Table 1. Validation of LDF according to the OMERACT filter

	TRUTH				DISCRIMINATION				FEASIBILITY
	Face	Content	Construct	Sensitivity in situations of change			Sensitivity in situations of no change		
				HC vs SSc	PRP vs SRP	LcSSc vs DcSSc		In clinical trials	
Basal	ND	NA	PV	PV	V	PV	PV	V	ND
Cold challenge	ND	V	ND	PV	V	ND	PV	ND	ND
Heat challenge	ND	V	PV	PV	V	PV	PV	ND	ND
PORH kinetics	ND	ND	ND	V	PV	V	ND	ND	ND
amplitude	ND	ND	ND	PV	PV	UV	ND	ND	ND

Conclusion: This systematic review emphasizes the very preliminary validation status of LDF in the assessment of the FBP in SSc. No single application method has emerged as fully validated according to the OMERACT filter.

REFERENCES

- [1] Herrick A, et al. ARD 1998; 57:70-78
- [2] Boers M, et al. The OMERACT handbook. Ottawa, ON, Canada: OMERACT; 2017

Only those studies which were found of good quality according to the Good Methods Checklist were considered and only the results where p-values were given were considered in this table. OMERACT= Outcome Measures in Rheumatologic Clinical Trials; HC= healthy controls; PRP= primary Raynaud's phenomenon; SRP= secondary Raynaud's phenomenon due to systemic sclerosis; LcSSc: limited cutaneous disease; DcSSc: diffuse cutaneous disease; PORH= post-occlusive reactive hyperaemia; NA= not applicable; ND= no data; V= valid if agreement exists among studies; PV= partially valid if disagreement exists among studies; UV= invalid if agreement about insignificant results exists.

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AB1330

SOLUBLE VASCULAR CELL ADHESION MOLECULE-1 AS AN INDEPENDENT MARKER FOR ENDOTHELIAL ACTIVATION IS ELEVATED IN ACTIVE RHEUMATIC DISEASES: A MULTIVARIATE ANALYSIS

Mara Oleszowsky¹, Widian Laaraj², Tanja Kottmann³, Matthias Seidel⁴. ¹Praxis für Rheumatologie, Köln, Germany; ²Universität Bonn, 53127 Bonn, Germany; ³CRO Dr. med. Kottmann GmbH and Co. KG, 59077 Hamm, Germany; ⁴Spitalzentrum Biel/Centre hospitalier Bienne, Chefarzt Rheumatologie/Médecin-chef rhumatologie, CH-2501 Biel/Bienne, Switzerland

Background: CRP and/or ESR are often unreliable indicators of disease activity. Serum markers of endothelial activation may be promising alternatives. We have recently shown that soluble vascular cell adhesion molecule-1 (sVCAM-1) is elevated in patients with positive antinuclear antibodies [1]. We also have described similar findings in another cohort of patients with a variety of rheumatic diseases [2] and now report a multivariate analysis of these data.

Objectives: CRP, ESR, age, disease and gender were correlated to sVCAM-1.

Methods: Cross-sectional study with 230 patients with rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriatic arthritis (PsA) and different vasculitides (VASC). Disease activities were determined using DAS28, BASDAI, BVAS, RF, ACPA, CRP or ESR. Treatment regimens were subgrouped for conventional DMARDs (cDMARDs) or sets of biologics (bDMARDs). sVCAM-1 (ng/ml) was determined in the serum by ELISA and data were compared to age- and gender-matched healthy controls (HC).

Results: Significant (p

0.05) overexpression of sVCAM-1 as compared to HC were found in the following groups and subgroups (subgroup data not shown): **RA** (n=136): 1.26-fold and in subgroups with bDMARDs, female gender, age >50 years, and RF≥15 IU/ml. **AS** (n=34): 1.71-fold and in subgroups with bDMARDs, age ≤50 years, female gender, CRP <3 mg/dl, and ESR<20 mm/h. **VASC** (n=25): 2.52-fold and in subgroups with cDMARDs, BVAS ≤10 and >10, disease duration ≤120 months, age ≤50 years, female and male gender, CRP ≤3 mg/dl, and ESR ≤20 mm/h. **PsA** (n=35): no significant changes. Linear regression analysis showed that CRP and ESR but not sVCAM-1 were correlated to each other (r=0.637, p<0.001). In addition, multiple linear regression showed that sVCAM-1 was independently

associated with age and disease (RA, AS, VASC). However, sVCAM-1 had no impact on CRP, ESR and gender.

Conclusion: sVCAM-1 is an objective disease marker in patients with RA, AS and VASC. sVCAM-1 is not correlated with CRP and ESR and may thus provide additional information of disease activity. Prospective studies are needed to establish sVCAM-1 as a marker of rheumatic diseases, especially in vasculitis.

REFERENCES

- [1] Oleszowsky M, Seidel MF. Serum Soluble Vascular Cell Adhesion Molecule-1 Overexpression Is a Disease Marker in Patients with First-Time Diagnosed Antinuclear Antibodies: A Prospective, Observational Pilot Study. Biomed Res Int. 2018;8286067. doi: 10.1155/2018/8286067. eCollection 2018. 1;2018:8286067.
- [2] Laaraj W, Seidel MF. Soluble vascular adhesion molecule-1 is overexpressed in patients with vasculitis, rheumatoid arthritis and ankylosing spondylitis. Ann Rheum Dis. 2018, 77(suppl. 2018), A1185, DOI: 10.1136/annrheumdis-2018-eular.5850

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AB1331

URINE METABOLIC PROFILE IN RHEUMATOID ARTHRITIS DEVELOPMENT

Oliveira Marianne Schrader de¹, Barbara Jonson Bartikoski¹, Jordana Miranda de Souza Silva¹, Rafaela Cavaleiro Do Espírito Santo¹, Stephen Peter Young², Ricardo Xavier¹, Laboratory of Autoimmune Diseases. ¹Clinicas Hospital de Porto Alegre, Rheumatology Department, Porto Alegre, Brazil; ²Institute of Inflammation and Ageing, Birmingham, United Kingdom

Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by increased mortality and associated with metabolic disorders including dyslipidaemia, insulin resistance and cachexia. Since the metabolomic profile is known to vary in response to different inflammatory conditions, metabolome analysis could substantially contribute to diagnosis and prognosis.

Objectives: To analyse the urine metabolic profile and assess its correlation with body composition parameters and disease activity of RA patients.

Methods: Seventy-nine RA patients, according to ACR/EULAR 2010 classification criteria, aged between 40 and 70 years, were recruited and followed for 12 months. Disease activity, body composition, fatigue and urine metabolome were measured. Body composition was assessed by total body dual-energy x-ray absorptiometry (DXA) for measurement of appendicular lean mass index (ALMI). Disease activity was assessed by Disease Activity Score-28 with erythrocyte sedimentation rate (DAS28-ESR). Fatigue as assessed by the Functional Assessment of Chronic Illness Therapy (FACIT). Nuclear Magnetic Resonance spectroscopy (NMR) measurements were performed to evaluate the profile of metabolic changes during the 12mo follow-up, resulting in the identification of 48 metabolites in urine collected at the baseline and after one year. Frequency analysis, Pearson Correlation and Multivariate data analysis with orthogonal projections to latent structures (OPLS) method were performed and a statistical significance was considered as p<0.05.

Results: The study population was characterized by the majority of women (86.7%), mean age 56 years old, mean disease duration of 8 years, around 80% with positive anti-CCP and RF. There was a significant increase of citric acid, creatinine, L-serine and urea during the follow-up, metabolites that are involved in the muscular-related metabolism. There was no substantial variation in the DAS28-ESR (baseline: 3.8, after

12 months: 4.0) and there was no significant correlation between changes in the metabolome pattern and DAS28-ESR score ($p > 0.05$). Fatigue was negatively correlated with L-serine/creatinine ($r = -0.4$, $p < 0.001$). Appendicular lean mass index (ALMI) also showed a positive difference which correlated with the increase of urea and creatinine ($r = 0.3$, $p < 0.019$).

Conclusion: This prospective metabolomic analysis indicated that the RA might be associated with amino acid metabolism alterations probably related to inflammation injury to muscle and fatigue. These findings suggest that urine metabolome analysis may be an interesting approach to study and monitor the systemic impact of RA.

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AB1332

COST EFFECTIVE BIOMARKER IN PREDICTING SLE IN DEVELOPING COUNTRIES – NEUTROPHIL LYMPHOCYTE RATIO (NLR), PLATELET LYMPHOCYTE RATIO (PLR), MPV

V.S. Srikanth¹, M Gopala Krishna Pillai¹, (Col.) Vishal Marwaha², Shruthi Rajkumar¹. ¹AIMS Hospital, Internal Medicine, Kochi, India; ²AIMS Hospital, Rheumatology, Kochi, India

Background: SLE is a disease which is easily missed in regular clinical practice. In developing countries due to lack of investigation modalities and rheumatologist, early identification of the diseases process is delayed. By the time the patient reaches a higher medical care centre there is a significant time loss and advancement of the disease. NLR, PLR, RDW and MPV can be calculated from a complete blood count which will be available at any grass route health centre.

Objectives: To identify Cost effective biomarkers in predicting SLE in developing countries. Focussing on markers - Neutrophil Lymphocyte Ratio (NLR), Platelet Lymphocyte Ratio (PLR), MPV.

Methods: This is a retrospective hospital based observational study conducted screening patients admitted from January 2016- November 2018 in with a diagnosis of SLE. We identified 150 patients with SLE and their NLR, PLR, and MPV data were collected and were correlated with equal control group without SLE

Results: We found that NLR, PLR, and MPV were highly significant with a p-value of 0.001 to be used as bio marker and also when further analysis was done using ROC curve with an area under curve of 76%, 81% and 78% respectively when compared with the control group.

Conclusion: We conclude that NLR, PLR, and MPV is cost-effective bio marker which costs (< 1 Euro) in predicting SLE and also play a great in monitoring following up referring patient to higher centre for biopsy at a golden period which will aid in early management which will limit the mortality and morbidity associated with the disease

REFERENCES

- [1] Qin B, Ma N, Tang Q, Wei T, Yang M, Fu H, Hu Z, Ling Y, Yang Z, Zhong R. Neutrophil, to Lymphocyte ratio (NLR) and Platelet to Lymphocyte Ratio (PLR) were useful markers in assessment of inflammatory response and disease activity in SLE patients. *Mod Rheumatol*. 2016;26(3):372-6. doi: 10.3109/14397595.2015.1091136. Epub 2016 Mar 4.
- [2] Wu Y1, Chen Y1, Yang X2, Chen L1, Yang Y3. Neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) were associated with disease activity in patients with systemic lupus erythematosus. *Int Immunopharmacol*. 2016 Jul;36:94-99. doi: 10.1016/j.intimp.2016.04.006. Epub 2016 Apr 22.
- [3] Soliman WM1, Sherif NM1, Ghanima IM1, El-Badawy MA2. Neutrophil to Lymphocyte and Platelet to Lymphocyte Ratios in Systemic Lupus Erythematosus: Relation With Disease Activity and Lupus Nephritis.
- [4] *Reumatol Clin*. 2018 Aug 27. pii: S1699-258X(18)30167-0. doi: 10.1016/j.reuma.2018.07.008. [Epub ahead of print]

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AB1333

CELL-FREE DNA AND BIOLOGICAL TREATMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS

Vanda Mlynarikova¹, Frantisek Malis¹, ^{2,3}Peter Celec⁴, Barbora Vlkova², Eموke Stenova⁵. ¹National Institute of Rheumatic Diseases, Rheumatology Department, Piestany, Slovakia (Slovak Republic); ²Comenius University Faculty of Medicine, Institute of Molecular Biomedicine, Bratislava, Slovakia (Slovak Republic); ³Comenius University Faculty of Medicine, Institute of Pathophysiology, Bratislava, Slovakia (Slovak Republic); ⁴Comenius University Faculty of Natural Sciences, Department of Molecular Biology, Bratislava, Slovakia (Slovak Republic); ⁵University Hospital, Comenius University Faculty of Medicine, 1st Department of Internal Medicine, Bratislava, Slovakia (Slovak Republic)

Background: Cell free DNA (cfDNA) are DNA fragments released from the cell nucleus into extracellular compartment and is therefore detectable in plasma or serum. The most common reason for this release is tissue damage, cell death and inflammation of diverse origin. In regard to autoimmune diseases, increased levels of cfDNA has been found in plasma/serum in patients with systemic lupus erythematosus (SLE), rheumatoid arthritis (RA) and Sjögren's syndrome. The results of some published works, appointing the correlation between levels of cfDNA and RA activity, are controversial, that's why the position of cfDNA as a potential new biomarker remains unclear.

Objectives: The aim of our study was to describe the effect of biological therapy on the concentration of cfDNA and explore the correlation between therapeutic response DAS28 score and cfDNA levels. This potential correlation could define cfDNA as a new marker of treatment response and also potentially also clarify the role of cfDNA in the pathogenesis of RA.

Methods: Plasma samples of 40 patients with RA were collected before, as well as 3 and 12 months after starting treatment with tumor necrosis factor α -inhibitor (TNF α -inhibitor). Total cfDNA was quantified fluorometrically. Treatment response was evaluated by using DAS 28 scoring system and C-reactive protein.

Results: The treatment with TNF α -inhibitors showed statistically significant changes of DAS28 and cfDNA. According the EULAR treatment response defined by DAS28 changes, patients with good response showed statistically significant decrease of cfDNA in month 3 ($p < 0.005$), but the improvement in month 12 was just on the border of statistical significance ($p = 0.059$). There were also only slight changes in group with moderate DAS 28 response in month 12 ($p = 0.054$). In the entire group there was found slight positive ($r = 0.44$), statistically significant ($p = 0.0073$) correlation between the levels of cfDNA and DAS 28 score after 12 month of treatment.

Conclusion: Even if treatment with TNF α -inhibitors decreases plasma cfDNA, there are other markers with better correlation with disease activity. We consider, that the changes in cfDNA levels after biological treatment could determine the role cfDNA more as a consequence of the inflammation, rather than the cause of inflammation in this autoimmune disease, but further research is needed.

REFERENCES

- [1] 1. Zhong XY, von Mühlhelen I, Li Y, et al. Increased Concentrations of Antibody-Bound Circulatory Cell-Free DNA in Rheumatoid Arthritis. *Clin Chem* 2007 53(9):1609-1614.
- [2] Dunaeva M, Buddingh BC, Toes REM, et al. Decreased serum cell free DNA levels in rheumatoid arthritis. *Auto Immun Highlights* 2015 6(1-2): 23-30.
- [3] Abdelal IT, Zakaria MA, Sharaf DM, et al. Levels of plasma cell-free DNA and its correlation with disease activity in rheumatoid arthritis and systemic lupus erythematosus patients. *The Egyptian Rheumatologist* 2016 38:295-300.
- [4] Hashimoto T, Yoshida K, Hashimoto N, et al. Circulating Cell Free DNA: A Marker To Predict The Therapeutic Response for Biological Dmards in Rheumatoid Arthritis. *Int J Rheum Dis* 2017;20(6):722-730.
- [5] Laukova L, Konečná B, Vlková B, et al. Anti-cytokine therapy and plasma DNA in patients with rheumatoid arthritis. *Rheumatol Int* 2018;38 (8):1449-1454.

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