AB0244

DEVELOPMENT OF AN ADJUSTED MULTI-BIOMARKER DISEASE ACTIVITY (MBDA) SCORE FOR RHEUMATOID ARTHRITIS (RA) THAT ACCOUNTS FOR AGE, SEX AND ADIPOSITY, WITH SUBSEQUENT EVALUATION OF ABILITY TO PREDICT RISK FOR RADIOGRAPHIC DAMAGE

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Background: The MBDA score, based on 12 serum proteins, is a validated tool for assessing disease activity in RA patients. MBDA biomarkers may be influenced by age, sex and adiposity.

Objectives: To develop and validate an adjusted MBDA score that accounted for these three factors, using BMI or serum leptin as proxies for adiposity.

Methods: The MBDA score as a continuous variable was adjusted to account for age, sex and a proxy for adiposity (serum leptin) using data from 325,781 RA patients for whom MBDA tests had been ordered as part of routine care. Leptin values came from the MBDA test. As an alternative to using leptin to adjust for adiposity, a cohort of 1411 patients from 5 studies/registries (BRASS, Corrona-CERTAIN, InFoRM, OPERA, RACER) was used to adjust for BMI, which was not available in the larger cohort, adding this BMI adjustment to that for age/sex from the larger cohort. Both types of adjusted MBDA score use the low, moderate, and high disease activity cutpoints of the original MBDA score. The two adjusted MBDA scores and other variables were evaluated for the prediction of radiographic progression (RP) in the 2 cohorts with available data (OPERA, BRASS) using univariate and multivariate linear regression analyses. Rate of RP was assessed as the change in modified total Sharp score (Δ mTSS) per year after MBDA testing.

Results: The MBDA score increased with age, BMI and leptin concentration. In univariate analysis of the combined OPERA and BRASS cohorts (n=555), the significant variables predicting Δ mTSS were leptin-adjusted MBDA score, seropositivity for RF or anti-CCP, BMI-adjusted MBDA score, MBDA score, BMI, CRP, baseline mTSS, disease duration, DAS28-CRP, SDAI, CDAI and DAS28* (table 1). The leptin- and BMI-adjusted MBDA scores were the first and third most significant univariate predictors of Δ mTSS. To compare them directly, DAS28-CRP, MBDA score, BMI-adjusted MBDA score and leptin-adjusted MBDA score were combined in pairs in regression analyses of Δ mTSS; the BMI-adjusted (p=0.0027) and leptin-adjusted MBDA score were significant (p=0.00063) after adjusting for DAS28-CRP (p=0.87 and 0.74, respectively) and the leptin-adjusted MBDA score was significant (p=0.024 and 0.020, respectively) after adjusting for either the MBDA (p=0.32) or BMI-adjusted MBDA scores (p=0.094).

Abstract AB0244 – Table 1. Univariate Linear Regression Analysis of the Association of Clinical and Laboratory Variables with Δ mTSS in the OPERA and BRASS Combined Cohort

Variable	n	F-statistic	p-value
Leptin-adjusted MBDA Score	555	17.1	0.000040
RF or Anti-CCP Status	555	14.8	0.00013
BMI-adjusted MBDA Score	555	14.4	0.00016
MBDA Score	555	12.9	0.00036
BMI	555	10.9	0.001
log _e (CRP)	555	6.8	0.0093
Baseline mTSS	555	5.3	0.022
log _e (Disease duration + 1)	401	4.8	0.030
DAS28-CRP	536	4.6	0.032
SDAI	533	4.3	0.040
CDAI	533	3.9	0.049
DAS28*	536	3.1	0.079
Gender	555	1.5	0.23
Smoking Status	478	0.8 (2 df)	0.46
Age	555	0.1	0.76

DAS28* = DAS28 with no CRP or ESR component, i.e., $0.56(\text{TJC28})^{1/2} + 0.28(\text{SJC28})^{1/2} + 0.014(\text{GH})$.

Conclusions: We developed two adjusted MBDA scores that combine molecular and biometric variables to account for age, sex, and adiposity. The leptin-adjusted MBDA score, significantly outperformed DAS28-CRP and the original MBDA score in predicting radiographic progression in RA patients. These results suggest that the leptin-adjusted MBDA score may offer improved clinical utility for the personalised management of patients with RA.

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AB0245

PERFORMANCE OF THE EULAR DEFINITION OF ARTHRALGIA SUSPICIOUS FOR PROGRESSION TO RHEUMATOID ARTHRITIS IN COMBINATION WITH MUSCULOSKELETAL ECOGRAPHY WITH DOPPLER (USMD) IN CLINICAL PRACTICE

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Background: The treatment at an early stage of rheumatoid arthritis (RA), even in the undifferentiated phase, which can prevent the progression and even the reversal of the inflammatory process¹. Identification in the preclinical phase is complicated. The detection of joint inflammatory activity through the use of UsMD would be useful for diagnosis in arthralgia suspicious for progression to RA (CSA)².

Objectives: To assess the usefulness of the EULAR definition of CSA in clinical practice.

To Describe the clinical, serological and ultrasound characteristics and the CSA evolution over time (0, 3, 6 months).

To determine the clinical and ultrasound characteristics that could influence in the RA progression.

Methods: A longitudinal prospective study that includes 27 patients referred from primary care (PC) or Rheumatology consultations with CSA according to EULAR criteria of more than 8 weeks and less than 6 months of evolution. All patients were evaluated at 0–3–6 months, including at each visit: serological parameters (RF, ACPA, ESR, CRP), measures of functionality (HAQ) and activity (DAS28); and image (Xray and UsMD). The ultrasound examination included: carpus (palmar and dorsal planes), MCFs 2°–5°, extensor cubital tendons, ankles, posterior tibialis, 5° MTFs and painful IFPs in a comparative and bilateral model. The Us scans were performed by the same researcher without access to the clinical data of the patients, collected by another independent researcher. Proportions were compared using the chi-square test to see which factors were related to RA development.

Results: 27 patients with CSA criteria according to EULAR definition have included. 59.3% were derived from PC, 92.6% were women with a mean age of 48.5 years (DS 11.95) and active labour 77.8%. Ten patients (37%) were smokers and dyslipidemias with an atherogenic index of 3.19 (DS1.04). 60.95% presented slight overweight with a BMI of 27.65 Kg/m² (DS 5.7). The most frequent form of presentation was polyarticular 12 (50%) followed by oligoarticular. 57.7% of the cases had symmetric involvement and 81.5% a duration of symptoms between 6–16 weeks. 52% patients presented RF + and 4 ACPA and ANA+. During the follow-up: 8 patients (29.6%) were classified as RA (ACR/^{EULAR 2010} all of them derived from Rheumatology, 3 (11.1%) microcrystalline arthritis, 1 Sjogren primary syndrome and 15 (55.5%) presented degenerative or tendinosis pathology.

In those patients who progressed to RA, we only found a statistical association with the presence of high RF +and with the presence of doppler at the carpal level ($p=0.048$).

Conclusions: The results of our study suggest that the EULAR definition of CSA, although more useful when used by rheumatologists, does not reach sufficient accuracy for the diagnosis of RA, while the presence of subclinical synovitis detected by UsMD could be useful. The highest levels of RF were related to the presence of synovitis in our cohort, unlike ACPA. Further studies would be needed to recommend its introduction into clinical practice and, in our opinion should be considered in future sets of classification criteria.

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AB0246

GENETIC VARIABILITY WITH TOLL-LIKE RECEPTOR 10 AFFECTS SUSCEPTIBILITY TO RHEUMATOID ARTHRITIS AND MODULATES RESPONSE TO BIOLOGICAL TREATMENT

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Background: Genetic variability in Toll-like receptor 10 (TLR10) may change the balance between pro- and anti-inflammatory responses, and hence modulate the susceptibility to infection and to autoimmune disease including rheumatoid arthritis (RA).

Objectives: Therefore we aimed to assess the possible associations of the TLR10 genetic variants with RA susceptibility and/or response to treatment

Methods : TLR10 gene (rs 11096957, N241H, A>C) polymorphism was genotyped by LightSNIP assay in 303 RA patients (237F/66M) and in 140 healthy individuals from Polish population.

Results: RA patients with the AC genotype showed predisposition to disease development [OR 1.99 (1.32–3.01); $p=0.001$], while the AA homozygosity seemed to play a protective role [OR 0.63 (0.42–0.95); $p=0.034$]. Response to treatment with TNF-alpha inhibitors was more effective after 6 months as compared to 3 months ($p=0.001$), especially in female patients ($p=0.05$). Women carrying the A allele responded better to treatment after 6 months of anti-TNF treatment as compared to those with the CC genotype ($p=0.053$). Response to biological treatment was more effective in patients with low stage of disease ($p=0.01$), with rheumatoid factor (RF) positivity ($p=0.01$) and with double positivity against cytrulinated (CCP) protein and RF ($p=0.003$). RF-positive patients (especially women, $p=0.001$) characterised with a higher degree of the disease as compared to RF-negative cases ($p=0.01$). Men had a higher activity of the disease before anti-TNF treatment ($p=0.05$), therefore the remission of the disease was more common in women ($p=0.04$).

Conclusions: These results imply that the TLR10 polymorphism has an important role in RA and may potentially influence risk of the disease and effectiveness of biological treatment.

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AB0247

LACK OF AGEING WITH LONG TERM METHOTREXATE: OBJECTIVE MEASUREMENTS OF COGNITION, AUDIOMETRY, AND SLEEP

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Background: Methotrexate (MTX) has long been known to improve the cardiovascular system. Myocardial infarction, strokes, and mortality are significantly reduced in patients compliant with long term MTX.¹ Hearing loss at middle age is an independent major risk factor for dementia,² and sleep over 8 hours is associated with better health. MTX use may affect all of these risk factors.

Objectives: Our hypothesis is that the cardiovascular benefits of long term MTX treatment would translate into improved cognition, improved hearing, and better sleep patterns.

Methods: Cambridge Cognition (CamCog based in Cambridge) developed cognitive objective testing to study brain function. Camcog is widely used to assess cognitive function in atherosclerotic disease, dementia and ageing. The CamCog tests are computer based. Programs used in this trial included "PAL", paired associates learning for new learning memory and "SWM", spatial working memory along with new strategic thinking during the test. These tests provide 22 assessments per patient. In separate testing, each patient was scored on the mini-mental state examination, including serial 7's, WORLD spelled backward, memory retention of 3 items, and drawn forms such as clock faces.² Sleep patterns were assessed by questionnaire.

Results: There were 88 patients with RA between the ages of 80–101 years who had been treated with MTX a minimum of 20 years. The average PALFAM score for the group was 16.3 (sd 2.7) with a maximum score of 20. The SWMBE score for errors for the group was 2.2 (sd 4.4) with the best score 0 errors. In all 22 scoring categories of the CamCog tests, the 88 long term MTX users scored in the top quintile, and better than average for published results for healthy people at age 65. All scores were statistically significant ($p<0.01$) compared to healthy 65 year olds. It was not possible to compare age, sex matched normal individuals because the normative CamCog database only extends to age 90. All 88 subjects scored above 24 on the mini-mental testing (reflecting no cognitive impairment on that test). The audiometry testing was much better than expected for age, in the top tertile. Of the 88 patients on long term MTX, 3 had hearing aides. Sleep duration averaged 8.5 hours/pm which is considered excellent for maintaining cognition.³

Conclusions: This is a subset of people with cardiovascular risk due to age and RA. The CV risk assessment tool* for our subgroup predicted 10 year risk for MI or CVA at 54%. We did not see MI or CVA over 20 years, despite RA. Expanding on that physiology, we found 88 RA patients on long term MTX had above average cognitive testing, completed mini-mental test, drawings, audiometry close to the scores expected for people 3 decades younger. One reason these preliminary results cannot be generalised to other populations is that only RA patients were studied with long term MTX. Also our group were 80–101 years old and there may be a survival advantage in this subgroup since all were healthy at age 65. A study in a larger general population given MTX for several years would be needed to evaluate the benefit in cognition, hearing, and sleep.

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* ASCVD algorithm in the ACC/AHA Guidelines on the Cardiovascular Risk

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AB0248

EVALUATION OF SUBCUTANEOUSLY (SC) INJECTED TC 99M TILMANOCEPT LOCALIZATION IN ACTIVE RHEUMATOID ARTHRITIS (RA) SUBJECTS BY PLANAR AND SPECT/CT

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Background: In rheumatoid arthritis (RA), infiltrating macrophages play a critical role in the immunopathogenesis of the disease by generating pro-inflammatory cytokines and chemokines and by contributing directly to joint damage. Current imaging modalities do not directly assess activated macrophage-mediated disease processes in RA. Use of non-invasive imaging to detect macrophage infiltration of synovial joints may allow for more sensitive identification of synovitis and earlier recognition of RA, identify joints at risk for progressive inflammation and destruction, provide a better means of quantifying joint inflammation and disease activity, and measure or even predict response to macrophage-directed therapy. Tc 99 m tilmanocept is a synthetic radiopharmaceutical imaging agent that binds with high affinity to the mannose receptor (CD206) located on the cell surface of synovial macrophages. We investigated whether subcutaneous (SC) administration of tilmanocept labelled with Tc 99 m could specially image macrophage mediated inflammation in RA but not in healthy control (HC) subjects.

Objectives: To investigate whether subcutaneous (SC) administration of tilmanocept labelled with Tc 99 m could specially image macrophage mediated inflammation in RA but not in healthy control (HC) subjects.

Methods: Subjects received a SC injection of either 50 µg or 200 µg tilmanocept radiolabeled with 2mCi Tc99m in 0.4 mL. 18 subjects were enrolled as follows – Cohort 1: HC: 50 µg/2mCi; n=5; Cohort 2: HC: 200 µg/2mCi; n=4; Cohort 3: RA 50 µg/2mCi; n=4; Cohort 4: RA 200 µg/2mCi; n=5. Subjects were imaged with whole body planar scans at 2–3 hours and 4–6 hours post injection as well as separate 5 min planar images of both hands. If there were areas of increased localization, SPECT images were obtained.