AB1250

DIAGNOSTIC SIGNIFICANCE OF THE PROCALCITONIN TEST IN RHEUMATOLOGY

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Background: Immuno-inflammatory rheumatic diseases (IIRDs) are often complicated by the infectious process, which may be due to both the disease itself and immunosuppressive therapy. At the same time, clinical symptoms and traditional laboratory tests are often uninformative in patients with active IIRDs, and negative results of bacteriological research do not exclude the presence of infection. One of the markers of bacterial inflammation – the procalcitonin test (PCT) – can play an important role in the early detection of infection in IIRDs.

Objectives: The aim of the study is to assess the diagnostic significance of PCT in rheumatology.

Methods: The study included 340 patients (227 women, 113 men, age 39.1±20.8 years) with different IIRDs: systemic lupus erythematosus (SLE) – 74, rheumatoid arthritis (RA) – 71, juvenile arthritis (JA) – 53, systemic vasculitis (SV) – 33, systemic scleroderma (SSD) – 27, ankylosing spondylitis (AS) – 18, adult-onset Still's disease (AOSD) – 13, other IIRDs – 51. The serum concentration of PCT was determined by the quantitative electrochemiluminescent method using the Cobas E 411 analyzer (Roche, Switzerland).

Results: In patients without infection (n=181), the median (Me) PCT level was 0.11 ng/ml [0.05; 0.17]; higher values of PCT were found in patients with AOSD (0.39 ng/ml [0.14; 0.51]), systemic form of JA (0.17 ng/ml [0.11; 0.5]) and SLE (0.16 ng/ml [0.10-0.45]). In RA, SV, SSD, AS without infection, Me PCT was 0.07 ng/ml [0.03; 0.12]. The infectious process was detected in 159 patients: generalized – in 11, local – in 148. Depending on the severity of the intoxication syndrome, local infections are divided into severe (n=70) and light (n=78). Infections of the lower respiratory tract, urinary system, skin and soft tissues prevailed. In patients with generalized infection, Me PCT level was 3.6 ng/ml [0.49; 11.3]. In 10 patients of this group, the level of PCT exceeded 2 ng/ml, in 5 patients – 10 ng/ml. In severe local infection, Me PCT was 0.45 ng/ml [0.23; 1.19], in light – 0.12 ng/ml [0.05; 0.16]. In generalized infection, the level of PCT was significantly higher than in patients without infection (p<0.0001), as well as with mild (p<0.0001) and severe local infection (p<0.0001). In patients with severe local infection, the level of PCT was higher compared to patients without infection (p<0.0001) and with mild local infection (p<0.001). There were no significant differences in PCT in the groups of patients with light local infection and without infection. In SLE patients with infection, the level of PCT and CRP (but not ESR) was higher than in patients without infection; a correlation was found between the level of PCT and CRP (r=0.53, p<0.001) in the presence of infection. In AOSD, systemic form of JA, RA, SV, SSD, AS, significant differences in the levels of PCT, ESR, CRP in patients with infection and without infection were not obtained, correlations were not revealed. According to the ROC-analysis, the diagnostic significance of determining PCT in generalized infection is excellent, in severe local infection – very good, and in differentiation of generalized infection from local infection – very good.

Conclusion: PCT is a significant diagnostic test that allows to recognize generalized and severe local infections in patients with IIRDs. In order to more accurately diagnose the infectious process, a multi-marker approach is needed.

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Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.905

AB1251

VALIDITY OF RHEUMATOID ARTHRITIS DIAGNOSES IN FINNISH BIOBANK PATIENTS

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Background: Finnish healthcare registers are used in medical research, but there is little data about the validity of these registers in rheumatology.

Objectives: The aim of our study was to determine the validity of rheumatoid arthritis (RA) diagnoses in patients participating in the Finnish Biobanks.

Methods: We reviewed the electronic patient charts of 125 patients with at least one visit with a diagnosis of seropositive RA, 125 patients with at least

one visit with a diagnosis of seronegative RA and 250 age-and-sex matched controls. Patients were randomly selected from Finnish biobank participants. We evaluated whether the patients' diagnosis of RA recorded in the hospital discharge registry at the participating hospital was correct according to chart review and expert opinion. In the control group it was investigated whether the diagnosis of RA was written in the patients' chart, but the diagnosis code was not recorded.

Results: The positive predictive value (PPV) of a single hospital registry diagnosis of seropositive RA was 0.74 but rose to 0.98 in patients with a special reimbursement for seropositive RA and 0.98 in anti-citrullinated protein antibody positive patients. For seronegative RA, the PPV of a diagnosis was 0.72 and in patients with a special reimbursement for seronegative RA 0.89. The PPV was higher in patients with more than one visit with the diagnosis: 0.92 if the patients had at least 5 visits with seropositive RA and 0.88 with at least 5 visits with seronegative RA. Negative predictive value for RA diagnosis was 0.99.

Conclusion: These results demonstrate that the validity of RA diagnoses in healthcare registers can be markedly improved with data about special reimbursement for medication, number of visits and serological data.

Disclosure of Interests: Anti Palomäki Consultant of: Pfizer, Speakers bureau: Pfizer, Sanofi, MSD, Johanna Paltta Consultant of: Lilly, Abbvie, Laura Piriä Consultant of: Novartis, MSD Finland, Roche, Bristol-Myers-Squibb, Pfizer, Sanofi, Abbvie, Oy Eli Lilly Finland Ab, UCB Pharma Oy Finland, Jansen-Cilag, Mylan, Sandoz, Boehringer-Ingelheim, Paid instructor for: Boehringer-Ingelheim, MSD Finland, Speakers bureau: Boehringer-Ingelheim, Pfizer Finland, Hanna-Kaisa Heikkilä: None declared, Pia Isomäki Consultant of: Abbvie, BMS, Eli Lilly, MSD, Novartis, Pfizer, Roche, Sanofi, Johanna Huhtakangas Consultant of: Boehringer Ingelheim, Tuulikki Sokka-Isler: None declared, Oili Kaipiainen-Seppänen Speakers bureau: Boehringer Ingelheim, Kari Eklund Consultant of: Celgene, Lilly, Speakers bureau: Pfizer, Roche

DOI: 10.1136/annrheumdis-2020-eular.3890

AB1252

CAN THE HUPI BE MORE USEFUL THAN OTHER INDICES IN THE SEARCH OF BIOMARKERS FOR RA?

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Background: The Hospital Universitario La Princesa Index (HUPI) was developed to tackle metric shortcomings of DAS28 and SDAI, and has shown better accuracy and responsiveness than these widespread indices.¹

Objectives: To compare the performance of HUPI, DAS28, and SDAI in explaining the variability of radiographic progression, HAQ and the distribution of a biomarker of damage such as IL6.

Methods: Two cohorts were assembled with data from a clinical trial (ACT-RAY) and an early arthritis register (PEARL). Radiographic progression, measured as the change (Δ) of Genant or Sharp/Van der Heijde indices at week 52 in ACT-RAY and PEARL respectively, Δ HAQ and serum IL6 (ELISA; R&D Systems) levels, the latter only available in PEARL, were the outcome variables. HUPI, DAS28, SDAI, sex and age were the independent variables.

For each index, linear regression models adjusted for sex and age were developed using standardized variables. The overall performance of the model, as well as that of the specific index it included, were evaluated using the adjusted R². Differences between models were assessed with the likelihood ratio test. Also, The *fpfitci* command (Stata v14) was used to estimate the predicted distribution of the described variables using fractional polynomials and plotting the resulting curves.

Results: The performance of the models and indices are shown in table 1. The variability of radiographic progression was better explained by the SDAI model in ACT-RAY whereas HUPI did it so in PEARL. The latter also performed better for explaining HAQ in ACT-RAY (figure 1) and IL6. Sex modified the performance of DAS28 and SDAI in their respective models. The relation between all the described outcomes predicted using fractional polynomials and each index was also more linear for HUPI than its comparators. (see an example in figure 2).

Table 1. Adjusted R^2 of the models and indices. R^2_m : adjusted R^2 of the models; R^2_i : adjusted R^2 of the index included in the model; LR: Likelihood-Ratio test comparing HUPI models vs other indices¹.

OUTCOME	INDEX	ACT-RAY		LR	PEARL		LR
		R^2_m	R^2_i		R^2_m	R^2_i	
RADIOGRAPHIC PROGRESSION	HUPI	0.025	0.024	ref	0.110	0.020	ref
	DAS28	0.031	0.030	<0.000	0.102	0.011	<0.000
	SDAI	0.051	0.050	<0.000	0.109	0.019	<0.000
HAQ	HUPI	0.353	0.323	ref	0.477	0.448	ref
	DAS28	0.329	0.298	<0.000	0.472	0.442	<0.000
	SDAI	0.334	0.303	<0.000	0.486	0.457	<0.000
IL6	HUPI	-	-	-	0.212	0.184	ref
	DAS28	-	-	-	0.204	0.176	<0.000
	SDAI	-	-	-	0.201	0.172	<0.000

Figure 1. Box plots comparing the adjusted R^2 of each index estimated in models for HAQ in ACT-RAY.

Figure 2. Curves for comparison of predicted serum IL6 using fractional polynomials for HUPI and DAS28.

Conclusion: Although all indices explained the outcomes' variability similarly, HUPI did it better than DAS28 and SDAI for almost all outcomes except for Δ Genant and HAQ in PEARL.

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Disclosure of Interests: Sebastian C Rodriguez-García Speakers bureau: Novartis Farmaceutica, S.A., Merck Sharp & Dohme España, S.A., Sanofi Aventis, UCB Pharma, Nuria Montes: None declared, José Ivorra: None declared, Ana Triguero-Martinez: None declared, Luis Rodríguez Rodríguez: None declared, Isabel Castrejón: None declared, Loreto Carmona Grant/research support from: Novartis Farmaceutica, SA, Pfizer, S.L.U., Merck Sharp & Dohme España, S.A., Roche Farma, S.A, Sanofi Aventis, AbbVie Spain, S.L.U., and Laboratorios Gebro Pharma, SA (All through institution), Isidoro González-Alvaro Grant/research support from: Roche Laboratories, Consultant of: Lilly, Sanofi, Paid instructor for: Lilly, Speakers bureau: Abbvie, MSD, Roche, Lilly

DOI: 10.1136/annrheumdis-2020-eular.713

AB1253

EVALUATION OF CYSTEINE-RICH 61 IN RHEUMATOID ARTHRITIS AS A DIAGNOSTIC MARKER AND PREDICTOR OF ATHEROSCLEROSIS

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Background: Matricellular protein Cysteine-rich protein 61 (Cyr61) is involved in chronic inflammatory disorders like rheumatoid arthritis (RA) and atherosclerosis.

Objectives: This study aimed to assess the value of serum Cyr61 in diagnosis of rheumatoid arthritis, evaluating its correlation with disease activity and its relation to atherosclerosis.

Methods: Cross-sectional study included 105 RA patients classified into active and inactive groups according to disease activity score (DAS28) with 50 healthy age and gender-matched controls. Full clinical and laboratory assessment was done including enzyme-linked immunosorbent assay (ELISA) measurement of Cyr61. Bilateral assessment of carotid intima-media thickness (CIMT) was done using high resolution-ultrasonography. Comparison of Cyr61 between RA patients and controls, correlation between Cyr61 and disease activity and CIMT were analyzed with appropriate statistical analyses.

Results: Significant elevation of Cyr61 in RA patients compared to controls (235.62±62.5 vs. 73.11±18.2) respectively. The cut off value of Cyr61 was 99.25 pg/ml, with area under the curve (AUC) =0.995, P <0.001, 98 % sensitivity and 95% specificity. Cyr61 was inversely correlated with DAS28 and its components in RA patients (r=- 0.92, r=- 0.94) (p<0.001). There was a significant positive correlation between Cyr61 levels and CIMT in inactive and active RA patients (r=0.88, r=0.47) respectively.

Conclusion: Serum Cyr61 as a potential diagnostic biomarker in RA is inversely correlated with disease activity. High Cyr61 in RA is a risk factor for atherosclerosis. Disruption of serum Cyr61 is engaged in the pathogenesis of both rheumatoid arthritis and atherosclerosis which is a clue for a future treatment strategy of RA.

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Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.752

AB1254

PHENOTYPING OF MULTIPLE BIOFLUIDS FOR LIQUID BIOMARKERS FOR DIAGNOSTICS AND PERSONALIZED MEDICINE OF RHEUMATOID ARTHRITIS, SPONDYLOARTHRITIS AND OSTEOARTHRITIS

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Background: Inflammatory and autoimmune diseases include multifactorial pathomechanisms and systemic responses. The etiology of the joint diseases rheumatoid arthritis (RA), spondyloarthritis (SpA) in relation to osteoarthritis (OA) remain incomplete and establishing the correct diagnose remains nontrivial. Advances in high-throughput molecular technologies have increased investigations into the