validity of the survey responses, any completed survey with greater than or equal to 2 inconsistent responses of the easiest sets of trade-off questions and choices that were only either to the right or left side on the survey were excluded. As the pair-wise rankings were consistent, PAPRIKA utilizes linear programming that analyzes the individual expert responses with the coefficient reported as the relative weights of the JAMRIS-SIJ measurement components [13]. The individual expert relative weights derived from the conjoint analysis were averaged for all experts to derive the relative weights for the JAMRIS-SIJ (Table 1).

Table 1. Conjoint analysis survey-derived relative percentage weight for the measurement components of the JAMRIS-SIJ. Following the grading of an image, the percentage weight of each component grade was added to constitute the domain percentage disease severity score ranging from 0–100% for seven inflammation and five damage domain items, respectively. The percentage weights are reported as group means relative weights. BME; bone marrow edema, IEC; inflammation in erosion cavity, JSE; joint space enhancement, JSF; joint space fluid, FML; fat metaplasia lesion. ICC: intraclass correlation coefficient.

	Inflammation Domain Grades										
	0	1	2	3	4	5	6	7	8	ICC (2,1)	ICC (2,k)
Osteitis	0	3.9	7.7	11.2	14.4	17.2	19.8	23.3	24.7	0.66	0.97
BME	0	3.2	6.4	9.5	12.6	15.6	18.5	21.4	24.3	0.59	0.96
IEC	0	5.3	10	13.7	16.9	–	–	–	–	0.52	0.95
JSE	0	4.5	8.2	10.9	13.1	–	–	–	–	0.34	0.90
JSF	0	2.8	5.1	7.1	9.1	–	–	–	–	0.17	0.78
Capsulitis	0	3.9	7.3	–	–	–	–	–	–	0.41	0.92
Enthesitis	0	4.6	–	–	–	–	–	–	–	0.76	0.98
All Items	–	–	–	–	–	–	–	–	–	0.60	0.96
	Damage Domain Grades										
	0	1	2	3	4	5	6	7	8	ICC (2,1)	ICC (2,k)
Ankylosis	0	10	20.2	30.7	41.3					0.79	0.98
Erosion	0	3.7	7.2	10.6	13.9	16.9	19.8	22.5	25.1	0.60	0.96
Backfill	0	3.9	7.5	10.8	13.9					0.59	0.96
Sclerosis	0	1.8	3.6	55.2	6.6	7.8	8.9	9.8	10.7	0.23	0.83
FML	0	1.6	3.1	4.5	5.7	6.6	7.5	8.3	9.1	0.33	0.90
All Items										0.73	0.98

2.2. JAMRIS-SIJ Vignette Ranking Exercise

Full profile magnetic resonance (MR) image + grade and a JAMRIS-SIJ grade-only vignette ranking exercise was performed to test the convergent and face validity of the partial-profile CAS-derived average JAMRIS-SIJ weights. All the participant experts were invited to complete the JAMRIS-SIJ grade-only vignette ranking, and a subset of twelve experts were additionally invited to complete the image + grade vignette ranking. The vignette ranking was completed before the CAS, allowing experts to rank the vignettes based on their prior expertise before being influenced by the effect of completing the conjoint analysis survey.

The MR image vignettes (Figure A3) are comprised of 14 bilateral SIJ-MRI studies represented by six coronal obliques MRI slices of T1-weighted (w), T2-w fat-suppressed (FS) or short tau inversion recovery (STIR), and T1-w FS post-contrast sequences to represent the SIJ pathologies according to the JAMRIS-SIJ scoring system [9]. Enthesitis was excluded from the inflammation domain measurement item for the image vignette ranking because the MR images provided did not include the optimized imaging planes for the assessment of enthesitis.

Twelve imaging experts in the imaging study cohort individually ranked the image vignettes in order of increasing severity or equivalence of inflammation or damage in the SIJ MR image. The vignettes were also scored using the JAMRIS-SIJ by consensus of three radiologists who did not participate in the ranking exercise to control confirmation bias. Two of the radiologists had more than 10 years of experience after training and one radiologist was in-training under the supervision of an experienced radiologist. Ten radiologists and two rheumatologists with experience in rheumatologic imaging completed the image + grade vignette ranking and constituted the imaging expert cohort (Figure A3 and Table S1). The MR image + grade vignette ranking was based on the individual items of the JAMRIS-SIJ system found on the MR images and reported by the JAMRIS-SIJ item grades, with a caution to avoid ranking the image vignette based on the composite of imaging findings to prevent obscuring the relative weights of each measurement item in arriving at the decision to rank order the vignette.

The JAMRIS-SIJ grade-only vignettes were prepared identical to the MR image vignettes, excluding the MR images. All imaging experts (except one radiologist who did

not participate in the MR image + grade vignette ranking) completed the JAMRIS-SIJ grade-only vignettes (Figure A4 and Table S1). Participants were instructed not to change their JAMRIS-SIJ ranking after receiving the image vignettes as MR images were used to illustrate the scores, but instead, rank the image + grade vignettes separately. The weighted score for the 14 vignettes was derived by multiplying each expert's CAS-derived weights by the vignette's consensus JAMRIS-SIJ grades. The correlation of the CAS-derived JAMRIS-SIJ weights against the MR image + grade and JAMRIS-SIJ grade-only vignettes was tested. This correlation test cumulatively assessed the face, content, and convergent validities of the JAMRIS-SIJ relative item weights; the implicit item preference by PAPRIKA through transitivity of the adaptive partial profile CAS and the JAMRIS-SIJ.

2.3. Statistical Analysis

The absolute agreement among experts on their relative weights of the JAMRIS-SIJ in the CAS was assessed by calculating the two-way random single and average measure intraclass correlation coefficient (ICC) model 2,1 and 2,k (ICC 2,1 and 2,k) for grades above zero for each JAMRIS-SIJ item. Moreover, expert agreement in the vignette ranking exercise was assessed using the ICC, as described above [14]. The Spearman rank correlation was utilized to assess the correlation of the ranking of MR image + image vignettes and the JAMRIS-SIJ grade-only vignettes with CAS-derived weighted JAMRIS-SIJ ranking. For ICC interpretation, values $\leq$ 0.50 were defined as poor, 0.51–0.75 as moderate, 0.76–0.90 as good, and $\geq$0.91 as excellent reliability [14]. For the Spearman rank correlation coefficients, values $\leq$ 0.40 were defined as poor correlation, 0.41–0.60 as moderate, 0.61–0.80 as substantial, and $\geq$0.81 as high correlation. Statistical analysis was performed using the SAS software version 9.4 (SAS Institute Inc., Cary, NC, USA).

3. Result

3.1. Summary of Survey Items

A total of 153 potential item-grade combinations in the inflammation domain (Figure A1) and 90 in the damage domain (Figure A2) involving two JAMRIS-SIJ measurement items were possible in the survey, which were completed either explicitly by experts through pairwise comparison (Figures A1 and A2) or implicitly through linear programming by the PAPRIKA algorithm 1000Minds software. The mean, range, and standard deviation (SD) of the number of item-grade combinations explicitly completed by experts was 35.6, 23–45, and 6.0 for the inflammation domain and 24.6, 17–28, and 2.7 for the damage domain, yielding 17 sets of relative weights unique to each expert. The average of the 17 relative weights from the experts was used as a template for the JAMRIS-SIJ weights (Table 1).

3.2. Conjoint Analysis Survey-Derived Relative JAMRIS-SIJ Weights

The average relative importance weights derived from the conjoint analysis survey had variable percentages depending on the grade and measurement items (Table 1). The relative weights for the highest grades among the inflammation items were osteitis (24.7%), bone marrow edema (24.3%), inflammation in erosion cavity (16.9%), joint space inflammation (13.1%), joint space fluid (9.1%), capsulitis (7.3%), and enthesitis (4.6%). Among JAMRIS-SIJ measurement items in the damage domain, the study average of the relative weights for the highest grades were ankylosis (41.3%), erosion (25.1%), backfill (13.9%), sclerosis (10.7%), and fat metaplasia lesions (9.1%). The complete set of average relative weights for the inflammation and damage domains is reported in Table 1.

3.3. Concordance of Conjoint Analysis Survey-Derived JAMRIS-SIJ Weights among Experts

The concordance of preference among the 17 experts in the conjoint analysis survey was moderate to excellent with ICCs for the inflammation domain survey of 0.60 (ICC 2.1) and 0.96 (ICC 2.k) (Figure A1 and Table 1) and damage domain survey of 0.73 (ICC 2.1) and 0.98 (ICC 2.k) (Figure A2 and Table 1). Item-wise agreement on the CAS-derived weights

for JAMRIS-SIJ item grades ranged from 0.17 to 0.76 for the inflammatory domain items and 0.22 to 0.78 for the damage domain items (Table 1).

3.4. Homogeneity of Vignette Rankings (by Conjoint Analysis Survey (CAS) Score and by Explicit Expert Rank)

The homogeneity of the 14 CAS-weighted JAMRIS-SIJ vignette scores was observed in the vignettes with the least and most severe SIJ disease, with significant variability in cases with mild disease (Figure 1A,B). For the inflammation domain, the ICC (2,1) of weighted JAMRIS-SIJ vignette scores among the 17 experts was 0.80 when using the scores as ratio-level percentage data (i.e., 0–100%), and 0.87 when converting the percentages to ordinal-level rank data (i.e., 1–14). For the damage domain, the ICC (2,1) of the vignette scores among the 17 experts was 0.83 when using the scores as ratio-level percentage data, and 0.99 when using their ordinal-level rank data. Five case vignettes had no significant osteochondral damage findings present, hence all of them receiving all-zero grades as per the JAMRIS-SIJ definitions. Therefore, these five vignettes were indistinguishable by the JAMRIS-SIJ damage domain weighted score. Instead, they were separated by the vignette's identification, ordered from the least to the greatest average grade-only vignette rank (Figure 2B).

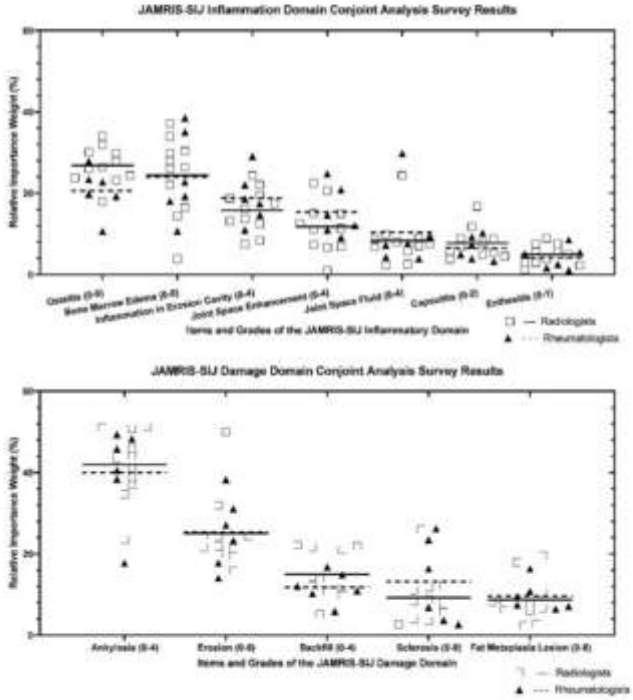

Figure 1. (**A**,**B**) Scatter plots of item weights derived from the conjoint analysis survey (CAS)-derived weights. (**A**) Scatter plots of inflammation domain item weights derived from the conjoint analysis survey (CAS)derived weights. Relative weights from all participants are plotted for each of the JAMRIS-SIJ inflammation domain items, with lines representing the median weight for radiologists (Square marker and solid line n = 11) and rheumatologists (triangular and broken line, n = 6). (**B**) Scatter plots of the damage domain item weights derived from the CAS-derived weights. Relative weights from all participants are plotted for each of the JAMRIS-SIJ damage domain items, with lines representing the median weight for radiologists (Square marker and solid line n = 11) and rheumatologists (triangular and broken line, n = 6).

The homogeneity of the 14 vignette ranks among the 16 experts by grade-only ranking was 0.83 for the inflammation domain, and 0.90 for the damage domain. For the imaging expert cohort, who also provided the concurrent grade + image ranking, the vignette ranks was 0.84 for the inflammation domain and 0.91 for the damage domain.

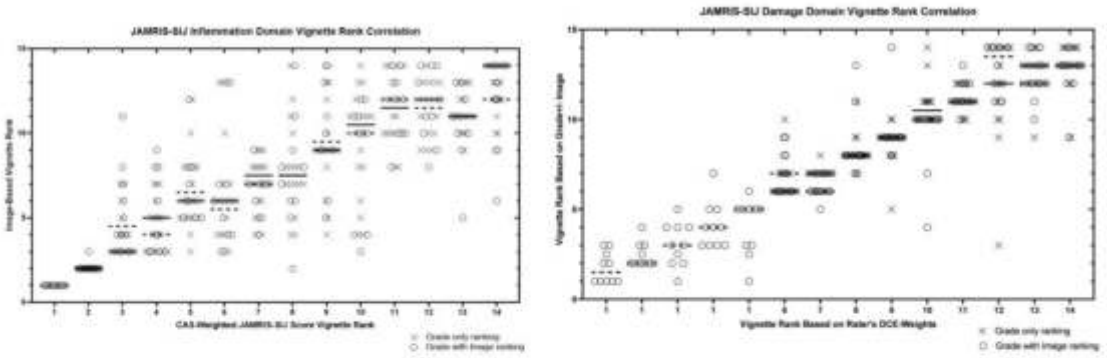

Figure 2. (**A**,**B**) Scatter plot of the of the JAMRIS-SIJ vignette ranks. (**A**) Scatter plot of the JAMRIS-SIJ vignette ranks produced by the full profile, MR image + grade ranking, ordered by consensus-graded, weighted JAMRIS-SIJ grade-only vignettes for the inflammation domain. Twelve imaging experts participated in the JAMRIS-SIJ image + grade ranking (circle maker), and 16 experts in the grade-only ranking (cross maker). For each of the 14 vignettes received, a consensus weighted grade rank on the x-axis and y-axis values for the image + grade ranks provided by the individual experts. Horizontal line denotes the median weighted score rank provided to each of the JAMRIS-SIJ MR image + grade vignettes. (**B**) Scatter plot of the of the JAMRIS-SIJ vignette ranks produced by the full profile, MR image + grade ranking, ordered by consensus-graded, weighted JAMRIS-SIJ grade-only vignettes for the damage domain. Twelve imaging experts participated in the JAMRIS-SIJ image + grade ranking (circle maker), and 16 experts in the grade-only ranking (cross maker). For each of the 14 vignettes received, a consensus weighted grade rank on the x-axis and y-axis values for the image + grade ranks provided by the individual experts. Horizontal line denotes the median weighted score rank provided to each of the JAMRIS-SIJ MR image + grade vignettes.

3.5. Correlation of JAMRIS-SIJ Vignette Ranking by MRI +/− Grade versus CAS Generated JAMRIS-SIJ Weights

Of the 17 CAS-survey respondents, 16 participated in the vignette ranking exercise (Figures 2 and 3). Each of the 16 experts provided two sets of vignette rankings, one produced by the expert's independent ranking of grade-only vignettes and one produced by applying the expert's CAS-derived weights to the grades (CAS weighted score rank). A subset of these experts (n = 12), who were imaging experts, also provided a third set of vignette rankings, derived using the grades of the vignettes as well as the representative MRI ("grade + image" ranking) to be correlated against their CAS-weighted score rank.

Correlation of the experts' grade-only vignette rank with their CAS-weighted score rank showed a median Spearman correlation of 0.84 (IQR: 0.80–0.94) for the inflammation domain and 0.93 (IQR: 0.90–0.96) for the damage domain (Figure 3, Table 2). Subgroup differences were observed for this grade-only ranking between rheumatologists and radiologists (n = 6 and 10, respectively; Table 2). The correlation of the radiologists' "grade + image" ranking against their CAS-weighted score rank showed a median Spearman correlation of 0.74 (IQR: 0.55–0.85) for the inflammation domain and 0.93 (IQR: 0.81–0.95) for the damage domain (Table 2).

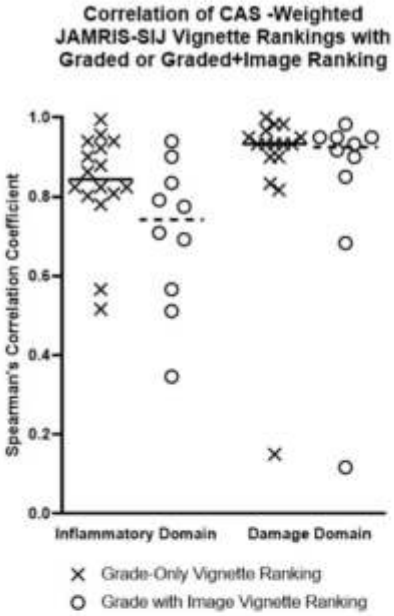

Figure 3. Correlation of CAS-Weighted JAMRIS-SIJ Vignette Ranking with Graded or Image Ranking. Spearman's rank correlation coefficients are plotted for each expert rater (radiologist and rheumatologist, n = 17) comparing their two methods of producing of vignette ranks, i.e., correlating the experts' grade-only or graded image-based full profile ranking with the ranking produced by applying the experts' own CAS-derived weights applied to consensus grades. Horizontal lines represent the median Spearman correlation for each subgroup of participants (X—grade-only vignette ranking, n = 17, O—grade + image vignette ranking, n = 12). The JAMRIS-SIJ MR image + grade vignettes.

Table 2. Spearman's correlation coefficients of four different datasets. Correlation of experts' preference for JAMRIS-SIJ measurement item weights for MR image, JAMRIS-SIJ score vignettes and a combination of MR image and score vignettes. CAS—conjoint analysis survey IQR—interquartile range.

		Spearman Correlation Coefficient of CAS-Weighted JAMRIS-SIJ vs. Graded ± Image Vignette Ranking			
Vignette Type	**Expert Cohort**	**Inflammation Domain**		**Damage Domain**	
		Median	IQR	Median	IQR
Grade only	All experts (n = 17)	0.84	0.80–0.94	0.93	0.90–0.96
	Rheumatologists (n = 6)	0.89	0.82–0.97	0.92	0.88–0.95
	Radiologists (n = 11)	0.82	0.73–0.93	0.94	0.91–0.97
Grade + Image	Radiologists (n = 10) Rheumatologist (n = 2)	0.74	0.55–0.85	0.93	0.81–0.95

4. Discussion

This study utilized a conjoint analysis of expert preferences to determine the relative weights of the measurement items within the JAMRIS-SIJ scoring system [15]. The experts in this study comprised eminent pediatric and adult rheumatologists and musculoskeletal radiologists with prior extensive experience in developing both adult and pediatric MR imaging scoring systems.

The relative weights of each grade for the inflammation and damage domain items are reported in Table 1. The two most important inflammation domain measurement items were bone marrow edema and osteitis, and their weights were equivalent (24.7% and 24.3%, respectively). Bone marrow edema and osteitis were 1.5 times more important

than inflammation in erosion cavity, 1.9 times more important than joint space fluid, and 5.3 times more important than enthesitis. For the JAMRIS-SIJ damage domain, ankylosis was the most important measurement item, which was 1.6 times more important than erosion and 4.6 times relative to fat metaplasia, which was the least important item among the five measurement items in the JAMRIS-SIJ damage domain. Erosion was rated second in relative importance by expert preference among the JAMRIS-SIJ damage domain, having 1.8 times more importance than backfill and 1.3 times more importance compared to sclerosis. The differential weights of the measurement items in the JAMRIS-SIJ are similar to the MRI scoring system for temporomandibular joint in JIA [16].

The presence of ankylosis signals advanced disease, which is in most cases a hallmark of irreversible osteochondral damage, while bone marrow edema and erosion are the preferred measurement items in discriminating the response to intervention in patients with JIA since these can be reversible entities, providing an objective metric for clinical decision making. The presence of bone marrow edema is indicative of active disease, providing clinical evidence for the initiation of therapy. Likewise, erosion has been reported to be a negative prognostic factor that warrants the use of more aggressive therapy in JIA, such as biologic agents [17].

The clustering of the relative weights of items in the inflammation domain was homogenous for both radiologists and rheumatologists, with a greater variability for bone marrow edema and joint space fluid. In the damage domain, there were substantial outliers of expert preference across all measurement items. This may be related to the complexities of the damage domain item definition and interpretation, further than in adults' occurrence of sacroiliitis, and resulting in part in the infrequent presence of the damage domain items among JIA patients. It may also be due to the availability and access to advanced imaging with prompt intervention that limits the progression of the JIA disease course to osteochondral damage.

Trends for the item weights at lower grades were not consistent with the highest grade weights. In the inflammation domain, inflammation in the erosion cavity at grade level 1 was 5.3%, which was higher in the point value than osteitis (3.9%) and bone marrow edema (3.2%). This was similar for joint space enhancement (4.5%) and capsulitis (4.6%). There were similar nonlinear trends in the intermediate grades in the inflammation domain items. However, in the damage domain, except for backfill, the item weights were consistent between grades. These grade-related differences in the JAMRIS-SIJ measurement items are likely due to the expert misperception on their preferences of SIJ MR imaging pathology at lower grades compared to higher grades among the measurement items. For example, the presence of bone marrow edema measured in 0–8 grades for a single quadrant of the SIJ MR image may suggest lesser disease compared to the presence of inflammation in an erosion cavity, which is measured in 0–4 grades in the superior half of an SIJ MR image. The differences in the measurement item levels of grades, for a four-grade level item, such as in the case of inflammation in erosion cavity, compared to an eight-grade level item, such as in the case of bone marrow edema, may distort the expert perception of the severity of the patient scenario of either inflammation or damage in the partial profile provided in the conjoint analysis survey. This may have resulted in scenarios where the experts have disproportionately weighted more disease for 0–4 grade level items and lesser disease for 0–8 grade level items.

The differences in the measurement value of osteitis and bone marrow edema are yet to be ascertained, as both measurement items are of uncertain origin that signal active disease and have similar clinical response to treatment. However, osteitis requires contrast enhancement for visualization, which is a significant limitation for its use in pediatric imaging due to the concern of contrast accumulation in the central nervous system after multiple scans and nephrogenic systemic fibrosis in patients with limited renal function [18,19]. Bone marrow edema may be present due to other causes unrelated to JIA, such as mechanical overload, trauma, infection, and neoplasm. In a recent study, bone marrow edema-like lesions were shown due to the normal variability in subchondral bone marrow signal in

growing children [20]. Whether osteitis and bone marrow edema should both be scored would sensibly depend on the imaging protocol used.

Determining whether a small amount of fluid in the joint space is pathologic becomes challenging when associated pathologic findings, such as bone marrow edema, are absent. Correlations found between joint effusion and bone marrow edema measurement items may be partially due to their pathogenesis. This could have contributed to the experts' preferences for relative weights of individual items. Further studies are needed in the future to improve our understanding on the inter-relationship of items which may help us reduce the variance among experts in allocating point values for individual measurement items.

Imaging outcome measurement tools are increasingly used to assess intervention effectiveness in musculoskeletal disease clinical trials, with evidence supporting the use of MRI as the preferred modality of choice in JIA [21]. To objectively assess JIA disease activity and change after therapeutic intervention, it is possible to use the multi-component JAMRIS-SIJ score without weighting each component. However, it is also desirable to generate a single composite score as a summary biomarker. If a single score is to be generated, this requires the relative weighting of its measurement items for clinical importance in some way. Ideally, this will improve the construct validity of the composite domain score by increasing the weighing of changes which are more specific and/or sensitive to JIA.

This study has some limitations. Chief among them is the expert-driven weighting method used. Experts' preferences vary considerably due to the expected differences among the patient population and in clinical experiences. The validity of experts' preferences was also limited by subject matter expertise, a criterion that is not impervious to fallibility. Moreover, the differential preferences of experts did not necessarily account for the inherent intercorrelation of the measurement items, for which there are gaps in the knowledge base in the literature. Furthermore, the sampling of the JAMRIS-SIJ full profile image vignettes was limited in this study as we tried to minimize the pragmatic issues related to survey fatigue that could have arisen from the assessment of a large sample of imaging vignettes at a single setting. This sample size limitation in this study may have influenced the coefficients of correlation of the JAMRIS-SIJ weighted scores and the JAMRIS-SIJ vignette ranking.

5. Conclusions

This study used a formal conjoint analysis-based survey to elicit expert preferences on the relative weights of measurement items and grades, which are necessary to generate single summaries for the two domains of the JAMRIS-SIJ from constituent items. The face and content validity of the partial profile CAS-derived JAMRIS-SIJ weights was high when compared to the full profile vignettes defined by grades with and without representative images. These weights may provide value, by helping to appropriately measure disease activity and treatment effectiveness in JIA clinical trials.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/jcm12072729/s1, Table S1: Distribution of individual experts with the years of experience into imaging and clinician expert cohort. The imaging expert cohort comprises of ten radiologist and two rheumatologists with imaging interpretation experience who ranked the JAMRIS-SIJ image+grade and grade-only vi-gnettes. The clinician expert cohort comprise of one radiologist and 4 rheumatologist who com-pleted only the JAMRIS-SIJ grade-only vignettes.

Author Contributions: Conceptualization, A.S.D., T.M.O., N.H. (Nigil Haroon), R.M. and M.T.; methodology, A.S.D., T.M.O., M.T., J.L.J., N.H. (Nele Herregods), J.D.A., J.S., S.J., A.B.M., I.S.-S., S.M.L.T. and M.Z.; software, T.M.O. and M.T.; validation, T.M.O., M.T., A.B.M., J.S., M.Z., S.J., S.M.L.T., N.H. (Nigil Haroon), J.L.J., R.M., N.H. (Nele Herregods), J.D.A., L.J., N.T., S.A., M.P., A.E.L., E.J.I.C., P.W., O.P., E.K., M.A.J.v.R., D.G.R., J.C., P.G.C., I.S.-S. and A.S.D.; formal analysis, T.M.O., M.T. and A.S.D.; investigation, T.M.O., M.T., A.B.M., J.S., M.Z., S.J., S.M.L.T., N.H. (Nele Herregods), J.D.A., J.L.J., R.M., N.H. (Nigil Haroon), L.J., N.T., S.A., M.P., A.E.L., E.J.I.C., P.W., O.P., E.K., M.A.J.v.R., D.G.R., J.C., P.G.C., I.S.-S. and A.S.D.; resources, A.S.D. and T.M.O.; data curation, A.S.D., S.J., T.M.O., J.S. and M.T.; writing—original draft preparation, T.M.O.; writing—review and editing, T.M.O., M.T., A.B.M., J.S., M.Z., S.J., S.M.L.T., N.H. (Nele Herregods), J.D.A., J.L.J., R.M., N.H. (Nigil Haroon), L.J.,

N.T., S.A., M.P., A.E.L., E.J.I.C., P.W., O.P., E.K., M.A.J.v.R., D.G.R., J.C., P.G.C., I.S.-S. and A.S.D.; visualization, T.M.O. and M.T.; supervision, A.S.D.; project administration, T.M.O. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the research ethics board (REB) of the Hospital for SickKids (REB number 1000059077).

Informed Consent Statement: Implied consent was obtained if study participants voluntarily completed and submitted the study questionnaires after receiving an invitation to participate in the study. The REB waived patient consent. The magnetic resonance images used for the image vignettes were anonymized.

Data Availability Statement: The data presented in this study are available on request from the corresponding author. The data are not available publicly due to privacy and ethical reasons.

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Conflicts of Interest: The authors declare no conflict of interest.

Appendix A

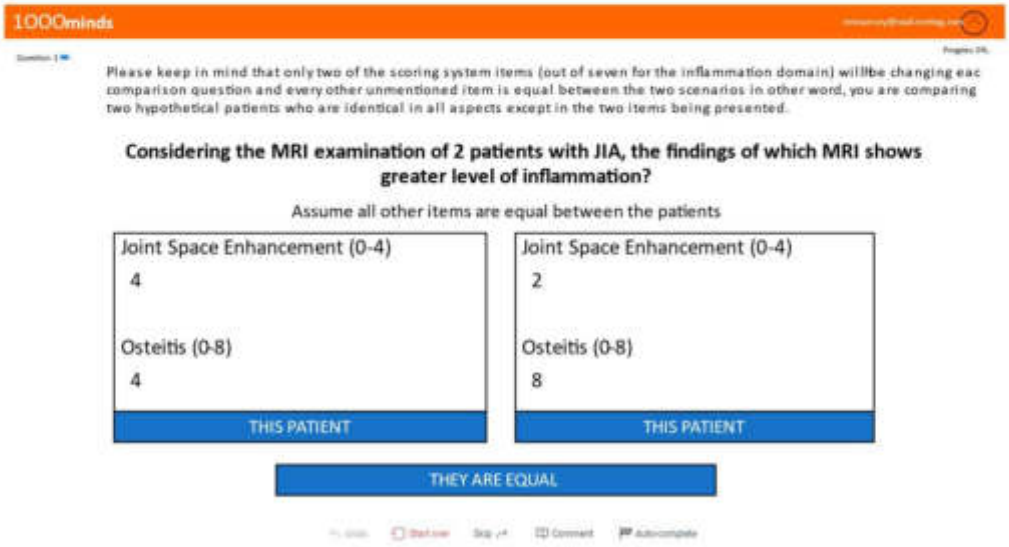


Figure A1. JAMRIS-SIJ inflammation domain item comparison. An example of an item comparison question presented by the 1000Minds software to the rating experts to elicit their preferences of the relative importance weights for the JAMRIS-SIJ inflammation domain items. The expert was asked to compare two hypothetical patients assuming all other features were equal: with a score of 4 each for joint space enhancement (JSE) and osteitis and patient; with a score of 2 for JSE and 8 for osteitis. The expert had to choose which patient showed greater inflammation or rate them as equal. The questions varied adaptively and were presented again until all necessary trade-off questions were completed by the expert to determine the relative weights for each domain.

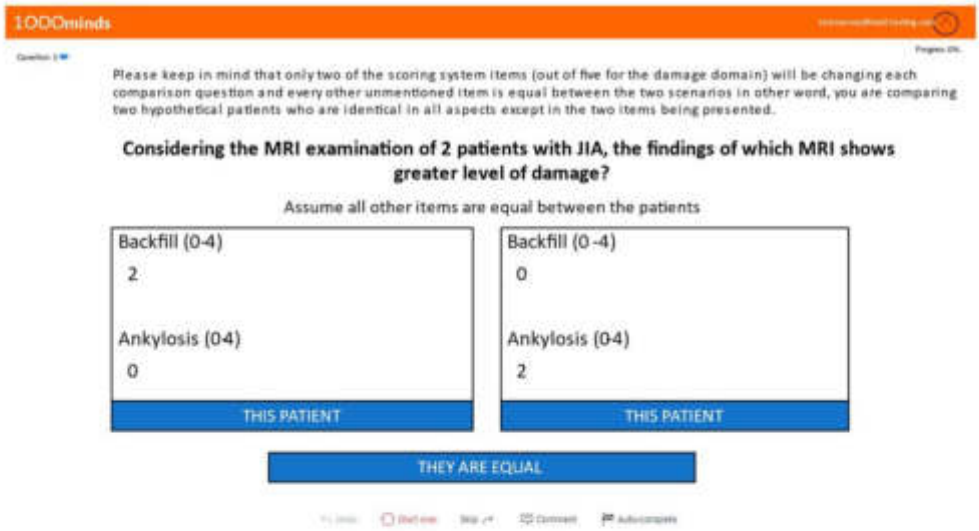
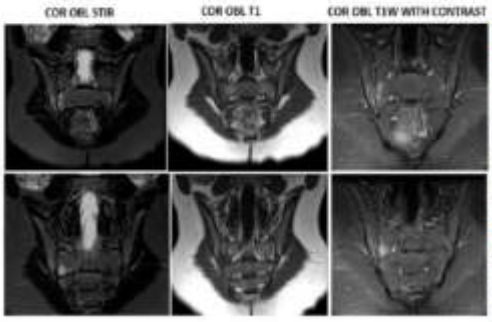


Figure A2. JAMRIS-SIJ damage domain item comparison. An example of an item comparison question presented by the 1000Minds software to the rating experts to elicit their preferences on the relative importance weights for the JAMRIS-SIJ damage domain items. The expert was asked to compare two hypothetical situations in patients with juvenile idiopathic arthritis assuming all other features were equal: with a score of 2 for backfill and 0 ankylosis and patient; with a score of 2 for ankylosis and 0 for osteitis. The expert had to choose which patient showed greater damage or to rate them as presenting with equal damage. The questions varied adaptively and were presented again until all necessary trade-off questions were completed by the expert to determine the relative weights for each domain.

Appendix B



Inflammatory	
BME	3
Join space enhancement	1
Osteitis	2
Capsulitis	0
Joint space fluid	0
Enthesitis	NA
Inflammation in erosion cavity	0
Damage	
Sclerosis	0
Erosion (RT=2, LT =1)	3
Fat Metaplasia	0
Backfill	0
Ankylosis	0

Figure A3. JAMRIS-SIJ image + grade vignette used for ranking exercise to test conjoint analysis survey (CAS)-derived weights. Fourteen image + grade vignettes were constructed corresponding to various combinations of pathologies in the JAMRIS-SIJ. Experts individually ranked the cases from the greatest to least level of inflammation and damage, respectively.

MRI Images not provided for grade-only vignettes

Inflammatory	
BME	3
Join space enhancement	1
Osteitis	2
Capsulitis	0
Joint space fluid	0
Enthesitis	NA
Inflammation in erosion cavity	0
Damage	
Sclerosis	0
Erosion (RT=2, LT =1)	3
Fat Metaplasia	0
Backfill	0
Ankylosis	0

Figure A4. JAMRIS-SIJ grade-only vignette used for ranking exercise to test conjoint analysis survey (CAS)-derived weights. Fourteen grade-only vignettes were constructed corresponding to various combinations of pathologies in the JAMRIS-SIJ. Experts individually ranked the cases from the greatest to least level of inflammation and damage, respectively.

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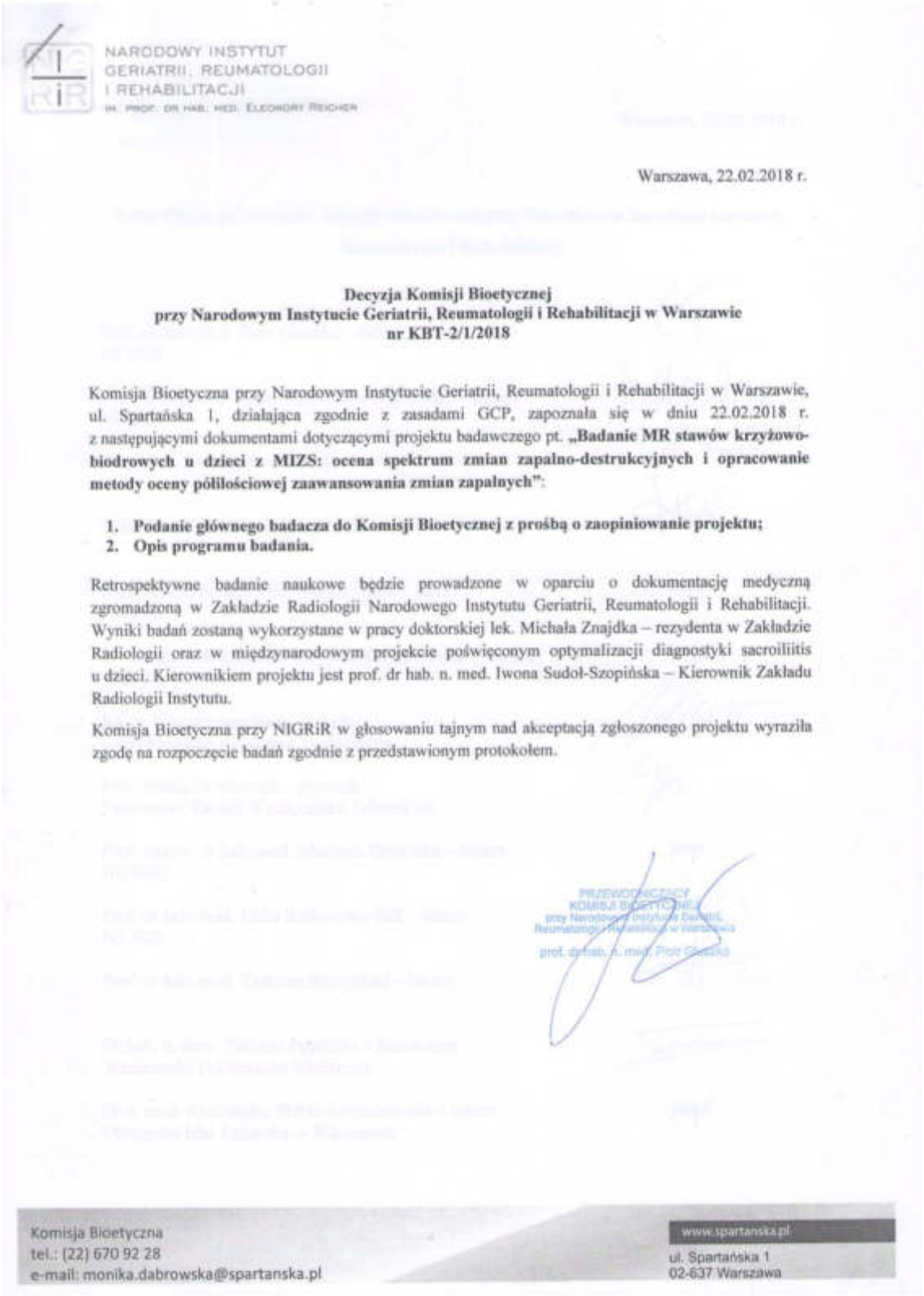
10. Spis rycin i tabel

Spis rycin

Spis tabel

11. Opinia Komisji Bioetycznej



NARODOWY INSTYTUT
GERIATRII, REUMATOLOGII
I REHABILITACJI
IM. PROF. DR HAB. MED. ELEONORY REICHER

Warszawa, 22.02.2018 r.

Decyzja Komisji Bioetycznej
przy Narodowym Instytucie Geriatrii, Reumatologii i Rehabilitacji w Warszawie
nr KBT-2/1/2018

Komisja Bioetyczna przy Narodowym Instytucie Geriatrii, Reumatologii i Rehabilitacji w Warszawie, ul. Spartańska 1, działająca zgodnie z zasadami GCP, zapoznała się w dniu 22.02.2018 r. z następującymi dokumentami dotyczącymi projektu badawczego pt. **„Badanie MR stawów krzyżowo-biodrowych u dzieci z MIZS: ocena spektrum zmian zapalno-destrukcyjnych i opracowanie metody oceny półilościowej zaawansowania zmian zapalnych"**:

1. **Podanie głównego badacza do Komisji Bioetycznej z prośbą o zaopiniowanie projektu;**
2. **Opis programu badania.**

Retrospektywne badanie naukowe będzie prowadzone w oparciu o dokumentację medyczną zgromadzoną w Zakładzie Radiologii Narodowego Instytutu Geriatrii, Reumatologii i Rehabilitacji. Wyniki badań zostaną wykorzystane w pracy doktorskiej lek. Michała Znajdka – rezydenta w Zakładzie Radiologii oraz w międzynarodowym projekcie poświęconym optymalizacji diagnostyki sacroiliitis u dzieci. Kierownikiem projektu jest prof. dr hab. n. med. Iwona Sudoł-Szopińska – Kierownik Zakładu Radiologii Instytutu.

Komisja Bioetyczna przy NIGRiR w głosowaniu tajnym nad akceptacją zgłoszonego projektu wyraziła zgodę na rozpoczęcie badań zgodnie z przedstawionym protokołem.

PRZEWODNICZĄCY
KOMISJI BIOETYCZNEJ
przy Narodowym Instytucie Geriatrii,
Reumatologii i Rehabilitacji w Warszawie
prof. dr hab. n. med. Piotr Głuszko

Komisja Bioetyczna
tel.: (22) 670 92 28
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ul. Spartańska 1
02-637 Warszawa

Warszawa, 22.02.2018 r.

Lista obecności członków Komisji Bioetycznej przy Narodowym Instytucie Geriatrii, Reumatologii i Rehabilitacji

Prof. dr hab. med. Piotr Głuszko – lekarz
NIGRiR ……

Prof. dr hab. med. Anna Filipowicz-Sosnowska – lekarz
NIGRiR ……

Dr n. hum. Ewa Kujawa – etyk ……

P. Barbara Kurek – pielęgniarka ……

Prof. nadzw. dr hab. med. Robert Gasik – lekarz
NIGRiR ……

Prof. nadzw. dr hab. med. Brygida Kwiatkowska – lekarz
NIGRiR ……

Ks. dr Włodzimierz Nast – ksiądz
Chrześcijańska Akademia Teologiczna ……

Mec. Maria Grzeszczyk – prawnik
Państwowy Zakład Wydawnictw Lekarskich ……

Prof. nadzw. dr hab. med. Marzena Olesińska – lekarz
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NIGRiR ……

Prof. dr hab. med. Tadeusz Styczyński – lekarz ……

Dr hab. n. farm. Tomasz Pawiński – farmaceuta
Warszawski Uniwersytet Medyczny ……

Dr n. med. Aleksandra Słabik-Ledóchowska – lekarz
Okręgowa Izba Lekarska w Warszawie ……

12. Oświadczenia współautorów publikacji

Warszawa 1.09.2024r.

Prof. Dr hab. Med. Iwona Sudoł-Szopińska
Narodowy Instytut Geriatrii, Reumatologii i Rehabilitacji
Ul. Spartańska 1, 02-637 Warszawa

OŚWIADCZENIE

Oświadczam, że w publikacji pt.: Imaging of Juvenile Spondyloarthritis. Part I: Classifications and Radiographs, Autorzy: Iwona Sudoł-Szopińska, Piotr Gietka, Michał Znajdek, Genowefa Matuszewska, Magdalena Bogucevska, Ljubinka Damjanovska-Krstikj, Slavcho Ivanoski, opublikowanej w Journal Of Utrasonography 2017;

DOI: 10.15557/JoU.2017.0025, mój wkład merytoryczny w przygotowanie publikacji polegał na:

Zaprojektowaniu pracy

Przygotowaniu manuskryptu

Analizie literatury.

Jako pierwszy i korespondencyjny autor powyższej międzynarodowej publikacji, oceniam swój wkład procentowy w publikację na poziomie 45%, doktora Michała Znajdka na poziomie 35%, pozostałych współautorów 5%.
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Z poważaniem,

Iwona Sudoł-Szopińska

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Warszawa 1.09.2024r.

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OŚWIADCZENIE

Oświadczam, że w publikacji pt.: Imaging of Juvenile Spondyloarthritis. Part II: Ultrasonography and Magnetic Resonance Imaging, Autorzy: Iwona Sudoł-Szopińska Michał Znajdek, Piotr Gietka, Violeta Vasilevska-Nikodinovska, Lukas Patrovic, Vladka Salapura; opublikowanej w Journal Of Utrasonography 2017;

DOI: 10.15557/JoU.2017.0025, mój wkład merytoryczny w przygotowanie publikacji polegał na:

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Z poważaniem,

Iwona Sudoł-Szopińska

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ul. Spartańska 1
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Gent, 26.09.2024

Dr. Eva Schiettecatte

Department of Radiology and Medical Imaging,

Ghent University Hospital,

Corneel Heymanslaan 10, 9000, Gent, Belgium

DECLARATION

I hereby declare that in the publication entitled: Common incidental findings on sacroiliac joint MRI in children clinically suspected of juvenile spondyloarthritis , Authors: Eva Schiettecatte, Jacob L. Jaremko, Iwona Sudoł-Szopińska, Michał Znajdek, Ramin Mandegaran, Vimarsha Gopal Swami, Lennart Jans, Nele Herregods, published in European Journal of Radiology Open; DOI:10.1016/j.ejro.2020.100225;

my substantive contribution to the publication consisted of:

Designing the paper

Preparation of the manuscript

Analysis of the literature

As first and corresponding author of the above international publication, I estimate my percentage contribution to the publication at 40%, Dr Michał Znajdek at 35%, the other co-authors at 5%.

I agree to submit the above publication by Dr Michał Znajdek as part of his doctoral dissertation in the form of a coherent series of scientific articles published in peer-reviewed scientific journals.

At the same time, I declare that the independent and separable part of the above publication shows an individual contribution of dr. Michał Znajdek in the design of the work, preparation of the manuscript, and analysis of the literature for this work.

Yours sincerely,

SickKids
THE HOSPITAL FOR SICK CHILDREN

Department of Diagnostic Imaging
The Hospital for Sick Children

UNIVERSITY OF TORONTO
FACULTY OF MEDICINE

September 4th, 2023

RE: Confirmation Letter for Michael Znajdek

Dear Sir / Madam,

I am pleased to write this letter in support of Dr. Michael Znajdek whom I had the chance to know as a member of the OMERACT Sacroiliac Joint (IJ) Working Group. I serve as Co-Chair of the MRI in Juvenile Idiopathic Arthritis OMERACT SIG over the past decade.

In this capacity I got to know the nice work that Dr. Michael Znajdek has done to our working group under the supervisor of Dr. Iwona Sudol-Szopinska. The contribution that Michael has made towards the success of several research projects conducted by the SIJ working group are remarkable and greatly appreciated.

With specific regard to the paper entitled: "Determination of Relative Weightings for the Component Pathologies of the OMERACT Juvenile Arthritis Magnetic Resonance Imaging Sacroiliac Joint Score", published in the Journal of Clinical Medicine 2023, 12, 272; doi.org/10.3390/jcm12072729, I am the senior and corresponding author, responsible for the coordination of the study prior to the submission of the manuscript for publication.

Based on the feedback received from Dr. Sudol-Szopinska and other investigators of our working group, and on the invaluable contribution of Michael towards the conduct of the study I attest that he substantially contributed to the study conduct. His contribution made it possible the accrual of cases for the study, local creation and validation of the tools to be used in the study, discussion of methods and results and edition of the manuscript, therefore his contribution can be counted as at least one third (33%) efforts compared to the first author of the paper.

I agree with the submission of the aforementioned publication as part of Dr. Michael Znajdek's doctoral dissertation.

If I can be of any further assistance, please do not hesitate to contact me.

Sincerely,

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13. Piśmiennictwo

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