AB0236

WHAT FACTORS ARE ASSOCIATED WITH THE EVOLUTION TOWARDS RHEUMATOID ARTHRITIS, USE OF BIOLOGICAL THERAPY AND DEVELOPMENT OF CARDIOVASCULAR EVENTS IN A COHORT OF PATIENTS WITH UNDIFFERENTIATED ARTHRITIS?

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Objectives: To describe the clinical-demographic characteristics and behaviour over time (12, 24 and 60 months) of a cohort of Undifferentiated Arthritis (UA), as well as to analyze which factors are associated with the evolution towards Rheumatoid Arthritis (RA), use of Biological Therapy (BT) and the development of Cardiovascular Disease (CVD).

Methods: Ambispective cohort study of patients with UA evaluated longitudinally from January 2009 to 2019. We analyzed baseline clinical and laboratory variables and a Multivariate Logistic Regression was performed to determine the factors associated with RA development after 5 years of follow-up. To analyze what factors were associated with the use of BT and the presence of CVD chi-square or Fisher's test were used for binary variables, and U-Mann Whitney for continuous variables.

Results: 180 patients were included, 55% were women, with an average age of 49.3 (SD 16.1) years. The average duration of symptoms before the first visit was 6.9 (SD 9.9) months. 47.2% were FR+, 41% ACPA+, 20.6% HLA-DRB1 shared epitope.

At the end of follow-up: 33.3% evolved to RA, 17.2% remained as palindromic rheumatism, 25% were diagnosed other chronic rheumatic diseases, 21.1% remitted spontaneously and 3.3% remained as UA. Of the 60 AR, 37 were diagnosed in the first year, 13 at second and 10 at 5 years of follow-up. During follow-up, 13 patients with RA started BT, and 12 patients presented CVD (7 of them died).

Table 1.: Factors associated with RA after 5 years of follow-up.

Baseline data	Total patients N=180	RA N = 60	No RA N =120	OR (95%CI)	p-value
Sex (women)	99 (45.7%)	34 (56.7%)	65 (54.2%)	1.11 (0.69-2.07)	0.751
Duration of symptoms (months)	7.7 (8.8)	7.5 (6.5)	7.8 (9.8)	0.99 (0.96-1.03)	0.864
Age at diagnosis	49.3 (16.1)	49.4 (14.5)	49.3 (16.9)	1.00 (0.98-1.02)	0.961
-Oligoarthritis	84 (46.7%)	20 (33.3%)	64 (53.3%)	2.34 (0.49-11.14)	0.284
-Polyarthritis	79 (43.9%)	38 (63.3%)	41 (34.2%)	6.95 (1.49-32.42)	0.014
Morning stiffness>1h	43 (23.9%)	22 (36.7%)	21 (17.5%)	2.73 (1.35-5.52)	0.005
RF+	85 (47.2%)	47 (78.3%)	38 (31.7%)	7.8 (3.78-16.1)	<0.001
ACPA+	73 (41.0%)	50 (83.3%)	23 (19.5%)	20.6 (9.1-46.7)	<0.001
High ESR	104 (57.8%)	40 (66.7%)	64 (53.3%)	1.75 (0.92-3.34)	0.089
Hight CRP	100 (55.6%)	40 (66.7%)	60 (50%)	2.0 (1.05-3.81)	0.035
HLADRB1 Shared epitope	37 (20.6%)	32 (53.3%)	5 (4.2%)	26.3 (9.39-73.55)	<0.001
Smoker	72 (40%)	25 (41.7%)	47 (39.2%)	1.11 (0.59-2.08)	0.747
Family history RA	39 (21.7%)	17 (28.3%)	22 (18.3%)	1.76 (0.85-3.64)	0.127
Tto glucocort (5mg/d)	88 (48.9%)	40 (66.7%)	48 (40%)	3.0 (1.57-5.74)	0.001
Tto dolquine (200mg/d)	50 (27.8%)	25 (41.7%)	25 (20.8%)	2.71 (1.38-5.34)	0.004
Tto mtx (15mg/w)	16 (8.9%)	14 (23.3%)	2 (1.7%)	17.9 (3.93-82.12)	<0.001

Table 1 identifies the factors associated with the development of RA. The MLR identified **ACPA +**, **OR (95% CI) = 10.69 (4.43 - 25.78)**, and the **HLA-DRB1 shared epitope OR (95% CI) = 9.18 (2.96 - 28.48)** **p <0.001** as factors associated to the development of AR. We failed to identify factors associated with the use of BT, possibly due to the sample size. The factors associated with the development of CVD, where only the use of glucocorticoids as a factor associated with the presence of CVD shows statistical significance.

Conclusion: 1) Useful clinical and laboratory characteristics have been identified to predict which patients are at risk of developing persistent arthritis. 2) HLADRB1 shared Epitope and ACPA are predictive factors of evolution to RA. 3) Possibly the continued use of glucocorticoids, even at low doses, may be related to the development of long-term CVD

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AB0237

WHAT DO SPANISH RHEUMATOLOGISTS THINK ABOUT THE EFFICACY OF THE DRUGS USED IN THE MANAGEMENT OF PATIENT WITH RHEUMATOID ARTHRITIS AND POOR PROGNOSIS FACTORS? PROGRESAR-2 PROJECT

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Background: Currently, patients with rheumatoid arthritis (RA) have a wide range of treatments available to achieve a good control of the disease and avoid progression. However, some patients, especially those with poor prognostic factors, need to switch drugs to achieve remission or low disease activity. If we can predict the response to a drug, given specific prognostic profiles, we may be able to choose the best drug for individual patients.

Objectives: To assess the degree of confidence of rheumatologists regarding the efficacy of biologic therapies and specific targeted synthetic molecules in patients with RA harbouring poor prognostic factors.

Methods: A Delphi survey was sent to a group of rheumatologists with the aim to capture the perceived efficacy of a group of drugs (antiTNF, T-cell co-stimulants, B-cells depletors, anti IL6, and JAK inhibitors) given different poor prognostic factors are present at the onset of the disease. These factors were: interstitial lung disease, elevated HAQ, positive rheumatoid factor (RF), presence of anti-citrullinated protein antibody (ACPA), elevated acute phase reactants (APR), and bone erosions observed by simple x-ray/ultrasound. The survey was circulated in two rounds, with feed-back from the first round. The degree of confidence in the efficacy of the therapies for each specific prognostic profile was collected on a Likert scale from 1 to 9. The mean (m) and standard deviation (SD) were calculated; agreement was considered if SD ≤1 and 80% of the scores were in one of the three levels (correspondingly it would be agreement on "ineffectiveness", "neutrality" and "effectiveness").

Table 1.:

Prognostic factor	Agreement on the efficacy of therapy m (SD)				
	AntiTNF	T-cell co-stimulants	Depletion of B cells	Anti IL-6	Jak inhibitors
Interstitial Lung Disease	2.5 (1.5)	8.6 (0.7)	7.0 (1.4)	6.2 (1.4)	5.1 (1.6)
High HAQ	8.1 (0.7)	7.4 (1.0)	7.0 (1.0)	8.1 (0.7)	7.9 (0.9)
RF positive	7.7 (0.8)	8.1 (0.6)	8.3 (0.5)	7.8 (0.8)	7.6 (0.8)
ACPA positive	7.8 (0.8)	8.6 (0.5)	8.2 (0.7)	7.5 (0.8)	7.4 (0.7)
Elevated APR	7.9 (0.7)	7.2 (0.7)	7.0 (0.9)	8.7 (0.5)	7.9 (0.9)
Bone erosions by Rx	8.1 (0.8)	7.9 (0.6)	7.3 (0.8)	8.2 (0.5)	7.8 (0.8)
Bone erosions by US	8.2 (0.9)	7.9 (0.7)	7.3 (1.0)	7.9 (0.8)	7.8 (0.8)

Conclusion: There is agreement among rheumatologists regarding the behaviour of particular drugs on particular prognostic profiles, except in the case of interstitial pulmonary involvement, HAQ, ACPA+ and acute

phase reactants, where there may be differences in the perception of efficacy. This perception of efficacy should be contrasted with scientific evidence

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AB0238 14-3-3H AND CALPROTECTIN PROTEINS IN PLASMA AS NEW BIOMARKERS IN EVALUATION OF THE ACTIVITY IN PATIENT WITH RHEUMATOID ARTHRITIS

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Background: The determination of rheumatoid arthritis (RA) activity remains an important clinical task nowadays and it is a long and difficult process. There is no single approach to assess the activity of RA. The gold standard for evaluating RA activity is composite indexes, for example, DAS28. However, composite indices are not reliable in evaluation of the disease activity in patients with RA, as having a subjectivity assessment. New biomarkers that reflect the immune inflammatory process in joints in RA is of great scientific importance. 14-3-3 η and calprotectin markers in plasma are considered as promising.

Objectives: To assess the value of 14-3-3 η and calprotectin in plasma as additional markers in RA activity determination.

Methods: 48 patients were examined with reliable diagnosis of RA, according to the ACR 2010 criteria. The mean age was 59 years, mean duration of the disease was 12.8 years. 4 patients in the group were in remission, 2 had low degree of RA activity, 20 - moderate, 22 - high. RA activity was determined according to the DAS28 ESR index. The concentrations of 14-3-3 η and calprotectin in the blood plasma were determined by ELISA (LLC «SPF «Abris+»). The obtained results were compared with laboratory (ESR, CRP) and clinical (tender joint count (TJC), swollen joint count (SJC), VAS, DAS28) parameters of RA activity.

Results: 14-3-3 η and calprotectin proteins in plasma and ESR highly correlated with DAS28 ($r = 0.84$; $r = 0.65$; $r = 0.53$), while CRP had moderate correlation with RA activity ($r = 0.34$). 14-3-3 η and calprotectin proteins had high correlation with TJC ($r = 0.68$; $r = 0.61$) and moderate correlation with SJC ($r = 0.56$; $r = 0.41$); ESR and CRP had weaker correlation ($r = 0.15$; $r = 0.13$; $r = 0.02$; $r = 0.08$) respectively.

The ROC analysis showed that sensitivity, specificity, and diagnostic accuracy of high RA activity determination are significantly higher for 14-3-3 η (AUC = 0.98, $p < 0.001$) and calprotectin (AUC = 0.89, $p < 0.001$) than for ESR (AUC = 0.81, $p < 0.001$) and CRP (AUC = 0.72, $p < 0.001$). The proteins 14-3-3 η and calprotectin reflect the relationship with the SJC (AUC = 0.89, $p < 0.0001$; AUC = 0.79, $p = 0.002$) with higher diagnostic accuracy, sensitivity and specificity, comparing with ESR (AUC = 0.63, $p = 0.19$) and CRP (AUC = 0.51, $p = 0.88$).

It was also found, that calprotectin (AUC = 0.8, $p < 0.001$) and 14-3-3 η (AUC = 0.79, $p < 0.001$) had greater sensitivity and specificity, as well as diagnostic accuracy, in TJC determination, compared with ESR (AUC = 0.57, $p = 0.4$) and CRP (AUC = 0.52, $p = 0.8$). Determining the relationship between biomarkers and the patient's subjective assessment of RA activity (VAS), significant difference between 14-3-3 η (AUC = 0.68, $p = 0.06$), calprotectin (AUC = 0.63, $p = 0.16$), ESR (AUC = 0.64, $p = 0.14$) and CRP (AUC = 0.56, $p = 0.57$) was not detected.

Conclusion: 14-3-3 η and calprotectin proteins in plasma are new promising biomarkers of immunoinflammatory process in joints in RA

assessment, because they are more sensitive and specific markers of the disease activity, than conventional acute-phase proteins ESR and CRP.

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AB0239 EFFECT OF SMOKING ON THE EFFICACY OF TNF INHIBITORS IN THE TREATMENT OF CHRONIC INFLAMMATORY IMMUNE-MEDIATED DISEASES: SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Chronic inflammatory immune-mediated diseases, as rheumatoid arthritis (RA), psoriatic arthritis (PsA), psoriasis (Ps), ankylosing spondylitis (AS), ulcerative colitis (UC) and Crohn's disease (CD), have higher risks of morbidity and mortality and a great impact on quality of life of patients¹. Drug inhibitors of tumor necrosis factor (TNF inhibitors) have demonstrated an adequate efficacy and security profile in these patients when classical treatments (as disease-modifying antirheumatic drugs) have been failed or patients were intolerant. TNF inhibitors are used to control inflammatory response and to improve quality of life, pain, functional capacity and progression of the disease². Studies in RA show that smoking habit is related to more articular and extra-articular damage, worse prognosis, higher basal activity and higher risk of seropositive RA. It has been related also to greater number of different treatments and higher doses needed for patients by pharmacokinetic and pharmacodynamic processes. Data published until now suggest that smoking habit decreases efficacy of TNF inhibitors³.

Objectives: To analyze the smoking habit influence on the efficacy of TNF inhibitors in patients diagnosed of chronic inflammatory immune-mediated diseases (RA, PsA, Ps, AS, UC, CD).

Methods: It was made a systematic literature search using Cochrane Library, Medline, the Web of Science and Embase databases. Meta-analyses were performed using a random-effects model.

Results: 37 of 3677 identified articles met the inclusion criteria. No documents with GOL were found. The analysis of all the diseases together gives a significant decrease on the response to TNF inhibitors in smoking patients [OR 0.812 (0.662-0.996), $p=0.046$]. This response also has a significant decrease in IBD maintained response in smoking patients [OR 0.467 (0.257-0.848), $p=0.012$]. A non-significant decrease in the treatment response of smoking patients with IBD clinical remission was found, in smoking patients versus ex-smoking and never smoking patients with IBD response, in ex-smoking patients versus never smoking patients with IBD partial response, in current and ex-smoking patients versus never smoking patients with IBD partial response, in current smoking patients versus ex-smoking patients with IBD partial response, in current smoking patients versus never and ex-smoking patients with IBD partial response, in current smoking patients versus never smoking patients with IBD partial response, in patients with AR EULAR and in patients with AR EULAR moderate response.

Conclusion: Smoking habit is a poor prognosis factor in RA, AS, Ps, PsA, UC and CD. Its leaving will decrease cardiovascular risk, joint and bowel damage, will increase the efficacy of TNF inhibitors and will benefit the health of patients, not only in their particular disease, and it can be the first step on their treatment.

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