AB0105

A SYSTEMATIC REVIEW OF THE MULTI-BIOMARKER DISEASE ACTIVITY SCORE FOR THE DIAGNOSIS AND TREATMENT IN RHEUMATOID ARTHRITIS

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Background: Biomarkers are important tools that can be used in the diagnosis and monitoring of rheumatoid arthritis (RA). The multi-biomarker disease activity (MBDA) score has shown a clinical value in the overall management of patients with RA.

Objectives: To systematically explore the role of MBDA score for diagnosis and treatment of RA.

Methods: A systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) recommendations. Key words used included: 'Rheumatoid Arthritis', 'Biomarkers', 'Diagnosis', 'Treatment', 'Outcome', 'Response to treatment', 'Disease Activity', and 'MBDA'. The literature search included papers published in 2020 and in the English language.

Results: This literature search has yielded 5 studies that investigated the impact of MBDA score on the diagnosis, treatment or disease progression of RA and have reported clear and clinically validated diagnostic or therapeutic effects. The first study prospectively investigated 130 patients with RA, and has shown that the MBDA score moderately correlated with disease activity at baseline ($r = 0.36$ for adjusted MBDA score, $r = 0.44$ for unadjusted MBDA score) and at 16 weeks follow up ($r = 0.20$ for adjusted MBDA, $r = 0.30$ unadjusted MBDA) but did not predict treatment response to methotrexate. There was also moderate correlation between MBDA scores and erythrocyte sedimentation rate (ESR) at baseline ($r = 0.54$ and 0.59) and week 16 ($r = 0.42$ and 0.51). The second was a cross-sectional study, which included 104 patients (50% female) and demonstrated that adjusted and unadjusted MBDA score correlated similarly with clinical disease activity. Adjustment for leptin reduced the influence of adiposity, particularly among women but significantly estimated higher disease activity in thin men and women. However, MBDA score predicted disease activity and response to tofacitinib treatment, measured by musculoskeletal ultrasound score (MSUS), in RA patients as demonstrated by the third prospective study that included 25 patients (all $p < 0.05$). Correlation was found between baseline MSUS and MBDA score, and with 12-week changes in clinical disease activity ($r = 0.45$ – 0.62 , $p < 0.05$). Regression analysis showed associations between baseline MBDA score and 6-week (all $p < 0.05$) and 12-week change in change in clinical disease activity ($p = 0.03$). The fourth prospective study which included 92 patients with RA, showed that MBDA could predict response to treatment of methotrexate with or without prednisolone. The improvement was faster in the first month of treatment followed by gradual improvement over the following 6 months. Changes from baseline to 12 months for disease activity and MBDA score showed a significant correlation for methotrexate and prednisolone ($r = 0.57$, $p = 0.002$), methotrexate and placebo ($r = 0.57$, $p = 0.001$) and for all groups ($r = 0.56$, $p < 0.001$). The final prospective study which included 148 patients, showed that MBDA predicted remission in RA and could differentiate between small differences in disease activity (low disease activity vs remission states). Baseline MBDA score discriminated baseline remission, area under the curve (AUC) 0.68–0.75, and intermittent/sustained remission (AUC 0.65–0.74). MBDA also predicted long term remission after one year.

Conclusion: MBDA appears to be a useful tool in day-to-day clinical practice that can be used in the diagnosis, monitoring of treatment and prediction of outcomes of patients with RA. MBDA correlated well with disease activity and response to treatment. It is also a good predictor of long-term disease remission.

Disclosure of Interests: None declared

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AB0106

ASSOCIATED FACTORS FOR PRESENTING WITH MODERATE TO HIGH DISEASE ACTIVITY ON THE FIRST RHEUMATOLOGY VISIT IN AN OUTPATIENT CLINIC-BASED COHORT OF COLOMBIAN RA PATIENTS: A REAL-WORLD CROSS-SECTIONAL STUDY

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Background: Rheumatoid arthritis (RA) is characterized by autoantibody formation and expansion such as the rheumatoid factor (RF), anti-citrullinated protein

antibodies (ACPA), and antinuclear antibodies (ANA). Autoantibody identification has been considered as crucial not only for the diagnosis but also for its eventual association with the disease activity, to the extent of playing a pivotal role as a poor prognostic factor among patients¹.

Objectives: Our aim was to assess the eventual association between certain clinical-epidemiological factors and presenting with moderate to high disease activity on the first rheumatology visit in an outpatient clinic-based cohort of Colombian RA patients.

Methods: We conducted a cross-sectional analytic study utilizing the database of an outpatient clinic based in the Rheumatology Department at *Fundación Santa Fe de Bogotá University Hospital*. Data were collected from May 2013 until Sep. 2020 and included age, gender, autoimmune- and non-autoimmune comorbidities, family history of autoimmunity (including RA), smoking and alcoholism personal history, previous DMARD and oral steroid use, nutritional status, disease duration defined as established or early RA (disease duration of ≤ 1 year before starting a DMARD), autoantibody profile information (RF, ACPA, and ANA), and disease activity, assessed by the DAS28- ESR. Multiple logistic regression with backward selection was performed to build the final fitted model.

Results: Data from a total of 1229 patients were included in the analysis. Our population was primarily female ($n = 938$, 76.3%), the majority had an initial diagnosis of established RA ($n = 952$ (77.5%)), and presentation on the first consultation with moderate to high disease activity was seen on 65.2% of the cases ($n = 801$). Being male and having an autoimmune comorbidity were statistically significant associated protective factors whereas strongly positive RF and ACPA levels, positive high ANA titres, and established RA were recognized as risk factors after adjustment for the effects of possible confounders such as age, smoking status, previous DMARD use, and family history of RA. Table 1 provides the complete results obtained from the multiple logistic regression model.

Table 1. Multiple logistic regression analysis's results.

	OR (95% CI)	p-value
Male	0,52 (0,39 – 0,69)	< 0,0001
Age	0,99 (0,99 – 1)	0,24
Autoimmune Comorbidities	0,41 (0,21 – 0,80)	0,009
Family History of RA	0,85 (0,61 – 1,14)	0,26
Current Smoking	1,26 (0,78 – 2,07)	0,29
History of Smoking	1,26 (0,81 – 2)	0,30
Previous DMARD use	0,91 (0,70 – 1,18)	0,45
RF strong titers i.e., > 80 U/ml	1,56 (1,21 – 2,02)	0,0007
ACPA strong titers i.e., > 80 U/ml	1,59 (1,19 – 2,11)	0,0016
ANA low positive titers i.e., < 1:640 dil.	0,94 (0,72 – 1,12)	0,67
ANA strong titers i.e., > 1:640 dil.	1,98 (1,23 – 3,27)	0,0063
Disease duration (established RA)	1,41 (1,05 – 1,90)	0,0277

Bold values indicate statistically significant.

Conclusion: These findings have significant implications for the understanding of the disease activity evaluated on the first contact of a RA patient with a rheumatologist. Our data supports the consideration of being male as a protective factor; however, suggest that autoimmune comorbidities could also condition a lower disease activity for such scenarios, which may be explained by the fact that such patients were referred from- and already being treated by- other practitioners. Additionally, our research provides insights for the consideration of high ANA titers as a potentially poor prognosis factor to be identified as early as on the first visit. ANA's use on daily practice is an intriguing matter which could be usefully explored in further research with distinct methodological approaches.

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AB0107

CHANGES IN EXTRACELLULAR MATRIX BIOMARKER C3M CORRELATE WITH ABATACEPT RESPONSE IN SEROPOSITIVE EARLY RA

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Background: Effective biomarkers are needed to guide RA treatment selection, and the importance of evaluating synovial tissue is increasingly recognised.¹ Markers of extracellular matrix (ECM) turnover (e.g. C3M, a marker of interstitial tissue degradation)² may have clinical utility as disease-relevant and surrogate biomarkers of synovial joint pathophysiology.

Objectives: To evaluate baseline (BL) correlations of ECM biomarkers with disease activity and the predictive value of ECM biomarkers in patients (pts) with seropositive early RA in the exploratory head-to-head Early AMPLE study (NCT02557100), and to explore the impact of shared epitope (SE) status.

Methods: Biologic-naïve, MTX-inadequate responder adults with early (≤12 months' duration), active, moderate-to-severe RA were enrolled if they were anti-cyclic citrullinated peptide 2+ and RF+. Pts were randomised 1:1 to receive SC abatacept (ABA) 125mg weekly or SC adalimumab (ADA) 40mg every 2 weeks (wks) for 24 wks (single-blind period). Linear correlations between levels of ECM serum biomarkers (Nordic Biosciences) and disease activity (DAS28 [CRP], SDAI) at BL and change from BL (CfB) at Wk 24 were assessed in the overall population and by SE status (+/-); early (Wk 4) changes in biomarkers were also assessed.

Results: For SE+ (n=61) and SE- (n=18) pts at BL, mean (SD) DAS28 (CRP) was 5.3 (1.2) and 5.0 (1.0), and SDAI was 35.9 (16.2) and 34.0 (13.8), respectively. At BL in the overall population, significant medium correlations between C1M, C3M and C4M and disease activity were seen (Table 1). Correlations were generally higher in SE+ vs SE- pts, with C1M highly correlated with DAS28 (CRP) in SE+; correlations between C1M, C3M and C4M and disease activity were all significant in SE+ but not SE- pts. At Wk 24, overall CfB in C3M showed higher correlation with CfB in disease activity in pts receiving ABA (n=36; DAS28 [CRP]: 0.66 [p<0.0001]; SDAI: 0.53 [p=0.0009]) vs ADA (n=32; DAS28 [CRP]: 0.33 [p=0.0644]; SDAI: 0.39 [p=0.0267]); this was more pronounced in SE+ pts (ABA, n=27; DAS28 [CRP]: 0.70 [p=0.0001]; SDAI: 0.63 [p=0.0005] vs ADA, n=25; DAS28 [CRP]: 0.33 [p=0.1120]; SDAI: 0.41 [p=0.0445]). Changes at Wk 4 in C3M showed higher correlation with response to ABA vs ADA (Figure 1). Correlations between CfB (at Wks 4 and 24) in other biomarkers and response were generally similar between treatment groups.

Table 1. BL correlation of ECM biomarkers with BL disease activity

	Overall (N=77)		SE+ (n=60)		SE- (n=17)	
	DAS28 (CRP)	SDAI	DAS28 (CRP)	SDAI	DAS28 (CRP)	SDAI
CRPM	0.26 0.0207	0.20 0.0777	0.20 0.1324	0.12 0.3583	0.41 0.0981	0.41 0.1001
Osteocalcin	0.24 0.0380	0.23 0.0416	0.23 0.0763	0.20 0.1293	0.28 0.2818	0.33 0.1890
CTX-1	0.23 0.0440	0.20 0.0844	0.21 0.1104	0.17 0.1932	0.26 0.3089	0.28 0.2703
C1M	0.54* 0.0000	0.34* 0.0028	0.60* 0.0000	0.38* 0.0029	0.34 0.1822	0.26 0.3216
C2M	-0.05 0.6774	0.00 0.9759	-0.06 0.6565	0.01 0.9567	-0.02 0.9441	0.01 0.9813
C3M	0.44 0.0001	0.30 0.0080	0.47 0.0001	0.30 0.0199	0.33 0.1943	0.31 0.2301
C4M	0.39 0.0004	0.32 0.0049	0.47 0.0001	0.36 0.0047	0.10 0.7012	0.11 0.6767

Data are Spearman correlation coefficient, p value. Linear correlations by shading: light grey, low (0<-0.3); medium grey, medium (0.3<-0.6); dark grey, high (0.6-1). Pts with missing SE allele data not included.^an=75.^bn=58.C1M, C2M, C3M, C4M=MMP-mediated degradation products of collagen type I, II, III and IV, respectively; CRPM=neo-epitope of MMP-mediated degradation of CRP; CTX-1=neo-epitope of cathepsin-mediated degradation of type I collagen; MMP=matrix metalloproteinase; SE=-0 SE alleles; SE+=≥1 SE allele.

Conclusion: Significant BL correlation between C1M, C3M and C4M and disease activity was seen and was generally numerically higher in SE+ vs SE- pts. Early (Wk 4) change in C3M and later (Wk 24) treatment response were more highly correlated in pts receiving abatacept vs adalimumab. The predictive value of ECM biomarkers for treatment response warrants study in a larger population.

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Figure 1. Correlation between early changes in C3M and Wk 24 changes in efficacy parameters in the overall population and SE+ subpopulation

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AB0108

USING RNA SEQUENCING TO IDENTIFY GENE EXPRESSION SIGNATURES ASSOCIATED WITH RESPONSE TO ABATACEPT IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a common chronic autoimmune disease. Abatacept (CTLA4-immunoglobulin) is one of the biological disease-modifying antirheumatic drug (bDMARD) for RA patients with inadequate response to methotrexate. Recently, Yokoyama-Kokuryo et al. compared gene expression levels between abatacept responders and non-responders in RA patients using a microarray and found that type I IFN score and expression levels of nine genes may be used as a biomarker to predict response to abatacept. However, little study used RNA sequencing (RNA-seq) to identify whole blood gene expression signatures to predict therapeutic response to abatacept.

Objectives: The aim of this study is to identify gene expression signatures to predict therapeutic responses to abatacept in RA patients using RNA-seq.

Methods: This study is a single-center, prospective study. We used a PAX gene Blood RNA kit to collect whole blood at baseline and 4 weeks after abatacept treatment from RA patients. We also measured DAS28, physician global assessment, HAQ, ESR, CRP at baseline and 12 week to calculate EULAR response at 12 week. Patients with good EULAR response were defined as responders and those with moderate or no EULAR response were defined as non-responders.

Results: We finally conducted RNA-seq for whole blood from 7 RA patients initiating abatacept therapy. Of the 7 RA patients, one was non-responder and 6 were responders. We first use DESeq2 to analyze the differentially expressed genes of non-responder and responder before taking the drug. We used hierarchical clustering and PCA to evaluate the overall similarity of the samples, and group the patient data, and find that the nonresponder can be distinguished from responders. Subsequently, we analyzed the differentially expressed genes of the two groups of non-responder and responder patients before taking the drug. Before treatment, we found that 72 genes had a higher expression in the non-responder,