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AB0194 JOURNEY OF A PATIENT WITH RHEUMATOID ARTHRITIS: DELAY IN DIAGNOSIS AND TREATMENT

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Background: It has been shown that there is a window of opportunity for treatment in Rheumatoid Arthritis (RA). Several Argentinean studies showed an average of 8 months to arrive to a rheumatology visit and 12 months to receive DMARDs. There aren't recent studies.

Objectives: To establish delay time from onset of rheumatoid arthritis (RA) symptoms to the first rheumatology visit, to diagnosis of the disease and to the beginning of treatment with DMARDs; and to assess impact of such delay on structural damage, in a cohort of RA patients.

Methods: A retrospective study was performed including all patients with RA (fulfilling ACR/EULAR 2010 criteria) seen at a Prepaid Medical Health Plan between 2002–2015. Diagnosis delay and its impact on functional capacity measured by HAQ-A and structural damage by Sharp van der Heide score (SvdH) was estimated. Demographic and clinical data, and dates of diagnosis, onset of symptoms and HAQ-A were extracted from electronic medical records. SvdH score was performed by an experienced rheumatologist.

Results: 246 patients (mean age at diagnosis 67.25±14 years, 199 (81%) female) were included. Clinical presentation was polyarticular in 49% of the cases, oligoarticular in 47% and monoarticular in 3%. 79% had high titers of anti-cyclic citrullinated peptide antibodies, 12% low titers, and 9% were negative. Rheumatoid factor was positive in 82.5%. Mean time of follow up was 7 years (SD: 3.8). At the end of the follow-up, median HAQ-A (n=145) was 0.125 (IQR: 0–0.87). Hands and feet lastxray available were analyzed in 171 patients. Median SvdH score was 15 (IQR: 6–33). 242 patients (98.4%) received DMARDs as initial treatment: methotrexate monotherapy (76%) was the most frequent one. 41 patients (17%) received biological agents at some point of their disease. Table 1 shows different delay times in accessing rheumatology consultation, diagnosis and beginning of treatment.

At the end of follow up, 21 patients (12.28%) had noradiological damage (SvdH score =0). In the ROC curve (AUC 0.57, 95% CI: 0.45 - 0.69), 5.6 months of diagnosis delay was the best cut off value to discriminate the presence of erosions (SvdH erosions score >0), with a sensitivity and specificity of 54.17% and 61.90%, respectively. Delay in diagnosis greater than 12 months (n=70) was associated with significantly radiological damage: SvdH mean 30.91 (IC 95% 21.99–39.79) vs 21.32 (IC 95% 16.93–25.72); p=0.0325.

Table 1. different delay times

Variable	Mean (SD)	Median (IQR)
Time from first symptoms to first rheumatology visit (months)	9.21 (20.50)	3 (1–7)
Time from first symptoms to diagnosis (months)	14.2 (24)	4.8 (2.4–13)
Time from first symptoms to DMARDs indication (months)	16.9 (25.4)	7 (3–17)
Time from first symptoms to biological indication (years)	6.2 (4.8)	5.7 (2.4–7.2)

Conclusions: In a Prepaid Medical Health Plan with ease of referral, there is still a significant delay in diagnosis and treatment of RA patients. Delay in diagnosis greater than 12 months was associated with more radiological damage.

Disclosure of Interest: None declared

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AB0195 IS THERE AN ASSOCIATION BETWEEN PERIODONTITIS AND LEVELS OF ANTI-CITRULLINATED PEPTIDES ANTIBODIES IN RHEUMATOID ARTHRITIS?

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Background: Positivity of anti-citrullinated peptides antibodies (ACPA) indicates severity in Rheumatoid Arthritis (RA). There is evidence for chronic periodontitis (PD) in RA autoimmune response by periodontopathogenic bacteria such as *P.gingivalis*, through citrullination of L-arginine.

Objectives: 1.To determine whether there is an association between PD and its severity with ACPA(+). 2.To assess relationship between PD and ACPA titres. 3.To identify association between certain periodontal parameters and ACPA titres and their possible cutoff points.

Methods: Observational, cross-sectional study RA patients ≥18 with ≥4 teeth, no tooth cleaning, antibiotic intake 6 months before. Socio-demographic and anthropometric variables, annual dental prophylaxis and comorbidities. Serum

ACPA detection: Ab IgG against CCP2 (ELISA) Eurodiagnostica: positive ≥25; ACPA titres stratification: Low (25–75), moderate (76–300) and high (>300). Periodontal parameters: plaque index (PI), bleeding on probing (BoP), probing pocket depth, clinical attachment level (CAL). CAL loss was categorized according to European Workshop 2005 (Tonetti): T level 0 (absence), T1 (mild), T2 (severe). Statistical analysis: t-student, Kruskal Wallis, Chi-squared tests by Stata program 13.1.

Results: 187 RA patients included (table 1), ACPA determined in 168 patients: 67.86% (+) with similar titres distribution: low 18%, moderate 26%, high 23%. PD: 182 patients (97.3%): T1 52.4%, T2 44.9%. Although prevalence of severe PD/ACPA(+) was higher compared to PD/ACPA(-) (69.2% vs 30.7%), there was no association between PD and ACPA positivity/titres. Regarding the association with periodontal parameters, there was tendency of association between ACPA(+) and number of periodontal pockets ≥5mm (NPP), OR 1.02 (95% CI 0.9–1.04) adjusted. There was a gradient effect, where NPP increased as ACPA titres increased, which was significant for high ACPA titres (p≤0.05, OR 1.03 95% CI 1.0–1.05). When ACPA(+) was related to %PI and BoP, a strong association was observed for PI, OR 10.32 (p<0.026), and only a tendency for BoP (p<0.062). With cutoff points of 8% PI and 65% BoP, a risk for ACPA(+) was detected with an OR 2.19 and OR 2.45, respectively.

Table 1

	RA (N)	RA (%)
Female sex	147	78.6
Mean age (SD)	54.4 (10.8)	
Follow up time, median (SD), years	8.88 (7.32)	
Early RA	35	18.7
Rheumatoid factor, seropositive	138	74.2
Disease Activity Ranges		
Remission	39	20.9
Low	45	24.1
Moderate	85	45.4
High	18	9.6
Medication RA		
Without Treatment	10	5.3
DMARDs	99	52.9
≥2 DMARDs	22	11.8
Biologic Drugs	56	29.9

Conclusions: 1. Despite higher prevalence of severe PD in ACPA(+) patients, we found no association between the presence of PD and ACPA positivity nor with serum titres. 2. On analysis of ACPA titres in relation to the severity of the periodontal parameters, there was a “gradient” risk, where NPP increased as ACPA titres increased, which was significant for high ACPA titres. 3. Risk cutoff points for ACPA(+) were 8% for PI and 65% for BoP.

Disclosure of Interest: None declared

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AB0196 VASCULAR ENDOTHELIAL GROWTH FACTOR IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: The level of vascular endothelial growth factor (VEGF) may reflect the intensity of angiogenesis, which is an important step in the initiation and development of chronic rheumatoid arthritis (RA).

Objectives: to study features of VEGF level changes in the blood of RA patients, depending on the duration of the disease, the degree of activity, the level of antibodies to cyclic citrullinated peptide (anti-CCP)

Methods: 194 patients were examined with a diagnosis of RA (verified according to criteria ACR/EULAR 2010), without concomitant pathology. Among the examined patients with RA women predominated 168 (86.6%), and there were 26 men (13.4%). The age of patients was 22 to 65 years (mean age 47.7±10.22 years), mean duration of the disease was 3.82±3.43 years. Assessment of RA activity was done by DAS 28 index, using blood CRP in the formula. 152 patients were positive for the presence of anti-CCP (≥20 U/ml) (78%) and 42 (22%) - negative. Serum CRP concentrations (Vector-Best, Russia), anti-CCP (Orgentec, Germany), VEGF (BCM Diagnostic, Canada) were determined by ELISA. Statistical processing of the data was performed using non-parametric methods, univariate (ANOVA) variance analysis on a personal computer using a licensed software packages (“Microsoft-Excel” and “Statistica-Stat-Soft”, USA)

Results: Analysis of VEGF level changes in the blood depending on the duration of RA revealed that the measure was high in patients with small diseases duration 0–23 months (472.96 (341.1; 582.1) pg/ml) compared with the group 5 years (324.1 (199.2; 556.2) pg/ml) (p<0.04). Analysis of VEGF level in blood depending on the degree of RA activity showed that the VEGF concentration in blood increased with increasing degree of RA activity and it was the greatest - 564.4 (340.1; 758.4) pg/ml in the group with a high degree (DAS28 >5.2) compared to the minimum (DAS28 ≤3.2) - 230.5 (178.1; 385.3) pg/ml, and moderate (DAS28 3.3–5.2) - 356.4 (278.9; 553.1) pg/ml, (p<0.001; p=0.005, respectively). Using ANOVA variance analysis, it was found that the degree of RA activity influenced the VEGF levels in the blood (KW =17.37; p<0.001).

Analysis of the VEGF levels in the blood depending on the level of anti-CCP

showed a significant increase in VEGF level (343.35 (190.62; 561.28) pg/ml) in the group of high positive ACCP (>60 U/ml) compared with the group of low positive ACCP (≤ 60 U/ml) - 470.23 (324.3, 676.85) pg/ml ($p=0.005$). Using ANOVA variance analysis, it was found that the level of anti-CCP in the blood of studied RA patients influences the VEGF level in blood (KW =7,88; $p=0.005$)

Conclusions: In patients with RA duration <2 years VEGF levels in the blood was 30% higher than in patients with a prolonged course of RA. Concentration of VEGF in the blood increased 2-fold with a high degree of RA activity. Levels of VEGF in the blood were 1.5 times higher in the patients with anti-CCP levels >60 U/ml compared to low positive anti-CCP patients. The high level of VEGF may be a marker of severe clinical course of RA, the high rate of disease progression and the development of early joint destruction

Disclosure of Interest: None declared

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AB0197 SUBCLINICAL INTERSTITIAL LUNG DISEASE IN EARLY RHEUMATOID ARTHRITIS

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Background: Interstitial lung disease (ILD) is a severe extra-articular complication of Rheumatoid Arthritis (RA). The decrease in DLCO diffusion is the most sensitive value for the detection of ILD. DLCO is also a prognostic factor.

Objectives: To study the prevalence of subclinical lung involvement in early RA.

Methods: Cross-sectional study of lung involvement in early RA. The following criteria were used: A) RA according to the EULAR-2010 criteria. B) Early RA if evolution from the onset of symptoms to the diagnosis of RA was less than one year. C) Lung affection if DLCO diffusion was lower than 80%. In each patient we evaluate: a) presence of dyspnea according to MMRC (Modified British Medical Research Council) scale; B) Respiratory function tests (FVC, FEV1, FEV1/FVC; C) DLCO; classifying the degree in: i) normal >80% (mild decrease 80–60%); ii) Moderate decrease (60–40%) and iii) Severe reduction (<40%); D) Chest x-ray: assessed by radiologist. E) Joint activity of RA (DAS28), F) CRP and ESR. G) RF, CCPA, H) Presence of atheroma plaque on carotid ultrasound. Quantitative variables were expressed as mean±SD or median [IQR] and were compared with the Student t or Mann Whitney U test, respectively. Dichotomous variables were expressed as percentages and compared using the chi-square test. Statistical analysis was performed with the SPSS 15.0 program.

Results: 20 patients (15 women/5 men) with early RA were studied; mean age of 54.1±13.4 years. Some patients were using disease-modifying antirheumatic drugs (DMARDs) prior to performing respiratory function tests (PFR): methotrexate (7) 3 of them with less than 14 days of treatment, hydroxychloroquine (4), sulfasalazine (1). The table shows the main characteristics of patients according to presence of lung disease. We observed a decrease in DLCO in 15/20 patients (75%) who were mild (DLCO <80%) in 4 (27%); Moderate (DLCO <60%) in 9 (60%) and severe (DLCO <40%) in 2 (13%). Chest x-ray showed these alterations in 3 patients: signs of air trapping, laminar atelectasis and scarring tracts. There were no alterations in FVC in any patient.

Table 1

	With lung involvement (n=15)	Without lung involvement (n=5)	P
Age, mean	56.3±13.11	55.6±15.69	0.55
Sex (W/M)	13/2	3/2	0.03
Smokers or ex smokers, n (%)	10 (66.7)	1 (20)	0.06
CCP Antibody, positive n (%)	8 (53.3)	2 (40)	0.60
Titer, median [IQR]	430.5 [165.8–1874.2]	47 [35–59]	0.23
RF Positive, n (%)	8 (53.3)	2 (66)	0.6
RF titer, median [IQR]	213 [67.5–334.75]	135 [74–196]	0.6
ESR mean/ CRP mean	32.1±21.4/ 4.7±7.8	24.6±21.8/ 0.80±0.83	0.84/0.21
DAS28, mean	5.04±1.03	4.48±0.85	0.49
Bone erosions X ray, n (%)	1 (6.7)	1 (20)	0.60
Carotid plaque, n (%)	8 (53.3)	2 (40)	0.60
Extra articular manifestation, n (%)	3 (20)	0	0.16
– Sjögren Syndrome	2		
Abnormalities in thorax Rx, n (%)	3 (20)	0	0.16
Dyspnea, n (%)	1 (6.7)	0	0.60
DMARDs, n (%)	8	4	0.60
Methotrexate, n (%)	5 (55)	2 (50)	
Hydroxychloroquine, n (%)	2 (33)	2 (50)	
Sulfasalazine, n (%)	1 (12)	0	

Conclusions: We find a high frequent of lung involvement in early RA, in most of cases subclinical. Performing Respiratory function tests may help in early detection of lung involvement. These results should be ratified in larger series.

Disclosure of Interest: None declared

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AB0198 DIFFERENTIAL CHARACTERISTICS OF PATIENTS DISCONTINUATING SEVERAL BIOLOGIC THERAPIES IN A COHORT OF RHEUMATOID ARTHRITIS PATIENTS

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Background: The treatment of Rheumatoid Arthritis (RA) has been transformed in the last decade with the introduction of biologic therapy. Nevertheless, a substantial proportion of patients (pts) are found to be primary or secondary nonresponders and will receive several biologics during the course of the disease. Evidence is lacking on the characterization of patients failing several agents and those who have adequate clinical response to their first biological treatment.

Objectives: To compare demographic, clinical and analytical characteristics in a cohort of RA pts who have failed treatment with at least two biological agents ("switchers") and another cohort of RA patients showing a sustained clinical good response to their first therapy ("maintainers"). As a secondary objective, reasons for therapy discontinuation were also evaluated.

Methods: A total of 186 patients under biological therapy of the RA-PAZ cohort were included in this observational study. In this cohort, 63 pts were switchers and 123, maintainers. Baseline demographic data and clinical disease activity (DAS 28 -ESR), clinical improvement (delta-DAS 28) and serological data (CRP and ESR) were evaluated at baseline and sixth months after starting the first biological treatment. Serum anti-drug antibodies (ADA) were measured by bridging ELISA at the last visit available during the follow-up period under the first treatment. Reasons for discontinuation of the first therapy and the number of biologic treatments received during the course of the disease were also evaluated.

Results: Demographic and clinical characteristics of both groups are shown in Table 1. Mean Age (49,96±10,82 vs 53,77±12,91, $p=0.046$) and disease duration (6,79±6,19 vs 9,97±8,56, $p=0.001$) prior to biologic therapy initiation were lower in the switchers. Furthermore, a higher proportion of switchers had extraarticular manifestations in comparison to the maintainers (18/63 (28,6%) vs 16/121 (13,2%), $p=0.016$). Clinical activity at baseline (DAS28: 5,74±1,26 vs 5,01±1,14, $p=0.01$) and after 6 months of starting the first biological therapy (DAS28: 4,45±1,6 vs 3,22±1,1, $p=0.001$) were statistically significant higher in the switchers. At the last visit under the first biologic, there were also more ADA-positive pts in the switchers (6/25 (24%) vs 1/73 (1,4%), $p=0.01$). Moreover, duration under biologic treatment was higher in this group. In terms of the reason for discontinuation of the first biologic, 22,2% of pts showed primary lack of efficacy; 38,1%, secondary loss of efficacy; 33,3%, adverse effects; 4,8% interrupted because of other reasons and 1,6% because of

Pts characteristics	Switchers n=63	Maintainers n=123	P value
Baseline characteristics at the initiation of the 1st biological therapy (1BT)			
Female, n/N (%)	49 / 63 (77,8%)	102 / 122 (83,6%)	NS
BMI (kg/m ²) ± DS	27,31 ± 5,37	26,23 ± 4,96	NS
Smoking habit	38 / 61 (62,3%)	69 / 115 (60%)	NS
• Non-smoker	11 / 61 (18%)	19 / 115 (16,5%)	
• Smoker	12 / 61 (19,7%)	27 / 115 (23,5%)	
• Ex smoker			
Age at the starting of the 1BT ± DS	49,96 ± 10,82	53,77 ± 12,91	P=0,046
Time from diagnosis to 1BT ± DS (y)	6,79 ± 6,19	9,97 ± 8,56	P=0,001
Co-therapy (DMARDs) ± DS	27,31 ± 5,37	26,22 ± 4,96	NS
Auto-antibodies (UI/ml)	50 / 63 (79,4%)	93 / 121 (76,9%)	NS
• FR +, n/N (%)	97 / 118 (82,2%)	53 / 62 (85,5%)	NS
• ACPA +, n/N (%)			
Erosions, n/N (%)	36 / 52 (69,2%)	67 / 101 (66,3%)	NS
Extraarticular manifestations, n/N (%)	18 / 63 (28,6%)	16 / 121 (13,2%)	P=0,011
Monotherapy, n/N (%)	3 / 63 (4,8%)	6 / 122 (4,9%)	NS
Baseline activity ± DS	5,74 ± 1,26	5,01 ± 1,14	P=0,001
• DAS – 28 ± DS	13,82 ± 20,8	10,26 ± 13,6	NS
• PCR ± DS	33,63 ± 22,03	29,4 ± 18,36	NS
• VSG ± DS			
6 months after the initiation of the 1st biological therapy			
Six months activity ± DS	4,44 ± 1,61	3,22 ± 1,10	P=0,001
• DAS-28 ± DS	1,40 ± 1,6	1,77 ± 1,2	NS
• Delta-DAS 28 ± DS			
Last visit available after the initiation of the 1BT			
ADA+, n/N (%)	6 / 25 (24%)	1 / 73 (1,4%)	P=0,01
At the last visit available after the initiation of the 1st biological therapy			
Age, mean ± DS	61,23 ± 11,8	61,05 ± 12,8	NS
Time of follow-up until the last visit available ± DS, (years)	16,48 ± 7,5	16,71 ± 9,9	NS
Mean time under biologic ± DS, (y)	9,48 ± 4,3	6,72 ± 4,6	P=0,001