

Association of positive psychological variables with disease activity, functional disability and erythrocyte sedimentation rate in patients with rheumatoid arthritis: a preliminary study

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SUMMARY

Rheumatoid arthritis (RA) is a chronic autoimmune disease which has shown positive correlations between negative psychological variables and disease activity in transversal studies and in the follow-up. However, the association of positive psychological variables with disease parameters including disease activity (DAS-28), functional disability (HAQ) and erythrocyte sedimentation rate (ESR) has not been investigated. Patients with RA attending the external consultation of a third level hospital were invited to participate and fill in a questionnaire with personal, disease and psychological variables; body mass index was also obtained as well as ESR. A total of 49 patients were included. The three dependent variables correlated among them, with the highest correlation for DAS-28 and HAQ ($r=0.645$, $p<0.01$), followed by somatization and HAQ ($r=0.614$, $p<0.01$) or DAS-28 ($r=0.537$, $p<0.01$). In addition, HAQ showed negative correlations with environmental mastery ($r=-0.366$, $p<0.01$), personal growth ($r=-0.292$, $p<0.05$) and monthly extra money ($r=-0.328$, $p<0.05$), and borderline negative correlations with emotion perception ($r=-0.279$, $p=0.053$) and self-acceptance ($r=-0.250$, $p=0.08$). ESR showed a significant negative correlation with emotion perception ($r=-0.475$, $p<0.01$). In conclusion, we observed important correlations of positive psychological variables with disease activity, functional disability and ESR that could be addressed in order to prevent or treat these disease features.

Key words: Rheumatoid arthritis, disease activity (DAS-28), functional disability (HAQ), ESR.

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INTRODUCTION

Rheumatoid arthritis (RA) is a chronic autoimmune disease that causes inflammation of the joints and surrounding tissues and has a prevalence of 0.2-1.2% (1, 2). To date, some studies have shown a significant association between basal negative psychological variables (anxiety and depression) and disease activity in the follow-up (3, 4), as well as positive associations between psychological distress and disease activity in transversal studies (5).

In addition, the inflammation marker C reactive protein (CRP) has shown significant correlations with depression in transversal studies of RA patients (1, 6). However, the association of positive psychological variables, which means psychological characteristics and/or abilities that are related with a higher psychological wellbeing (*i.e.*, self-acceptance, optimism and emotional intelligence), with disease variables has rarely been reported in RA patients (7). The study of the correlation between these psychological variables and disease activ-

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ity or functional disability could be useful in order to detect which abilities can be increased in preventive or intervention programs. With this respect, we did not find studies researching this association. On the other hand, although some studies have shown a significant negative association between positive effect and CRP in different populations (8-11), no studies evaluating the association of positive psychological variables and inflammation markers (CRP, erythrocyte sedimentation rate (ESR) or interleukins) in RA were identified. Therefore, we decided to perform a research study evaluating the association of a wide number of positive psychological variables with disease activity, functional disability and ESR in a sample of RA patients, in order to determine which psychological factors could be causally related with these disease variables.

Accordingly, we choose a group of positive psychological variables that could be related with disease activity, functional disability and ESR, in addition to three negative psychological variables: depression, anxiety and somatization. In this report, the variable somatization was measured as the sum of 15 different somatic symptoms, which, in the general population, is positively correlated with stress, depression and anxiety (12, 13). The measurement of somatization has neither been investigated in a RA population.

■ PATIENTS AND METHODS

Patients with RA attending the external consultation of rheumatology of a third level public hospital (before the COVID 19 pandemic period) were invited to participate, signed an informed consent and answered a questionnaire with personal, disease and psychological variables. Finally, the body mass index was measured and the ESR, measured within the last 5 days before the consultation, was obtained from medical records.

Personal variables

Among personal variables, age, schooling, presence of a romantic partner, job,

children, monthly extra money excluding necessary expenses, number of daily free hours, weekly hours of physical activity, and frequency of smoking, measured with 6 categories including never, 2-4 times a year, once in the month, 2-3 times in the week, 4 or more times in the week; the presence of 16 different diseases (diabetes, hypertension, overweight, thyroid problems, allergies, asthma, gastritis/gastric ulcer, colitis/irritable colon, migraine, acne, neurodermatitis, sinusitis, kidney/bladder problems, anorexia/bulimia, anxiety and depression problems that require medication); and additional diseases in the last 6 months were all reported.

Disease variables

Among disease variables, time since diagnosis, number of medications, functional disability measured with the Health Assessment Questionnaire (HAQ) (14), and disease activity measured with the DAS-28-CRP, evaluated by a rheumatologist (15), were recorded. The 4-item Morisky medication adherence scale (MMAS-4) (16) was used to assess treatment adherence. Finally, the use of steroids was also documented and analyzed in the bivariate and multivariate analysis.

Psychological variables

We measured somatization with the patient health questionnaire 15 (17); depression with the center for epidemiologic studies depression scale (18) [Spanish version (19)]; anxiety with the generalized anxiety disorder test (20); positive and negative emotions with the positivity-self scale (21), the 6 subscales of the shortened version of psychological well-being scale (self-acceptance, autonomy, environmental mastery, personal growth, positive relations with others and purpose in life) (22); and optimism with the life orientation test (LOT-R) (23). In addition, we measured 5-6 items of 4 subscales of the trait emotional intelligence questionnaire: self-motivation (5 items), emotion perception (5 items), assertiveness (6 items) and emotion regulation (6 items), (these items are described in Supplementary file 1) (24).

Statistical analysis

Descriptive data were presented with means and standard deviations for continuous variables and frequencies and percentages for binary/categorical ones. Associations between continuous variables were assessed with Pearson and Spearman tests for parametric and non-parametric distribution respectively. Finally, a multivariate analysis was carried out with the multiple regression tests, using the stepwise method for the 3 dependent variables (DAS-28, HAQ and ESR). This analysis was performed in order to detect the main variables associated with HAQ, DAS-28 and ESR, adjusting by the other measured variables, in order to identify possible psychological predictors of the three dependent variables, which are considered the main indicators of RA activity and disability. In this sense, the variable somatization was not included in the 3 analyses (because this variable is more a consequence than a predictor of HAQ, DAS-28 and ESR). Likewise, HAQ and DAS-28 were neither included in the analyses of ESR, and HAQ was not included in the analysis of DAS-28 (because these variables are considered a consequence and not a cause of the dependent variables).

All statistical analyses were carried out with the software SPSS v. 25.0 and a $p < 0.05$ was considered as significant.

■ RESULTS

Forty-nine patients with RA were included, most of them were female (93.9%), with a mean age \pm SD of 46.98 \pm 9.5 years. The majority of them had a romantic partner (67.40%), had children (83.70%) and did not have a job (51%). The most common schooling level was high school (Table 1). The main treatments used were azulfidine (87.76%), methotrexate (71.43%), non-steroidal anti-inflammatory drugs (63.27%), chloroquine (24.49%), steroids (24.49%), hydroxychloroquine (4.08%) and anti-depressants (4.08%).

The bivariate analysis showed that DAS-28 was positively correlated with somatization ($r=0.537$, $p < 0.01$), HAQ ($r=0.645$, $p < 0.01$) and ESR ($r=0.340$, $p < 0.05$). HAQ was

positively correlated with DAS-28, somatization ($r=0.614$, $p < 0.01$), ESR ($r=0.309$, $p < 0.05$) and age ($r=0.285$, $p < 0.05$) and negatively correlated with environmental mastery ($r=-0.366$, $p < 0.01$), monthly extra money ($r=-0.328$, $p < 0.05$) and personal growth ($r=-0.292$, $p < 0.05$). A borderline positive correlation was found between HAQ and the number of medications ($r=0.248$, $p=0.085$), and negative borderline correlations were found with emotion perception ($r=-0.279$, $p=0.053$) and self-acceptance ($r=-0.250$, $p=0.08$). ESR was positively correlated with DAS-28 and HAQ and negatively correlated with emotion perception ($r=-0.475$, $p < 0.01$). Borderline negative correlations were found with having a romantic partner ($r=-0.251$, $p=0.09$) and treatment adherence ($r=-0.264$, $p=0.08$) (Table 2); in addition, negative tendencies were observed for assertiveness ($r=-0.238$, $p=0.115$) and anxiety ($r=-0.214$, $p=0.158$) and positive tendencies for positive emotions ($r=0.235$, $p=0.120$) and daily free hours ($r=0.213$, $p=0.159$).

DAS-28 only showed positive correlations with HAQ, ESR and somatization; however, this variable showed a borderline positive correlation with having children ($r=0.260$, $p=0.085$) and weekly physical activity hours ($r=0.258$, $p=0.087$).

In the multivariate analysis for HAQ, the included variables were DAS-28 and depression, as positively correlated variables, and monthly extra money, as negative correlated variable. The multivariate analysis for ESR showed that positive emotions, schooling and having children were positively correlated with ESR while emotion perception and having a romantic partner were negatively correlated with ESR (Table 3). For DAS-28, we only detected a marginal association with sociodemographic, including having children, the sum of diseases and having a romantic partner, the latter being negatively associated.

■ DISCUSSION AND CONCLUSIONS

We could observe that the 3 dependent variables had a positive significant correla-

Table 1 - Descriptive statistics of studied variables.

Variable	All patients (N=49)
Female gender, N (%)	46 (93.9)
Age, mean±SD	46.98±9.5
With children, N (%)	41 (83.7)
With job, N (%)	24 (49.0)
With romantic partner, N (%)	33 (67.4)
Schooling, N (%)	
- Elementary	13 (26.5)
- High school	23 (46.9)
- Preparatory	6 (12.2)
- Bachelor's degree	5 (12.3)
- Master's degree	2 (4.1)
Monthly extra money, mean±SD	1.37±0.57
Daily free hours, median (range)	3 (0-24)
Number of diseases, median (range)	2 (0-6)
BMI mean±SD	26.47±4.00
Weekly physical activity hours, median (range)	3.5 (0-42)
Smoking frequency, median (range)	1 (1-5)
Psychological variables	
Somatization, mean±SD	1.53±0.30
Depression, mean±SD	1.85±0.57
Emotional intelligence, mean±SD	
- Self-motivation	5.10±1.19
- Emotion regulation	4.42±0.89
- Emotion-perception	4.44±1.17
- Assertiveness	4.47±1.12
Psychological wellbeing, mean±SD	
- Self-acceptance	4.75±0.94
- Positive relations with others	4.05±1.12
- Environmental mastery	4.55±0.92
- Personal growth	4.92±0.83
- Purpose in life	4.85±1.05
- Autonomy	4.19±0.95
Positive and negative emotions, mean±SD	
- Positive emotions	3.48±0.59
- Negative emotions	2.43±0.72
Anxiety, mean±SD	2.15±0.69
Optimism, mean±SD	3.60±0.70
Disease variables	
Time since diagnosis in years, median (range)	5 (1-27)
Number of medications, median (range)	5 (2-11)
ESR, mean±SD	33.46±21.85
DAS-28, mean±SD	3.50±1.22
HAQ, mean±SD	0.97±0.72
Treatment adherence (Morisky-Green), median (range)	3 (0-4)

Monthly extra money was measured with 5 ordered categories, from 1=nothing, to 5=more than 150 US dollars. Frequency of smoking was measured from 1=never, to 6=4 or more times in the week, somatization (patient health questionnaire 15) was measured from 1=without disturbance, to 3=much disturbance; depression (center for epidemiologic studies depression scale) was measured from 1=no day, to 4=almost all days; the 4 subscales of emotional intelligence (trait emotional intelligence questionnaire) were measured from 1=totally disagree, to 7=totally agree; the 6 subscales of psychological well-being scale were measured from 1=totally disagree, to 6=totally agree; positive and negative emotions (positivity-self scale), were measured 1 = never to 5 = always; anxiety (generalized anxiety disorder test) was measured from 1=not at all, to 4=almost all the days and optimism (Life Orientation Test) was measured from 1=totally disagree, to 5=totally agree. Adherence was measured from 1=no adherent, to 4=totally adherent.

SD, standard deviation; BMI, body mass index; ESR, erythrocyte sedimentation rate; DAS-28, disease activity; HAQ, functional disability.

tion among them, with DAS-28 and HAQ presenting the highest correlation ($r=0.645$, $p<0.01$), followed by somatization and HAQ ($r=0.614$, $p<0.01$), and somatization and DAS-28 ($r=0.539$, $p<0.01$). This find-

ing is explained by considering that the three variables are related with physical signs and symptoms.

When we analyzed the correlations of these three variables with personal and psycho-

Table II - Correlations of studied variables with disease activity, functional disability and erythrocyte sedimentation rate.

Variable	Disease activity (DAS-28)	Functional disability (HAQ)	Erythrocyte sedimentation rate (ESR)
Age	0.082	0.285*	0.044
With romantic partner (Yes=1, No=0)	-0.147	0.014	-0.251
With children (Yes=1, No=0)	0.260	0.161	0.151
With job (Yes=1, No=0)	0.175	-0.042	-0.021
Schooling	0.001	-0.050	0.153
Monthly extra money	0.028	-0.328*	0.150
Daily free hours	0.036	0.043	0.213
Number of diseases	0.185	0.227	0.037
Body mass index	0.072	0.113	0.167
Weekly physical activity hours	-0.258	-0.109	0.079
Smoking frequency	0.040	0.010	0.004
Somatization	0.537**	0.614**	0.025
Depression	-0.070	0.209	-0.052
Self-motivation	0.069	-0.046	0.057
Emotion regulation	-0.038	-0.028	0.076
Emotion perception	-0.192	-0.279	-0.475**
Assertiveness	-0.073	0.032	-0.238
Self-acceptance	-0.103	-0.250	-0.075
Positive relations with others	0.143	0.066	0.039
Environmental mastery	-0.157	-0.366**	-0.176
Personal growth	-0.105	-0.292*	-0.044
Purpose in life	0.036	-0.229	-0.094
Autonomy	0.004	-0.016	-0.131
Positive emotions	0.088	-0.012	0.235
Negative emotions	-0.104	0.075	-0.129
Anxiety	-0.018	0.190	-0.214
Optimism	-0.091	-0.116	0.020
Number of medications	0.060	0.248	0.177
Time since diagnosis	0.056	-0.106	0.101
Disease activity	-	0.645**	0.340*
Functional disability	0.645**	-	0.309*
Erythrocyte sedimentation rate (ESR)	0.340*	0.309*	-
Treatment adherence	-0.232	-0.078	-0.264
Steroid use	-0.029	-0.049	0.268

Note: p values were obtained with Pearson's and Spearman's correlation tests; * $p<0.05$, ** $p<0.01$.

Table III - Multivariate regression analysis for functional disability and erythrocyte sedimentation rate.

Functional disability (HAQ)				
Variable	Beta	Beta coefficient	p value	Change in R score
Constant	-0.235	-	0.482	-
DAS-28	0.378	0.673	0.000	0.416
Monthly free money	-0.510	-0.425	0.000	0.172
Depression	0.028	0.230	0.020	0.053
Erythrocyte sedimentation rate (ESR)				
Constant	26.973	-	0.105	-
Emotion perception	-2.075	-0.567	0.000	0.135
With romantic partner	-14.576	-0.332	0.007	0.138
With children	19.208	0.338	0.007	0.089
Schooling	7.487	0.388	0.003	0.128
Positive emotions	0.775	0.223	0.063	0.044
DAS-28				
Constant	2.418	-	0.000	-
With children	1.149	0.346	0.023	0.063
Sum of diseases	0.202	0.268	0.069	0.065
With romantic partner	-0.677	-0.264	0.073	0.067

DAS-28, disease activity.

R of the model for HAQ:0.801, R of the model for ESR:0.731, R for DAS-28:0.442.

logical variables, HAQ showed a significant negative correlation with monthly extra money, environmental mastery and personal growth. The negative correlation with monthly extra money could be explained by the effect of additional income in health maintenance and in a higher quality of life, which is also related with better treatments for the disease. The negative correlations with the subscales of psychological wellbeing such as environmental mastery, which is related with a sense of mastery and competence in managing the environment, and with personal growth, which is related with a feeling of continued development (25), as well as the borderline negative correlations with self-acceptance and emotion perception, highlights the importance of these psychological abilities in order to prevent and potentially treat functional disability in RA patients. These findings are interesting, considering that the correlations found overcome that found for depression and anxiety, the most studied psychological variables in RA (1,6).

In the case of ESR we found that the highest negative correlation was for emotion perception, with borderline negative correlations for assertiveness, having a romantic partner and treatment adherence. The negative moderate correlation with emotion perception is a new, interesting finding, that emphasizes the ability to identify the emotions in order to diminish inflammation in these patients, although only longitudinal studies will clarify the possible causal relation of these variables. Nevertheless, it is interesting that this correlation overcomes the one found for treatment adherence; however, treatment adherence showed a higher tendency to be negatively correlated with DAS-28 than emotion perception. These findings suggest an important role of these two variables in diminishing inflammation and disease activity. In the multivariate model for ESR, we observed the expected negative correlation with emotion perception, as well as the unexpected positive correlation with positive emotions, being feeling “inspired” the

positive emotion more correlated with ESR in the bivariate analysis ($r=0.420$, $p<0.01$). This finding suggests that some positive emotions could increase inflammation in patients with inflammatory diseases, which coincides with a previous report in breast cancer survivors, where only low arousal positive affect was associated with lower levels of CRP (9). This is an interesting finding that suggests that in inflammatory diseases like RA, positive affect could present an opposite relationship with inflammatory markers when compared with the general population (8-11). Another interesting finding is the positive tendency of a correlation between ESR and daily free hours ($r=0.213$, $p=0.159$), which coincides with the positive correlation found between somatization and daily free hours ($r=0.361$, $p=0.011$), possibly indicating that daily free hours could have an inflammatory and somatizing effect in RA patients. In the multivariate model for DAS-28, we detected that only socio-demographic variables were marginally included in the model, which coincides with the lack of significant associations in the bivariate analysis, suggesting that psychological variables are less associated with disease activity when compared with socio-demographic or clinical variables. However, studies with larger sample size are needed to determine these associations.

The main limitations of the study are the small sample size that impede to detect low correlations as significant; in addition, only three participants were men, which did not permit us to perform separated analyses by sex; finally, additional variables that could be confounding factors, including sleep quality and stress, were not measured. The measurement of these factors could have modified the interactions between the studied variables in the multivariate analysis. In conclusion, we observed interesting and not previously reported positive and negative correlations between positive psychological variables and disease activity, functional disability and ESR in RA patients. The negative correlations between environmental mastery and personal growth with HAQ, and between emotion perception and

ESR are of particular interest. However, further longitudinal studies with larger sample sizes and with new variables will clarify the influence of these factors in RA patients.

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