($p=0.040$), but not ESR levels, as well as to the standard Ultrasound Score of 7 joints ($p\leq 0.025$) (2). The MR-derived thermo-score could also discriminate patients in high [mean (SD) 9.2 (5.6)], moderate [mean (SD) 7.1 (3.5)] and low disease activity/remission [mean (SD) 4.2 (1.8)] ($p=0.015$), or aged-matched healthy subjects [mean (SD) 5.0 (1.7)] ($p=0.002$). Moreover, individual changes from baseline to follow-up end mirrored the corresponding DAS28 changes in 7/10 patients.

Conclusions: Increased in-depth temperatures of small joints detected by MR, which are indicative of local inflammation, may serve as an additional biomarker in RA. Optimization of MR equipment and technique may result in an objective measurement of RA disease activity in clinical practice.

References:

- [1] E. Zampeli, et al. Detection of subclinical synovial inflammation by microwave radiometry. *PLoS ONE*. 2013;(8)5:e64606.
- [2] Backhaus M, et al. Evaluation of a novel 7-joint ultrasound score in daily rheumatologic practice: a pilot project. *Arthritis Rheum*. 2009;61(9):1194–201.

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AB0245 DISTRICT DIFFERENCES BETWEEN THE SEXES OF PREDICTIVE VALUE OF MATRIX METALLOPROTEINASE-3 AT BASELINE REGARDING CHANGES IN MODIFIED TOTAL SHARP SCORE AT 1 YEAR IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Matrix metalloproteinase (MMP)-3, also known as stromelysin-1, is expressed in inflamed synovium of patients with rheumatoid arthritis (RA). It degrades components of articular cartilage, such as proteoglycans. In Japan MMP-3 has been used as a clinical biomarker of joint destruction and its predictive value for radiographic progression has been reported.

Objectives: We aimed to confirm a relation between baseline MMP-3 and radiographic progression at 1 year and to examine the association of the MMP-3 level with ultrasonography (US) findings.

Methods: A total of 259 (213 women) consecutive patients with RA were enrolled. We collected baseline data, that included the patient's age, sex, disease duration, use of glucocorticoid or disease modifying antirheumatic drugs, Disease Activity Score-28, and modified total Sharp score (mTSS); MMP-3 and, C reactive protein levels; rheumatoid factor or anti-citrullinated peptide antibody status; and the power doppler score (PD) of US assessment of digits and wrists. Baseline MMP-3 level was analyzed in association with the baseline PD value and changes (Δ) in mTSS, erosion score (Δ ERN), joint space narrowing (Δ JSN) at 1 year from baseline by Pearson's correlation method. Correlations between Δ MMP-3 and Δ mTSS, or Δ PD were also analyzed. Multiple regression analysis was performed, with Δ mTSS as the outcome for baseline variables. Statistical analysis was performed separately by sex because the upper normal limits of MMP-3 differ between the sexes (men ≤ 121 ng/ml, women ≤ 59.7 ng/ml).

Results: There was a weak correlation between the baseline MMP-3 level and baseline PD score in men. There was also moderate correlations between baseline MMP-3 level and structural damage at 1 year only in men. There was no predictive value for baseline MMP-3 level in women in terms of structural damage at 1 year. Multiple regression analysis revealed that the baseline MMP-3 level correlated independently with the Δ mTSS only in men ($p=0.0031$), whereas in

Table 1

	Variables	Correlation coefficient	Confidence interval	p
Male patients				
Baseline MMP-3	Δ mTSS	0.501 ^a	[0.246, 0.691]	<0.001
	Δ ERN	0.336 ^b	[0.051, 0.571]	0.022
	Δ JSN	0.542 ^a	[0.299, 0.719]	<0.0001
	Baseline-PD	0.228 ^b	[-0.074, 0.492]	0.136
Δ MMP-3	Δ mTSS	-0.435 ^a	[-0.644, -0.165]	0.003
	Δ ERN	-0.325 ^b	[-0.562, -0.038]	0.028
	Δ JSN	-0.436 ^a	[-0.645, -0.167]	0.002
	Δ PD	0.134	[-0.170, 0.414]	0.387
Female patients				
Baseline MMP-3	Δ mTSS	0.0011	[-0.130, 0.132]	0.987
	Δ ERN	0.0188	[-0.113, 0.150]	0.780
	Δ JSN	-0.0148	[-0.146, 0.117]	0.826
	Baseline -PD	0.0985	[-0.040, 0.233]	0.163
Δ MMP-3	Δ mTSS	-0.0344	[-0.165, 0.098]	0.610
	Δ ERN	-0.0485	[-0.179, 0.083]	0.472
	Δ JSN	-0.0127	[-0.144, 0.119]	0.851
	Δ PD	0.134	[-0.0058, 0.270]	0.060

^aModerate correlation, ^bWeak correlation. Statistical analysis was performed using Pearson's correlation.

the women the baseline PD score was correlated independently with the Δ mTSS ($p=0.0003$).

Conclusions: The baseline MMP-3 level was a good predictor of deterioration of the mTSS at 1 year in male patients with RA, but not in female patients. On the other hand, the baseline PD score was a useful predictor of joint destruction in female patients with RA.

Disclosure of Interest: None declared

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AB0246 IMPACT OF TREAT TO TARGET STRATEGY WITH COMPLEMENTARY ULTRASOUND ON REAL WORLD RADIOGRAPHIC OUTCOMES IN EARLY RHEUMATOID ARTHRITIS OVER THE PAST DECADE

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Background: Treatment for rheumatoid arthritis (RA) has changed over the past decade. Early diagnosis and prompt aggressive treatment based on treat to target strategy, as well as complementary ultrasound have been adopted and proven to improve patient clinical and radiological outcomes in clinical trials.

Objectives: The aim of this study was to compare radiographic progression of early RA patients starting their first DMARD 10 years ago vs more recently in daily clinical practice.

Methods: We reviewed the medical records of consecutive patients with symptom of 3 years duration who fulfilled the 1987 ACR classification criteria or the 2010 ACR/EULAR classification criteria in a single center retrospectively. In the first cohort (2000s), 70 patients (55.3 $\pm$ 13.3y.o, Female 77%) who were diagnosed with RA during 2003–2005 were included. In the second cohort (2010s), 71 patients (54.5 $\pm$ 17.3y.o, Female 90%) who were diagnosed with RA during 2013–2015 were included. Radiographs of hands were assessed at baseline and one year after according to the van der Heijde modified Sharp score (range 0–280) without clinical information and chronological orders of radiographs in the individual patients.

Results: Mean changes in radiographic joint damage for joint space narrowing score, erosion score, total radiographic score were higher in 2000s than 2010s (0.92 $\pm$ 2.70 vs 0.28 $\pm$ 1.86; $p=0.010$, 0.54 $\pm$ 1.35 vs 0.35 $\pm$ 0.99; $p=0.390$, 1.45 $\pm$ 3.54 vs 0.68 $\pm$ 2.55; $p=0.015$, respectively). Radiographic progression defined as total radiographic score >0 and >5 were 31.4% vs 22.5% and 8.6% vs 8.5% between 2000s and 2010s ($p=0.230$ and $p=0.970$, respectively). Methotrexate (MTX) was frequently used for initial treatment in 2010s than 2000s (86% vs 55%, $p\leq 0.001$), and initial dose and maximum dose of MTX were higher in 2010s than 2000s (9.13 $\pm$ 2.09 mg/week vs 4.67 $\pm$ 1.54 mg/week; $p\leq 0.001$ and 12.04 $\pm$ 3.73 mg/week vs 8.13 $\pm$ 1.88 mg/week; $p\leq 0.001$, respectively). The mean duration from symptom onset to diagnosis was earlier in 2010s than 2000s (5.75 $\pm$ 5.04 months vs 7.85 $\pm$ 6.85 months, $p=0.001$). CRP at baseline and 1 year after were lower in 2010s than in 2000s (2.74 $\pm$ 1.90 mg/dL vs 3.35 $\pm$ 3.94 mg/dL; $p=0.001$ and 0.60 $\pm$ 1.19 mg/dL vs 1.20 $\pm$ 1.99 mg/dL; $p=0.03$ respectively). There were no significant differences in sex, age, positive rate of RF and ACPA, the Sharp score at baseline, steroid use, and biological agents use between two cohorts.

Conclusions: In recent 10 years, early diagnosis with complementary ultrasound and appropriate MTX use based on treat to target strategy led to prevent joint destruction of RA patients in daily clinical practice.

Disclosure of Interest: None declared

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AB0247 EVALUATION OF RHEUMATOID ARTHRITIS CASES WITH HIGH ANTI-CCP ANTIBODY LEVEL

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Background: Anti-cyclic citrullinated peptide antibodies (Anti-CCP Ab) are well-established serological markers that show high sensitivity and specificity in diagnosing early rheumatoid arthritis (RA). Furthermore, Anti-CCP Ab is reported to be associated with bone erosions of RA. Therefore, Anti-CCP Ab positive RA patient can be a candidate for intensive treatment.

Objectives: Upper measurement limit of Anti-CCP Ab increased recently up to 1200 units. High level of Anti-CCP Ab may be a predictor of the profound therapy for RA. To understand the importance of Anti-CCP Ab level, we evaluated RA patients with high titer Anti-CCP Ab in relationship to the other activity markers of RA and the intensity of the treatment for RA.

Methods: Total of 186 RA patients with Anti-CCP Ab higher than 30 units was included in this study. Baseline markers such as CRP, MMP-3, RF and anti-CCP Ab were measured at the entry of the study. Relationship among these markers were evaluated and examined using statistical significance for the single-factor ANOVA and the multiple comparisons. Among those cases 131 cases were treated conservatively with biologics and/or DMARDs and were followed up more than one year. We graded them from I to IV by the intensity of the treatment. Grade I: Biological agent. Grade II: Methotrexate (MTX) more than 12mg or combination with more than 3 DMARDs Grade III: MTX 6–11mg or combination

with two recommended DMARDS Grade IV: single use of DMARDS including MTX less than 5mg.

Results: There was no relationship between titers of Anti-CCP Ab and titers of RF. We found significant statistical correlation between anti-CCP antibody titers and inflammatory markers such as CRP and MMP-3. There was significant statistical correlation between CRP and MMP-3.

In terms of treatment intensity, strong intensity group showed high titer of anti-CCP Ab and CRP. Titer of RF and MMP-3 level did not have any relationship with the treatment intensity. In cases treated with biologics, anti-CCP Ab and CRP were significantly higher compared to non-biologic case group. In 80% of cases treated with biologics titer of anti-CCP was more than 200 units. However, non-biologic treatment was continued in more than 50% of cases with anti-CCP Ab higher than 200 units.

Conclusions: Even though we treated cases based on the severity of the symptoms of the patient and response in laboratory data, high anti-CCP Ab titers and CRP at the base line were most associated with the treatment intensity after 1 year. The results of our study suggest that the titer of anti-CCP Ab can be better a predictor of the treatment intensity than MMP-3 and RF.

Disclosure of Interest: None declared

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AB0248 THE IMPACT OF THERAPY ON ANTI-CARBAMYLATED PROTEIN ANTIBODY ISOTYPES AND SEROSTATUS IN PATIENTS WITH EARLY RA TREATED WITH ABATACEPT AND METHOTREXATE

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Background: Maturation of autoantibody responses has been suggested to be a proxy for disease maturation. Autoantibody responses against post-translationally modified antigens are present in autoimmune diseases and antibodies directed against carbamylated proteins (anti-CarP antibodies) are a marker of RA. Anti-CarP antibody analysis in patients with early RA offers the opportunity to estimate whether specific intervention during such early stages of autoantibody development may have an impact on the maturation of the anti-CarP antibody response.

Objectives: We assessed the relationship between changes in anti-CarP isotypes and rates of seroconversion to negative in patients with early RA.

Methods: In the Assessing Very Early Rheumatoid arthritis Treatment study (AVERT; NCT01142726), patients with early RA were treated with abatacept (ABA)+MTX, ABA monotherapy or MTX alone.¹ Patients in AVERT were anti-cyclic citrullinated peptide-2 positive at baseline for study entry.¹ In this *post hoc* analysis, concentrations of anti-CarP isotypes were measured using custom ELISAs. Anti-CarP ELISAs for immunoglobulin (Ig)G, IgM or IgA isotypes were performed in patient serum at baseline, and at Days 85 and 365 on treatment. Baseline levels of each anti-CarP antibody isotype and % seropositivity were comparable across the three treatment arms. Adjusted mean change from baseline was calculated using a longitudinal repeated measures model.

Results: At baseline, 51.3, 42.5 and 29.3% of all patients with serum available in AVERT were positive for IgG, IgM (indicative of an ongoing immunoresponse) and IgA anti-CarP isotypes, respectively. Overall, approximately 65% of patients were positive for at least one anti-CarP antibody isotype. Median % change from baseline (25%, 75%) for anti-CarP isotypes levels from baseline to Days 85 and 365 are shown (Table). Analysing patients who were positive at baseline for each of the isotypes, we observed that 19/48 (40%), 16/43 (37%) and 11/48 (23%) of the patients positive for the IgG isotype became negative on ABA+MTX, ABA and MTX, respectively, at 1 year. For the IgM isotype, 26/48 (54%), 14/36 (39%) and 15/38 (39%) became negative on ABA+MTX, ABA and MTX, respectively. For the IgA isotype, 12/26 (46%), 10/23 (43%) and 13/31 (42%) became negative on ABA+MTX, ABA and MTX, respectively.

Conclusions: Concentrations of all anti-CarP isotypes (IgM, IgA, IgG) were numerically reduced by abatacept+MTX therapy compared with MTX or abatacept alone. Abatacept+MTX trended towards higher rates of seroconversion to negative for all isotypes over 1 year of treatment. These results indicate that the extent of the anti-CarP antibody response can be modulated by intervention with abatacept on background MTX in anti-citrullinated protein antibody-positive patients with early RA.

References:

[1] Emery P, et al. Ann Rheum Dis 2015;74:19–26.

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AB0249 IDENTIFICATION OF INFLAMMATORY- AND IMMUNE DISORDER- RELATED PROTEINS AS PUTATIVE BIOMARKER CANDIDATES FOR IMPROVING RHEUMATOID ARTHRITIS MONITORING

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Background: Rheumatoid arthritis (RA) is a long-lasting inflammatory autoimmune disorder that ultimately leads to the destruction of joint architecture.

Objectives: Using the DAS28 activity index, 80 RA serum samples (40 with low activity and 40 with high activity) were selected in order to be analyzed by mass spectrometry. The aim of this study was to find possible protein biomarkers that could discriminate patients with different RA activity in the daily clinical routine.

Methods: In order to facilitate the complex measurement of these serum samples, a simple, fast and reproducible albumin-specific depletion method using ethanol was optimized and applied to this study. Four independent pools of the 40 high RA activity samples (10 samples per pool) and 4 pools of the 40 low RA activity samples were firstly albumin-depleted, and then the remnant serum proteins were digested and differentially labelled with iTRAQ 8-plex reagents. Subsequently, the 8 labelled pools were combined and cleaned using StageTips-C18. Finally, the pool mixture was fractionated by HPLC (Zorbax-C18) and the resulting fractions were analyzed by nanoLC-MS/MS using two different equipments for validation (MALDI-TOF/TOF and TripleTOF).

Results: The mass spectrometry analysis led to the identification of 186 proteins. Among these, Haptoglobin, Kininogen-1, Alpha-2-HS-glycoprotein, Serum Amyloid A, Afamin and Histidine-rich-glycoprotein, exhibited a differential relative abundance depending on the RA activity of the patients ($p < 0.03$) in both analysis. These proteins were also validated by other orthogonal techniques (western blot, ELISA and protein arrays).

Conclusions: In this proteomic study, 9 proteins were found to be modulated between patients with high and low RA activity. Most of these proteins are related with the RA process and the effects caused by this type of disease (inflammation and immune disorder in joints). Therefore, these proteins are possible biomarker candidates for improving RA monitoring. Future validation experiments and prospective studies are needed to facilitate their implementation in the clinical routine.

Disclosure of Interest: None declared

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AB0250 THE ADIPOSE TISSUE AS PREDICTIVE FACTOR OF DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS PATIENTS: EVALUATION OF BODY FAT COMPOSITION BY BIOELECTRICAL IMPEDANCE ANALYSIS AND ULTRASONOGRAPHY

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Background: Adipose tissue (AT) is an endocrine organ able to secrete the "adipokine" molecules that contribute to the low-grade inflammatory state in obese subjects and to the local inflammation that affects joints and bone (1,2). High-grade inflammation, in course of RA, leads to an altered body composition (3,4), characterized by the increasing of fat mass and the decreasing of lean mass, mostly not associated to body mass index (BMI) variations (3,5). The BMI is not able to differentiate visceral (VTH) and subcutaneous (STH) fat tissue and to distinguish between muscle mass and fat mass body composition (BC) (6,7). Alternative methods proposed for assessment of visceral fat deposition, are bioelectrical impedance analysis (BIA) and ultrasonography (US).

Objectives: The aim of the study is to investigate if BC, assessed by BIA and US,

Abstract AB0248 – Table 1. Median % change from baseline (25%, 75%) for anti-CarP isotypes

	Day 85			Day 365		
	IgG	IgM	IgA	IgG	IgM	IgA
ABA	-17.3 (-55.7, 0.0)	-26.3 (-57.9, 0.0)	-6.8 (-35.1, 0.0)	-31.2 (-67.4, 0.0)	26.0 (-81.2, 0.0)	-26.7 (-72.9, 13.0)
MTX	-19.3 (-53.6, 0.0)	-35.7 (-54.4, -6.9)	-27.2 (-42.4, -3.9)	-17.7 (-65.1, 0.0)	-38.3 (-63.7, 0.0)	-21.9 (-50.3, 0.0)
ABA+ MTX	-38.8 (-62.3, 0.0)	-44.2 (-59.5, -13.8)	-41.3 (-54.9, -28.3)	-55.7 (-76.7, 0.0)	-45.7 (-72.5, -0.2)	-46.4 (-66.7, 0.0)