THU0539

IMPACT OF BODY MASS INDEX ON THE AGREEMENT BETWEEN ULTRASOUND- AND CLINICAL ASSESSMENTS OF DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS: MULTICENTRE AND CROSS-SECTIONAL STUDY

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Background: Clinical assessment of swollen joint count (SJC) in rheumatoid arthritis (RA) might be affected by obesity in terms of obesity-related excess adipose tissue.
Objectives: To compare the level of agreement between synovitis evaluated by Power Doppler ultrasound (PDUS) and clinical examination (SJC as component of SDAI) in obese (O) (i.e. Body Mass Index (BMI) >30) versus non-obese (NO) (BMI≤30) RA patients.
Methods: RA patients ≥18 years fulfilling 2010 ACR-EULAR criteria were included in the cross-sectional multicentre (13 centres) French observational RABODI study (ClinicalTrials.gov Identifier: NCT03004651). Clinical synovitis was evaluated on 44 joints. ESR and CRP were collected and SDAI, DAS28, DAS were calculated. A standard US examination on 44 joints was performed by an independent investigator blinded to clinical data. US synovitis was defined by a synovial hypertrophy ≥1 and PD signal≥1 on a semi-quantitative scale according to the EULAR-OMERACT scoring system. Levels of agreement between number of synovitis defined by PDUS and clinical examination were compared in O versus NO patients using Chi2 test, and Kappas (k) and ORs were calculated. A patient was considered "discordant" if ≥1 joint was discordantly classified by PDUS and clinical examination. SDAI was calculated and compared, with SJC defined either by clinical examination or PDUS.
Results: 121 patients were included: mean (SD) age of 58.5 (12.7) years, mean disease duration of 11.1 (9.7) years. 81% were female, 84.3% anti-CCP positive, 63.6% had erosive disease. Mean SDAI was 12.6 (±10.2). 53 (43.8%) had a BMI >30 and 68 (56.2%) ≤30. 59 (48.7%) and 62 (51.2%) had a SDAI≤11 and >11, respectively. The 2 groups were comparable, except for weight (mean (SD) 65.4 (13.5) vs 96.7 (14.7) kg, p< 0.001), some comorbidities (diabetes, asthma and fibromyalgia more frequent in O patients), tender joint count (mean 4.04 (±5.23) in NO vs 7.38 (±8.64) in O, p=0.021). Mean number of SJC was 2.4 (3.3), and PDUS 6.7 (±6.3). Levels of agreement between clinical and PDUS findings were comparable in O vs. NO patients regarding SDAI and other scores (Table). Patients with ≥3 discordant joints were numerically higher in O patients compared to NO (26/53 (49.1%) vs 22/68 (32.4%), p=0.062). At the joint level, discordance was higher in O patients in MCP4 (p=0.057), wrist (p=0.089).

Table. Level of agreement between PDUS synovitis and SJC in obese versus normally weighted RA patients

Score with PDUS vs. SJC		BMI ≤ 30 N=68	BMI > 30 N=53	OR (95%CI)	P*
SDAI	Non-Discordant (ND)	63	46	**1.92 (0.57-6.42)**	**0.28**
	Discordant (D)	5	7		
	Kappa	**0.85**	**0.73**		
DAS28	ND	62	47	**1.32 (0.4-4.35)**	**0.64**
	D	6	6		
	Kappa	**0.81**	**0.77**		
DAS44	ND	63	52	**0.24 (0.03-2.14)**	**0.23**
	D	5	1		
	Kappa	**0.83**	**0.96**		
≥1 synovitis	ND	51	35	**1.54 (0.7-3.4)**	**0.28**
	D	17	18		
	Kappa	**0.50**	**0.32**		

Conclusion: In RA patients, despite a perceived higher difficulty to clinically detect SJ in O patients, the discrepancy between clinically- and PDUS defined synovitis was not significantly higher than in NO patients, and did not impact the extend of the definition of disease activity level.

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THU0540

A PHASE 2B STUDY OF INTRAVENOUSLY (IV) ADMINISTERED TC 99M TILMANOCEPT TO DETERMINE DIFFERENTIAL UPTAKE, REPRODUCIBILITY OVER TIME AND IMAGE STABILITY IN HEALTHY SUBJECTS AND IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA) ON STABLE TREATMENT

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Background: At present, there are no reliable noninvasive means to directly monitor disease activity in RA patients. Activated macrophages are a critical component of the inflammatory etiology of RA due to their role in prolonged RA joint inflammation and destruction through the release of pro-inflammatory cytokines and chemokines. Tc 99m tilmanocept is a radiopharmaceutical imaging agent that binds with high affinity to the macrophage mannose receptor CD206 that resides on activated macrophages. Previous clinical trials demonstrated safety and tolerability of Tc 99m tilmanocept, as well as a determination of optimal clinical dose and timeframe for RA imaging.
Objectives: The current phase 2b study aims to evaluate reproducibility and stability of imaging and will assess quantitative Tc 99m tilmanocept uptake cut points that reliably enable discrimination between joints of healthy people and RA patients.
Methods: The analysis cohort contained 18 healthy controls (HC) clinically free of inflammatory joint disease and 12 subjects with clinically diagnosed RA who are on stable anti-inflammatory and/or anti-rheumatic therapy. Each subject received a 150-mcg dose of tilmanocept radiolabeled with 10 mCi of Tc 99m in a 3mL IV injection. Injection was followed by planar imaging at 60 and 180 minutes for both HC and RA subjects on study Day 0 and repeated in RA subjects on Day 8. Images were quantitatively assessed to detect localization within synovial spaces of bilateral hands and wrists by determining average pixel intensity in each region of interest relative to average pixel intensity in a joint-specific reference region.
Results: Data obtained from the interim analysis support the hypothesis that Tc 99m tilmanocept imaging can provide robust quantitative imaging in HC and RA subjects. Repeat images within and between days demonstrate root mean squared differences that are approximately 10% or less of the observed localization of Tc 99m tilmanocept. Qualitatively, images of HC indicated no disease-related site-specific localization, whereas localization is present in RA subjects at levels expected given the difference in macrophage number and density in different pathotypes of RA. Notably, images from patients with active RA exhibit the same localization patterns on images taken in a test-retest fashion on the same day as well as in subjects with images acquired on Day 0 and Day 8 (see Figure 1). These results show low imaging readout variability, enabling reliable quantification of joints with RA-involved macrophage-mediated inflammation. Analysis of the HC and RA images was used to determine initial quantitative "cut-points" to differentiate between joints with and without the inflammation typically seen in RA.

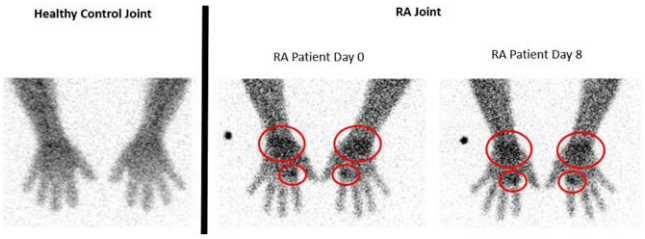

Figure 1. Tilmanocept consistently localizes in areas of macrophage-driven inflammation, demonstrating low variability. RA patients exhibit reproducible localization over a 1-week period. Typical of healthy subjects, no evidence of inflammation-related Tc 99m tilmanocept uptake was observed in the healthy control. Images on the right show same patient imaged on 2 different days.

Conclusion: Tc 99m tilmanocept imaging of the joints in healthy subjects as well as in patients with active RA under stable treatment is reproducible and stable over time. The results confirmed that the signal in joints of healthy subjects and RA patients can be quantified and used to establish cut points to distinguish inflamed and non-inflamed joints on a joint-by-joint basis. These results provide the foundation for a noninvasive, objective method to monitor activity in macrophage-driven inflammation in joints of patients with RA.

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THU0541 ANATOMICAL LOCATION OF SACROILIAC JOINT MRI LESIONS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS, POSTPARTUM WOMEN, PATIENTS WITH DISC HERNIATION, CLEANING STAFF, RUNNERS AND HEALTHY PERSONS

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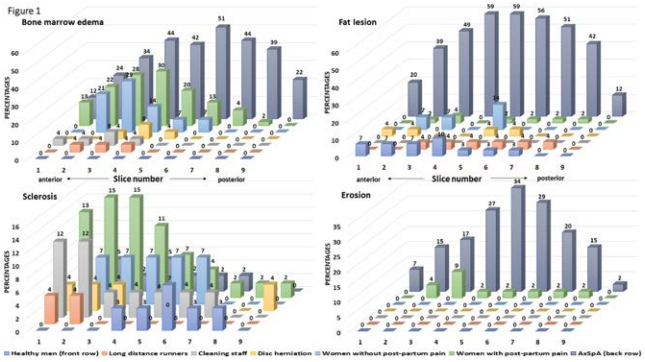
Background: Bone marrow edema (BME) on sacroiliac joint (SIJ) MRI is central in the Assessment of SpondyloArthritis International Society classification criteria for axial spondyloarthritis (axSpA). However, BME can be seen in other conditions and healthy persons. The presence of structural lesions may contribute to diagnosing axSpA.

Objectives: To investigate the location and distribution of SIJ MRI lesions in patients with axSpA and disc herniation, women with and without post-partum pain (PPP), cleaning staff, runners, and healthy persons.

Methods: In a prospective cross-sectional study of 204 participants, MRI of the SIJs was evaluated by two readers. MRI images were scored according to the SPARCC SIJ Inflammation[1] and Structural (SSS)[2] lesion definitions. Based on concordant reads, lesions were analysed according to location (unilateral/bilateral SIJ, upper/lower sacral/iliac quadrant/joint half, anterior (slice1-3)/central (slice 4-6)/posterior (slice 7-9) SIJ sections.

Results: BME was present in nearly all groups, in all quadrants, and primarily in the anterior SIJ section (Figure 1), but rarely as a bilateral feature, except in axSpA and women with PPP (Table 1). Fat lesion (FAT) was mainly found in axSpA, in all slices, and mostly bilaterally in the sacrum. In the other groups FAT was primarily located in the anterior and central SIJ sections. Sclerosis was only seen in the ilium, and was present in most groups, particularly in women with PPP, often bilaterally. Erosion was only seen in women with PPP (mostly unilaterally) and in axSpA (mainly bilaterally in the ilium). Backfill and ankylosis were only seen in axSpA.



Conclusion: Typical locations of common SIJ lesions in axSpA and non-axSpA were reported. In non-axSpA, except women with PPP, bilateral as well as posterior lesions were rare, while backfill and ankylosis were absent.

References:

[1] Maksymowych et al, *Arthritis Rheum, 2005*

[2] Maksymowych et al, *J of Rheumatol,* 2015

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Table 1. Participant characteristics and distribution of lesions – unilaterally/bilaterally in iliac/sacral quadrants

			AxSpA	Women with post-partum pain	Women without post-partum pain	Disc herniation	Cleaning staff	Long distance runners	Healthy men
Number of participants			41	46	14	25	26	23	29
Age			30.9 (6.4)	32.6 (3.3)*	33.1 (4.1)	35.2 (5.7)**	39.1 (4.6)***	32.7 (6.2)	30.9 (6.4)
Male sex			63	0***	0***	44	0***	78	100***
Low back pain VAS (0-10)			3.8 (2.8)	5.5 (2.4)**	0.4 (0.7)***	5.5 (2.4)*	0.8 (1.8)***	0.2 (0.5)***	0.1 (0.3)***
HLA-B27 positive			81	11***	7***	0***	0***	4***	14***
C-Reactive Protein >3 mg/l			59	17***	21**	20**	15**	17**	3***
	Quadrant:		**UNI / BI**	**UNI / BI**	**UNI / BI**	**UNI / BI**	**UNI / BI**	**UNI / BI**	**UNI / BI**
BME	Ilium	Upper	27 / 7	11 / 9	0 / 0	0 / 0	0 / 4	0 / 0	0 / 0
		Lower	22 / 17	15 / 13	21 / 0	0 / 0	0 / 4	4 / 0	0 / 0
	Sacrum	Upper	29 / 22	17 / 9	29 / 0	4 / 0	4 / 0	0 / 0	0 / 0
		Lower	24 / 20	9 / 9	4 / 0	4 / 0	0 / 0	0 / 0	0 / 0
FAT	Ilium	Upper	20 / 17	2 / 0	7 / 0	4 / 0	0 / 0	0 / 0	0 / 7
		Lower	17 / 29	0 / 0	7 / 0	4 / 0	0 / 0	0 / 0	0 / 3
	Sacrum	Upper	22 / 44	2 / 4	0 / 7	0 / 4	0 / 0	4 / 0	3 / 3
		Lower	17 / 42	2 / 2	4 / 7	0 / 0	0 / 0	4 / 0	3 / 3
Sclerosis	Ilium	Upper	5 / 2	4 / 4	0 / 7	4 / 4	4 /4	0 / 0	3 / 7
		Lower	0 / 0	9 / 9	7 / 0	0 / 4	15 / 0	4 / 0	0 / 0
	Sacrum	Upper	0 / 0	0 / 0	0 / 0	0 / 0	0 / 0	0 / 0	0 / 0
		Lower	0 / 0	0 / 0	0 / 0	0 / 0	0 / 0	0 / 0	0 / 0
Erosion	Ilium	Upper	22 / 24	4 / 0	0 / 0	0 / 0	0 / 0	0 / 0	0 / 0
		Lower	17 / 24	2 / 2	0 / 0	0 / 0	0 / 0	0 / 0	0 / 0
	Sacrum	Upper	10 / 5	2 / 0	0 / 0	0 / 0	0 / 0	0 / 0	0 / 0
		Lower	22 / 2	2 / 2	0 / 0	0 / 0	0 / 0	0 / 0	0 / 0

Values are % or mean (SD)

Mann-Whitney test was applied, tests are patients with axSpA compared with all other groups. P<0.05*; p<0.01**; p<0.001***

BI: bilateral; BME: Bone marrow edema; FAT: fat lesion; HLA-B27: Human Leukocyte Antigen B27;UNI: unilateral; VAS: Visual Analogue scale