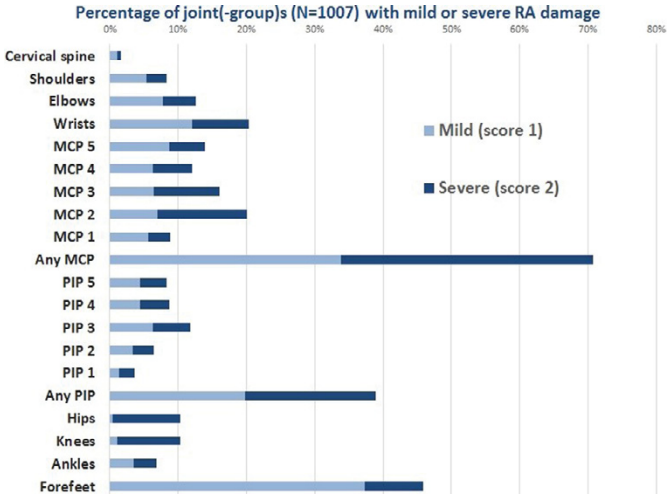
Objectives: Evaluate the feasibility of a simple clinical joint damage score and describe the increment over time in RA patients with varying disease duration.
Methods: Cross-sectional study in all patients with a clinical diagnosis of RA visiting the outpatient clinic in 2015 and 2016. Rheumatologists and nurses from the outpatient department of a large regional hospital received a single training to perform the RAAD score. Scores of 0 (no damage), 1 (mild) or 2 (severe: ankylosis, luxation or joint surgery) were assigned to 35 joints (maximum score: 70) with a disease activity score, and stored in the electronic patient record system. Baseline data including ACR 2010 criteria were also registered.
Results: In 1007 (67.3%) of 1496 RA patients seen over 2 years RAAD-scores were performed. 652 (64.7%) were female, average age (SD, range) was 62.6 (13.1, 19–95), disease duration 9.9 (9.6, 0–65) years. Rheumatoid factor and ACPA were positive in 70.6% and 70.3% respectively.
RAAD scores related to disease duration illustrate that at disease onset 86%, and after 20 years 37% of the patients has no joint damage (Table). Distribution over joints shows the classical predominance of damage in MCP, PIP and MTP joints (Image). Structural damage in shoulders or elbows was present in 8.3% and 12.5%, in knees and hips in 10,3% each. Despite current treatment strategies, irreversible joint damage of more than 5 joints is present in 6.3% within 10 years.

Table 1. Accumulation of irreversible joint damage score with disease duration, number (%)

RAAD-score	1st year (N=69)	2–4 yrs (N=228	5–9 yrs (N=253)	10–19 yrs) (N=239)	≥20 yrs (N=218)
0 (no joint damage)	59 (86)	158 (69.3)	145 (57.3)	81 (33.9)	80 (36.7)
1–5	8 (12)	65 (28.5)	92 (36.4)	103 (43.1)	42 (19.3)
6–10	2 (3)	4 (1.8)	11 (4.3)	34 (14.2)	28 (12.8)
11–20			4 (1.6)	13 (5.4)	36 (16.5)
>20		1 (0.4)	1 (0.4)	8 (3.3)	32 (14.7)
Average (range)	0,4 (0–6)	0,9 (0–23)	1,6 (0–37)	2,2 (0–18)	9,0 (0–59)



Conclusions: Clinical assessment of joint damage is a feasible parameter of long term outcome in RA. Reflecting overall joint damage, the RAAD-score provides a broader view than radiographic scoring of hands and feet and is easy to apply in routine care. Given the slow increment a single assessment per 5 years may suffice to compare structural joint damage across cohorts of patients.
References:
[1] Zijlstra T, Bernelot Moens H, Bukhari M. The rheumatoid arthritis articular damage score: first steps in developing a clinical index of long term damage in RA. Ann Rheum Dis. 2002;61:20–3.
[2] Hammer H, Odegard S, Fagerhol M, et al. Calprotectin is strongly and independently correlated with joint inflammation and damage in rheumatoid arthritis. Ann Rheum Dis 2007;66:1093–7.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4437

THU0107 ASSOCIATION OF GLOBAL DNA METHYLATION WITH MTX RESPONSE AND ADVERSE EVENTS IN EARLY RHEUMATOID ARTHRITIS

H. Gosselt[1], M.D. Rotte[1], M. Chisholm[1], M. Hazes[2], R.D. Jonge[3], S. Heil[1].
[1]Clinical Chemistry; [2]Rheumatology, Erasmus Medical Center, Rotterdam; [3]Clinical Chemistry, VUMC, Amsterdam, Netherlands

Background: Methotrexate (MTX) is a first-line therapy in early Rheumatoid Arthritis (RA). However, ~30% of treated patients do not respond to the medicine or need to abrogate treatment because of severe adverse events. Since MTX interferes with the folate cycle and thereby influences the methylation cycle, we hypothesize that methylation status at start therapy is associated with response and adverse events after three months of MTX treatment enabling personalized medicine.
Objectives: Examine global methylation status of early Rheumatoid Arhtritis patients before and after 3 months of MTX use between responders and non-responders and patients that do or do not experience adverse events.
Methods: To assess global methylation status, DNA was isolated at baseline from whole blood of 120 patients from the Treatment in the Rotterdam Early Arthritis Cohort (tREACH), a multicenter, stratified single-blind clinical trial of patients with early RA. Methylation status of 7 CpG sites within Long-interspersed nuclear elements (LINE-1) were analyzed and quantified by Matrix Assisted Laser Desorption Ionization time of flight Mass Spectrometry (MALDI-TOF MS). Results were compared between MTX responders and non-responders based on a low disease activity (DAS28 <3.2) at three months of treatment and patients experiencing ≤2 or ≥3 adverse events. Gastrointestinal adverse events were assessed separately.
Results: No statistical differences in the mean of 7 LINE-1 CpGs were observed between responders and non-responders, nor in patients experiencing ≤2 or ≥3 adverse events. However, methylation status of specific CpG sites within LINE-1 did show significant changes. Baseline CpG_2 methylation levels were positively correlated with the DAS28 score at t3 (p=0.018) and baseline methylation levels in CpG_5 and CpG_8.9 were significantly higher in patients experiencing ≥3 adverse events (p=0.018 and p=0.034, respectively). Besides, CpG_5 methylation levels were particularly increased in patients experiencing gastrointestinal adverse events (p=0.038).
Conclusions: Global methylation status is associated with non-response and adverse events to MTX in early RA patients and can therefore be implemented in future prediction models.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4686

THU0108 SUBCLINICAL CENTRAL NERVOUS SYSTEM DAMAGE IN PATIENTS WITH RHEUMATOID ARTHRITIS: DISEASE ACTIVITY AND CYTOKINES

I. Tekeoğlu, S. Sağ, A. Kamanlı, M.S. Sağ, K. Nas. *Department of Physical Medicine and Rehabilitation, Rheumatology, Faculty of Medicine, Sakarya University, Sakarya, Turkey, sakarya, Turkey*

Background: We aimed in this study to investigate blood-brain barrier (BBB) dysfunction in RA patients who had no neurological symptoms, and were receiving synthetic DMARD treatment.
Objectives: We investigated correlations between cranial MRI images and brain specific proteins (S100 Beta, GFAP), cytokines (IL-1 beta, IL-17) in plasma which had important roles in disease activity.
Methods: In our study, 57 patients (46 females and 11 males) were included included in RA group, and 34 patients (24 females and 10 males) in the control group. All of RA patients were receiving synthetic DMARD treatment. Demographic characteristics of all patients were recorded. Disease activity was evaluated by using DAS-28. Mini-mental test (MMT) was used for evaluation of cognitive functions, and Fazekas scale was used to evaluate cranial MR lesions. S100 beta, GFAP, claudin, IL-17, and IL-1 beta levels were measured in peripheral blood of both groups.
Results: Demographic characteristics were similar between the groups, and there was no statistically significant difference in gender, age, and body mass index (BMI) between patient and control groups (p>0.05). S100 beta, and GFAP levels were significantly higher in RA group (p<0.05). No difference was determined in hyperintense lesions diagnosed in cranial MR between patient and control groups (p>0.05). There were positive correlations between IL-17 S100 beta and GFAP, and IL-1 beta and S100 beta.
Conclusions: In our study, we have shown that blood-brain barrier may be damaged subclinically in RA patients, brain specific proteins related to BBB dysfunction may be increased in the peripheral blood, and BBB dysfunction may be related to cytokines which play an important role in disease pathogenesis. In conclusion, cytokines which circulate in the peripheral blood in RA may cause subclinical BBB damage. Further large scale studies with long-term follow-up are required which will support this hypothesis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2313

THU0109 UPDATED ESTIMATION OF THE EQ5D QUALITY OF LIFE QUESTIONNAIRE UTILITY VALUES THROUGH HAQ-DI MAPPING FOR SPAIN

I. Gorostiza[1], L. Ansola[2], E. Galindez[3]. *[1]Research Unit; [2]Research Unit; [3]Rheumatology, H. Universitario Basurto, Vizcaya, Spain*

Background: Rheumatoid arthritis (RA) deeply affects the quality of life (QoL) of patients. The preferred approach to evaluate treatment efficiency is to value health as patient preferences known as utilities, and subsequently, calculate Quality-Adjusted Life Years gained. A new 5-level of severity EQ5D has recently released and a new tariff proposed for Spain (Ramos-Goñi,2016). Although QoL questionnaires are not of routine use in clinical practice, it is possible to estimate it using the Health Assessment Questionnaire Disability Index (HAQ-DI)
Objectives: To develop a function that allows the estimation of EQ5D-5L utility values from HAQ-DI updated to the newest proposed tariff for Spain

Methods: Patients with RA from two teaching hospitals, participating in a prospective observational study completed the HAQ-DI and EQ5D-5L at 0–6-12 month follow-up visits. Inclusion criteria: ACR RA diagnosed patients, on biologic treatment and whose disease activity remained stable at least for 3 months EQ5D-5L is a standardized, generic instrument for describing and valuing health and QoL, consisting in a five-dimensional descriptive system (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) and a visual analogue scale. A country-specific tariff converts patient's answer to a 0–1 (full health) utility index. HAQ-DI is a self-completed questionnaire used to assess the functional ability using 20 items, distributed across 8 dimensions and resulting in a four-level disability scale (0–3). In addition, socio-demographic and clinical data where recorded.To estimate the EQ5D-5L utility index OLS models were built. As this index is bounded to the [-0.416, 1] interval, Tobit models were also considered. Hereafter, the index was transformed to the open interval (0,1) and estimated through beta regression with a logit link. To determine the relationship grade between the index and the HAQ-DI scale and obtain residuals without trend, GAM models were used. Best fitting models were determined by AIC, MAE and RMSE. All analyses were performed using R software

Results: 217 questionnaires fulfilled by 77 patients. Mean (SD) age was 57.0 (12.9), 87% women, AR duration 13.7 (7.1), mean DAS28 2.72 (1.00) and HAQ-DI 0.77 (0.60). Baseline EQ5D index: 0.768 (0.182). All the OLS estimation models resulted in the interval limits defined by the index, so Tobit models were not considered. When considering the linear model we obtained the best results with the HAQ-DI term and its third power: EQ5D5L = 0.9232 – 0.1760×HAQ – 0.0172×HAQ^3 (AIC=–221.62; MAE=0.0974; RMSE=0.1363); for beta regression, we obtained the best model with the HAQ-DI to the first power alone: logit (EQ_01) = 2.5821 – 1.1165×HAQ (AIC=–444.4; MAE=0.0691; RMSE=0.0958). Considering the AIC and the residuals together, we obtained the best fitting model with the beta regression approach, with neither age nor sex

Conclusions: So far, only a utility function using HAQ-DI and an older EQ5D-3L version was available for Spain (Carreño,2011). This updated utility function can be used as a practical approach to predict RA patients' QoL and EQ5D utility score for Spain when clinicians/researchers need them for clinical practice or cost-effectiveness analyses and generic QoL measurements are not available

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4836

THU0110 THE IMPORTANCE OF SUSTAINED REMISSION FOR LONGTERM OUTCOMES IN PATIENTS WITH RHEUMATOID ARTHRITIS

J. Smolen[1], C. Gabay[2], D. Aletaha[1], P. Emery[3], I. Sainsbury[4], Y. Zhang[4], A. Kavanaugh[5]. *[1]Medical Univ of Vienna, Vienna, Austria; [2]Univ of Geneva, Geneva, Switzerland; [3]Leeds Inst of Rheumatic & Musculoskeletal Medicine, Leeds, United Kingdom; [4]AbbVie, N Chicago, IL; [5]Univ of California, San Diego, CA, United States*

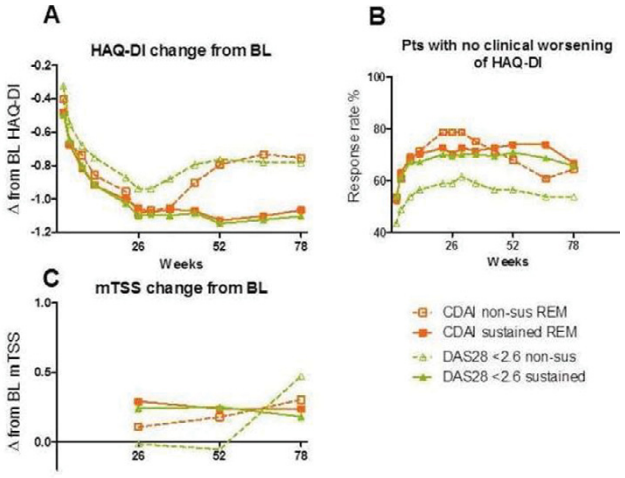
Background: In patients (pts) with rheumatoid arthritis (RA), the long-term impact of sustained versus (vs) transient clinical remission (REM) has not been assessed thoroughly, although REM duration has been shown to affect structural outcomes[1]. The relationship of different definitions of clinical remission (REM) with function and structural integrity has not been assessed.

Objectives: To explore the importance of sustained REM or disease control for long-term outcomes, and assess various definitions of REM in adalimumab (ADA) long-term trials.

Methods: Data are from 2 trials of ADA in early RA pts; In PREMIER, pts received ADA, methotrexate (MTX) or ADA+MTX for 2 years (yrs), after which they could enter an open label (OL) period for upto 8 yrs[2]. In OPTIMA, pts received ADA+MTX, or placebo (PBO) +MTX for 26 weeks (wks). Based on whether or not pts achieved DAS28-CRP <3.2 at wks 22 and 26, pts withdrew ADA, continued on PBO+MTX, ADA+MTX or OL ADA+MTX until Wk 78[3]. For this analysis, non-sustained REM/disease control was defined as meeting one of the following at 6 months but not 1 yr: DAS28-CRP <2.6; simplified disease activity index (SDAI) ≤3.3; clinical disease activity index (CDAI) ≤2.8. Sustained REM/disease control was defined as meeting these criteria at both 6 months and 1 yr. The mean change from baseline in health assessment questionnaire-disability index (ΔHAQ-DI), or modified total Sharp score (ΔmTSS), and the number of pts without clinical worsening of HAQ-DI (Δ≤0.22) were assessed over 78 wks for OPTIMA, or 5 yrs for PREMIER. NRI and LOCF were used for binary and continuous variables, respectively.

Results: In OPTIMA, by any of the REM criteria, pts in sustained REM had larger mean ΔHAQ-DI over time (Fig 1A) vs pts in non-sustained REM. Pts with non-sustained DAS28-CRP <2.6 vs non-sustained CDAI REM had numerically smaller ΔHAQ-DI up to Wk 52. Over time, more pts in sustained vs non-sustained REM using DAS28-CRP<2.6 (but not CDAI or SDAI criteria) did not have clinical worsening of HAQ-DI, possibly due to more suppression of inflammatory components upon achieving CDAI REM but not DAS28-CRP <2.6 in these early RA pts (Fig 1B). At Wk 78, ΔmTSS at Wk 78 was smaller for pts in sustained vs non-sustained DAS28-CRP <2.6, and similar for sustained and non-sustained CDAI REM (Fig 1C). Somewhat fewer pts at Wk 78 may have contributed to some variability. Trends were similar in PREMIER (not shown).

Conclusions: Pts who were in sustained disease control/REM had better clinical, functional and radiographic outcomes over the long- term, vs pts in a more transient state, regardless of the REM criteria used, although for CDAI REM, functional and radiographic outcomes were similar for sustained and non-sustained REM, in line with its higher stringency.



For LOCF: CDAI non-sustained REM N=28, CDAI sustained REM N=84, DAS28 <2.6 non-sustained, N=39, DAS28 <2.6 sustained, N=137; For NRI: CDAI non-sustained REM at Wk 26, N=22, at Wk 78, N=18; CDAI sustained REM at Wk 26, N=59, at Wk 78, N=56 DAS28 <2.6 non-sustained, at Wk 26, N=23, at Wk 78, N=21; DAS28 <2.6 sustained, at Wk 26, N=95, at Wk 78, N=90

References:
[1] Aletaha et al, Arthritis & Rheum. 2009;5:1242.
[2] Breedveld et al. 2006. Arthritis & Rheum;54:26.
[3] Smolen et al. 2014. Lancet;383:321.

Acknowledgements: AbbVie: study sponsor, contributed to design, data collection, analysis, interpretation; and writing, reviewing, approval of final version. Medical writing: Naina Barretto, of AbbVie.

Disclosure of Interest: J. Smolen: None declared, C. Gabay Grant/research support from: AbbVie Inc, Amgen, BMS, MSD, Pfizer, Roche, Celgene, Sanofi, and Regeneron., Consultant for: AbbVie Inc, Amgen, BMS, MSD, Pfizer, Roche, Celgene, Sanofi, and Regeneron., D. Aletaha Grant/research support from: AbbVie Inc., Pfizer, Grünenthal, Merck, Medac, UCB, Mitsubishi/Tanabe, Janssen, and Roche., Consultant for: AbbVie Inc., Pfizer, Grünenthal, Merck, Medac, UCB, Mitsubishi/Tanabe, Janssen, and Roche., P. Emery Grant/research support from: research grants and consulting fees from Pfizer, MSD, AbbVie Inc., Bristol-Myers Squibb, UCB, Roche, Novartis, Samsung, Sandoz and Lilly., Consultant for: research grants and consulting fees from Pfizer, MSD, AbbVie Inc., Bristol-Myers Squibb, UCB, Roche, Novartis, Samsung, Sandoz and Lilly., I. Sainsbury Employee of: AbbVie, Y. Zhang Employee of: AbbVie, A. Kavanaugh Grant/research support from: AbbVie Inc., Amgen, Astra-Zeneca, BMS, Celgene, Centocor-Janssen, Pfizer, Roche, and UCB., Consultant for: AbbVie Inc., Amgen, Astra-Zeneca, BMS, Celgene, Centocor-Janssen, Pfizer, Roche, and UCB.

DOI: 10.1136/annrheumdis-2017-eular.2779

THU0111 NOVEL AUTOANTIBODY PROFILES IN RHEUMATOID ARTHRITIS AND THEIR ASSOCIATION WITH RADIOGRAPHIC PROGRESSION IN THE SCOTTISH EARLY RHEUMATOID ARTHRITIS INCEPTION COHORT AND BIOBANK (SERA)

J. Nijjar[1], F. Morton[1], A. Gilmour[1], C. Paterson[1], H. Bang[2], D. van der Heijde[3], K. Raza[4], C. Buckley[4], D. Porter[5], I. McInnes[1]. *[1]University of Glasgow, Glasgow, United Kingdom; [2]Orgentec Diagnostika GmbH, Mainz, Germany; [3]LUMC, Leiden, Netherlands; [4]University of Birmingham, Birmingham; [5]NHS GGC, Glasgow, United Kingdom*

Background: Antibodies against citrullinated peptides are useful in the diagnosis of rheumatoid arthritis (RA) and are associated with poorer prognosis and greater radiographic progression. Novel autoantibodies recognising several post-translational modifications (PTM) are now emerging including anti-carbamyl, and anti-acetyl antibody classes. Less is known of their prognostic significance.

Objectives: To determine the prevalence of autoantibodies to modified vimentin and/or CCP2 (anti citrullinated (CCP), anti carbamylated (Carb), anti acetylated (Acet)) in a subset of the Scottish Early RA (SERA) inception cohort (n=212) and to correlate them with baseline and radiographic progression over 12 months.

Methods: Baseline and 12m hand and foot radiographs were scored by two readers independently, blinded to patient information and time order according to the Sharp van der Heijde score (SvH). Serum samples from the SERA biobank were analysed with recently published anti-modified protein assays. Patients with citrullinated antibodies (CCP) had antibodies to modified vimentin and/or antibodies to CCP2. Clinical, radiographic and autoantibody data were analysed in R.

Results: See Table 1.

In patients with early RA four main antibody profiles were detected: patients