Getting grip on preclinical rheumatoid arthritis

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CHAPTER 6

NO ADDED VALUE OF OPTIMAL SPECTRAL TRANSMISSION IMAGING IN PERSONS AT RISK OF RHEUMATOID ARTHRITIS

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KEY MESSAGE

OST imaging likely cannot contribute to diagnosis and prediction of arthritis in RA-risk individuals

Dear Editor,

Accurate prediction of rheumatoid arthritis (RA) development in individuals at risk of RA remains challenging. Previous studies showed that musculoskeletal ultrasonography (US) abnormalities can help predict clinical arthritis development in at-risk individuals[1,2]. However, performing US in every at-risk individual is not feasible due to time constraints, costs and high dependence on the examiner. Optimal spectral transmission (OST) imaging could be an objective, fast and low-cost alternative. It measures the transmission of light through tissue. Synovitis causes changes in the joint capsule and synovial fluid, decreasing light transmission[3]. In RA patients, OST correlated to US in detecting synovitis in the hand joints[4-8]. In at-risk individuals, OST might be an alternative for US to detect subclinical synovitis and possibly predict clinical arthritis. This is the first study of OST in an RA-risk population. To study the feasibility of OST in individuals at risk of RA, we 1) compared OST to US for detecting subclinical inflammation, 2) compared OST results between at-risk individuals, healthy controls and RA patients and 3) related OST and US to later occurring arthritis.

OST (HandScan, Hemics) and US measurement of the proximal interphalangeal (PIP), metacarpophalangeal (MCP) and wrist joints were performed in 35 prospectively followed patients with rheumatoid factor (RF) and/or anti-citrullinated protein antibody (ACPA) positive arthralgia without clinical arthritis[2]. For comparison, OST was also performed in 24 RA patients with active disease (≥2 swollen hand- or wrist joints), and 37 healthy controls, both groups age and sex matched (Blanken et al, manuscript submitted for publication). OST assigned each joint a score ranging from 0-3 (based on receiver operating characteristic (ROC) curves with DAS28 and US); a total score was calculated by summation of the 22 individual joint scores (range 0-66). Based on previous research[7], a predefined cut-off of ≥12.99 suggested the presence of inflammation (based on the ROC curve distinguishing RA patients from healthy controls). US greyscale (GS) and power doppler (PD) signal were scored using a four-grade semi-quantitative scale (0–3). GS grade ≥2 and/or PD grade ≥1 were regarded as abnormal (US abnormal score). Total GS and PD scores were calculated by summation of joint scores (range 0-66). Arthritis development was followed over a median (range) of 27 (26-28) months. Difference in US abnormal score between OST above and below cut-off was tested using the Chi-square test. Correlation between OST and US was analyzed using the spearman correlation test. Association with arthritis development was visually inspected using a scatter plot. Differences in OST score between the cohorts were analyzed using the one-way ANOVA test.

Baseline characteristics are shown in table 1. In the at-risk cohort, median OST total score was 12 (9-15) and 13 persons (37%) had a score above cut-off. Median US GS total score was 4 (2-9) and 14 persons (40%) had an abnormal GS score in ≥1 joint. Only 2 persons showed a PD signal. There was no difference in abnormal US score between OST above and below cut-off groups (Chi-square test p=0.568). Also, there was no correlation between OST and US on joint level (spearman correlation coefficients p>0.1) or between OST total score and GS total score on patient level (spearman correlation coefficient 0.01, p=0.948). Four individuals developed arthritis at median 14 (9-19) months (supplementary figure S1). Of them, 1 had an OST total score above cut-off, 3 showed GS signal (all in the highest GS total score quartile) and 2 showed PD signal. In contrast, 12 (39%) patients that did not develop arthritis had an OST above cut-off, 11 (36%) showed GS signal and none showed PD signal.

Table 1 Baseline characteristics

	At-risk individuals n=35	**RA patients n=24**	**Healthy controls n=37**
Age in years, mean (SD)	55 (10)	54 (12)	54 (8)
Female sex, n (%)	24 (69)	16 (67)	24 (65)
Arthralgia duration in months, median (range)	28 (16-52)	-	-
Disease duration in years, median (range)	-	6 (2-15)	-
DAS28, median (range)	-	4.6 (3.9-5.4)	-
ACPA positive (%)	12 (41)	18 (75)	-
OST total score, median (range)	12 (9-15)	17 (13-20)	12 (10-15)

ACPA: anti-citrullinated protein antibody; OST: optimal spectral transmission; RA: rheumatoid arthritis

Comparison of OST scores of at-risk individuals to healthy controls and RA patients (supplementary figure S2) showed that the mean OST score significantly differed between RA patients and at-risk individuals (p<0.001) and between RA patients and healthy controls (p=0.001). There was no difference between at-risk individuals and healthy controls (p=1.000).

In individuals at risk of RA, OST did not correlate with US. Additionally, although numbers are small, of the 4 individuals that developed arthritis, 3 showed GS signal and 2 showed PD signal while only 1 showed an OST score above cut-off. This seems in contrast to previous studies in RA patients, which did show a (moderate) correlation between OST and US in detecting synovitis[4-8]. In at-risk individuals with their inherently low level of inflammation, the OST background signal may be too high to detect subclinical synovitis, as suggested by the similar OST results in at-risk individuals and healthy controls, which

then results in a poor sensitivity for clinical arthritis prediction. In conclusion, using the current HandScan device and algorithm, it is unlikely that OST can contribute to the diagnosis and prediction of arthritis in persons at risk of RA. Future research should focus both on different optical imaging techniques and specific algorithms for this population.

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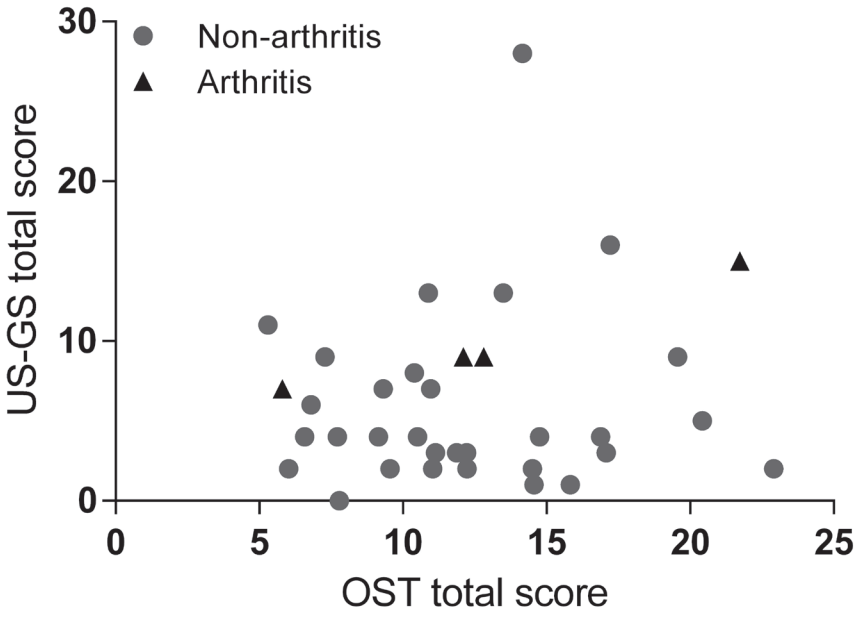
SUPPLEMENTARY MATERIAL

Supplementary figure S1: Ultrasound GS total score versus OST total score in individuals at-risk of RA

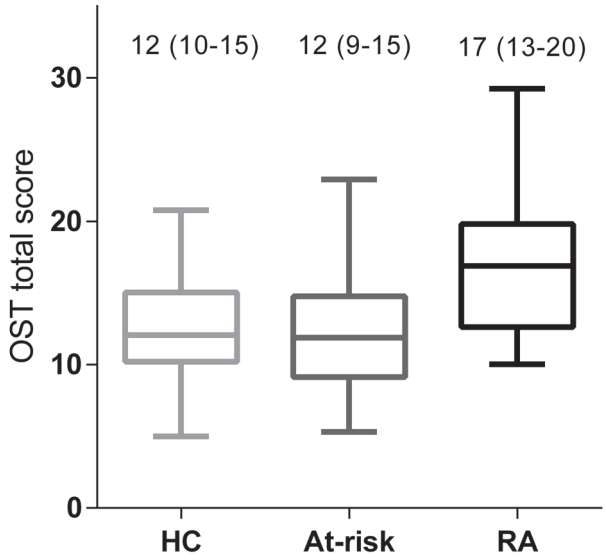
Supplementary figure S2: OST total score in the different cohorts

Supplementary figure S1: Ultrasound GS total score versus OST total score in individuals at-risk of RA



Non-arthritis: at-risk individuals that did not develop arthritis during follow up; Arthritis: at-risk individuals that developed arthritis during follow up
OST: optimal spectral transmission; US-GS: ultrasonography-greyscale

Supplementary figure S2: OST total score in the different cohorts



HC: healthy controls; At-risk: individuals at-risk of RA; RA: rheumatoid arthritis patients
OST: optimal spectral transmission