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Psychological distress over time in early rheumatoid arthritis: results from a longitudinal study in an early arthritis cohort

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Abstract

Objective. RA is a chronic disease with frequent psychological co-morbidities, of which depression and anxiety are two common manifestations. We aimed to identify predictive factors of psychological distress in a large prospective cohort of very early RA patients.

Methods. ESPOIR (Etude et Suivi des Polyarthrites Indifférenciées Récentes) is a multicentre, longitudinal and prospective cohort study of patients with early arthritis (<6 months disease duration). The study sample comprised 641 patients with very early RA according to the 2010 ACR/European League Against Rheumatism RA criteria from the ESPOIR cohort. Psychological distress was assessed over 3 years by the five-item Mental Health Inventory questionnaire at various time points (baseline, 6, 12, 18, 24 and 36 months). Logistic regression with a generalized estimating equation model was used to analyse the association of disease variables and risk of psychological distress.

Results. At baseline, 46.9% of RA patients were screened as positive for psychological distress. Over 3 years, psychological distress decreased significantly, with a prevalence of 25.8% at 36 months. The HAQ Disability Index (HAQ-DI) score was the most important factor predicting psychological distress over 3 years [odds ratio 2.10 (95% CI 1.41, 3.14)–3.59 (2.29, 5.63)]. Baseline biological and radiological variables and treatment regimens were not associated with distress.

Conclusion. Psychological distress in very early RA is frequent and the HAQ-DI score is a predictor of depression and anxiety in these patients. A psychological evaluation in patients with early RA is important for further individual psychiatric diagnosis and management.

Key words: early rheumatoid arthritis, depression, psychological distress, HAQ.

CLINICAL SCIENCE

Introduction

RA is a frequent chronic inflammatory disease with important impact on joint damage, impaired functional capacities and decreased quality of life [1]. Chronic medical illnesses are consistently associated with increased prevalence of depressive symptoms and disorders, and the risk of depression is increased 2- to 3-fold in patients with established RA [2]. Depression significantly increases the overall burden of illness in patients with RA. In RA, depression contributes its own additional burden and interacts with the disease course. As compared with medical outpatients without depression, those with depressive symptoms or disorders experience decreased quality of life [3]. Depression has also been linked to increased disease-related morbidity and mortality, with an increase in pain levels, functional disability, cardiovascular mortality and medical costs [4–9]. The interaction between depression and RA is considered to be bidirectional. Indeed, the impact of clinical RA on depression has been previously well described in established RA. Wolfe and Hawley [10], in 1993, indicated that ~20% of the variance in depression change scores (Arthritis Impact Measurement Scale

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depression score) was explained by changes in clinical variables, mainly by pain and the HAQ Disability Index (HAQ-DI). The impact of pain and functional impairment have been reported in the literature [11–12], as well as some psychological predictors and coping [11, 13].

The co-occurrence of depression and physical illnesses is important. Consequently, taking psychological distress into consideration is an important issue in the management of RA patients, especially because non-recognition of depression is common in RA [14].

In conjunction with recent concepts of early treatment and a window of opportunity, the management of psychological distress should occur as soon as possible. However, in contrast to established disease, few data are available in early RA and little is known about predictive factors of psychological distress in that population. Only seven studies have been performed in early RA and most of them have limitations. However, they suggested a relationship between pain [15–18], disease activity [15–16, 19] or functional disability [15–17, 19–20] and psychological distress such as depression, mainly with the initial level of depression [20–21] or coping [16, 20]. To detect depression early we need to identify patients at risk of psychological distress to provide further individual psychiatric evaluation and management. In the present study we aimed to evaluate the prevalence of psychological distress in a large cohort of patients with very early RA and to identify baseline predictors of psychological distress.

Methods

Participants

The study sample consisted of 641 patients with early RA according to the 2010 ACR/European League Against Rheumatism (EULAR) RA criteria [22] from the Etude et Suivi des Polyarthrites Indifférenciées Récentes (ESPOIR) cohort. The ESPOIR is a large French multicentre longitudinal and prospective cohort study of 813 patients >18 and <70 years of age with early arthritis (<6 months disease duration) [23]. Recruitment occurred between December 2002 and March 2005 and the follow-up is still ongoing. For the purpose of this study we focussed on the first 3 years. Several databases (clinical, biological and radiographic) were created for various studies. Details of the cohort have been described previously [23]. The ESPOIR cohort study was approved in July 2002 by the ethics committee of Montpellier, France (no. 020307), allowing future clinical projects on the database. All patients gave their signed informed consent before inclusion.

Psychological and clinical assessments

Psychological distress was assessed at baseline and every 6 months during the first 2 years and at 3 years after inclusion. Short screening questionnaires for mental health are useful tools for research and clinical practice. Psychological distress was measured with the five-item Mental Health Inventory (MHI-5) questionnaire, version 1 [24]. The MHI-5 is a brief self-administered questionnaire and includes scales for anxiety and depression. It is a screening tool for identifying depressive and anxiety symptoms but not an instrument for formal diagnosis according to Diagnostic and Statistical Manual of Mental Disorders, 4th edn (DSM-IV) criteria for depression and anxiety [25]. It is part of the mental health subscale of the Medical Outcomes Study 36-item Short Form Health Survey (SF-36) [26]. The instrument contains the following five questions: How much of the time during the last month have you (i-9b) been a very nervous person?, (ii-9f) felt downhearted and blue?, (iii-9d) felt calm and peaceful?, (iv-9c) felt so down in the dumps that nothing could cheer you up?, (v-9h) been a happy person? These items are scored on a 6-point frequency rating scale. After linear conversion, possible scores on the MHI-5 range from 0 to 100, with a lower score representing more psychological distress. The MHI-5 is a well-validated and reliable measure of mental health status and is widely used. Several studies have demonstrated the instrument's good psychometric properties, with high sensitivity, specificity and validity for detecting DSM-IV diagnoses in the general population and in primary care patients [24, 27–29]. An MHI-5 score $\geqslant 52$ indicated minimal psychological distress and <52 major psychological distress (anxiety or depression) in several studies [27], particularly in comorbid conditions. MHI-5, as a part of the SF-36 questionnaire, has been translated into French with validation in a large study [30]. The MHI-5 score has been considered as a dichotomous variable (absence or presence of psychological distress) based on this cut-off of 52.

Potential baseline explanatory variables of psychological distress that were collected in the cohort database [23] were evaluated. Individual characteristics included age, sex, educational level (university, primary or secondary school), occupation according to the French classification of socio-professional (CSP) categories defined by the National Institute of Statistics and Economic Studies [31], marital status, family income (euros per month) and disabled condition for social security. The usual clinical RA measures were recorded: patient and physician global assessment of disease activity on a visual analogue scale (VAS), tender joint count (TJC), swollen joint count (SJC), 28-joint DAS (DAS28) [32] and French validation of the HAQ-DI [33]. ESR and CRP level (<10 mg/l), IgM and IgA RF (ELISA; Menarini, France; positive >9 UI/ml) and ACPA (ELISA; DiaSorin, France; positive >50 U/ml) were performed for all the patients using the same technique in a central laboratory (Bichat, Paris, France).

Radiological outcome was evaluated based on the van der Heijde modified total Sharp score and erosion score [34]. Treatment was also recorded during follow-up: corticosteroid use, synthetic and biologic DMARDs and clinical response according to EULAR criteria [35]. The MHI-5 and HAQ questionnaires were presented in French to the patients.

Statistical analysis

Statistical analysis was carried out in the Institute of Clinical Research in Montpellier I University. The threshold

for psychological status was an MHI-5 score $\leqslant 52$ and >52. Psychological distress was described at baseline and over 3 years. Analysis over time involved the Friedman test.

At each time point from baseline to year 3 we explained the dichotomous variables by covariables linked to the MHI-5 at 15% (with univariate model) using a multivariate logistical unconditional model (models 1–6 according each time analysis, at inclusion = model 1, at month 6 = model 2, at month 12 = model 3, at month 18 = model 4, at month 24 = model 5, at month 36 = model 6).

To synthesize the results over time, we used a generalized estimating equation (GEE) model (with autoregressive correlation matrix) with a logit link function. The level of significance was chosen as 5%.

Results

Patient characteristics and missing data

Of the 813 patients with early arthritis in the ESPOIR cohort, 641 (78.8%) met the 2010 ACR/EULAR criteria for RA. Mean disease duration since the first synovitis symptom was 3.4 months. Table 1 shows the patient characteristics of 641 patients. Over 3 years, 12% of the data were missing. At 3 years, complete data were available for 504 patients (78.6% of the initial sample).

Prevalence of psychological distress at baseline and over 3 years

Psychological distress was common in our cohort, with a prevalence of 46.9% at baseline (MHI-5 score <52; Fig. 1); 18.3% of patients maintained this high score after 3 years. The prevalence decreased over time according to the Friedman test ($P < 0.0001$), but 25.8% of patients still experienced psychological distress at 3 years; 7.5% of the patients were new onset. The decrease in prevalence occurred mainly at month 6 (32.6%).

Association of explanatory variables and psychological distress

We examined the concurrent association of explanatory variables and psychological distress at inclusion and at each visit using multilevel regression analysis. Six models were developed and are presented in supplementary Tables S1–S6, available at *Rheumatology* Online. Female sex was associated with psychological distress at inclusion and at 36 months ($P = 0.027$ and 0.028). The HAQ score was the most important variable associated with risk of psychological distress, with consistency over the models [odds ratio (OR) 2.10 (95% CI 1.41, 3.14)–3.59 (2.29, 5.63); $P = 0.0003$ to <0.0001; Table 2). Progression of the total modified Sharp score was associated with risk of psychological distress at 1 and 2 years ($P = 0.0272$ and 0.0457). The DAS28 with CRP (DAS28-CRP) was only significantly associated at 3 years ($P < 0.0001$), which may reflect the impact of treatment. Other variables that were significantly associated with psychological distress in some models included educational level, occupation, family income, TJC, patient global score and death of a relative. Neither biological variables nor treatment regimens were significantly associated with psychological distress at any time point.

Variables at each time point predictive of psychological distress (GEE model)

On GEE analysis, significant variables predicting psychological distress included female sex ($P = 0.0237$), low educational level ($P = 0.0125$) and occupation according to the CSP ($P = 0.0196$), high (>median) patient and physician global assessment of disease activity and poor functional status (HAQ-DI). The risk of psychological distress increased with increasing HAQ score [OR 2.23 (95% CI 1.81–2.75); Table 3]. Biological variables (inflammatory parameters or immunological status), radiological scores and treatment options were not associated with risk of psychological distress.

When we performed a sensitivity analysis by transforming continuous DAS28-CRP and HAQ scores into dichotomous variables the results were very similar, but DAS28 low disease activity ($\leqslant 3.2$) was also protective for risk of psychological distress, which was increased during the first year after diagnosis (data not shown).

Discussion

In this large cohort of patients with very early RA we found that many patients show psychological distress at baseline (46.9%) and over the first year after diagnosis. The prevalence of psychological distress decreases over time, mainly the first year after diagnosis, with a rate of 25.8% at 36 months. The HAQ-DI was the most important variable associated with psychological distress over 3 years. Baseline factors predicting risk of psychological distress included female sex, low educational level, family income, employee occupational status, high disease activity and poor functional status (high HAQ score).

The prevalence of psychological distress and depression varies widely in the literature depending on the definition and psychometric tools used (psychiatric diagnosis or self-questionnaire). However, in most studies of established RA, the prevalence of depressive disorder ranges between 13% and 20%, rates that are two to three times higher than in the general population [36]. Recently a report indicated that the respective prevalence may be as high as 50% in developing country populations [37]. In early RA or early inflammatory arthritis only a limited number of studies have evaluated psychological distress, and most of those studies were cross-sectional or with quite small sample sizes [15–21]. Nevertheless, our data are consistent with the recent report by Overman *et al*. [15], where psychological distress was common: 45% of the depressed mood scores reflected distress at baseline (anxiety and depressed mood scales of the Impact of Rheumatic Diseases on General Health and Lifestyle questionnaire). This prevalence is also consistent with the reported rates of 36% and 35.9% from two other early arthritis studies, both using a self-questionnaire for psychological assessment [Center for Epidemiologic Studies–Depression (CES-D) scale] [18]. The risk was

Table 1 Baseline characteristics of 641 patients with RA

Demographic or socio-economic variable	Value	Number of patients
Age, mean (S.D.), years	48.5 (12.20)	641
Female, *n*		641
Educational level, *n* (%)	499 (77.85)	641
Primary school	79 (12.32)	
Secondary school	367 (57.25)	
University	195 (30.42)	
Occupation, *n* (%)		641
Unemployed	26 (4.06)	
Working class	65 (10.14)	
Employee	306 (47.74)	
Farmer	23 (3.59)	
Artisan, craft	38 (3.59)	
Intermediate profession	98 (15.29)	
Liberal profession, senior executive	85 (13.26)	
Marital status, *n* (%)		641
Single	91 (14.20)	
Married	396 (61.78)	
Cohabitating	69 (10.76)	
Divorced	60 (9.36)	
Widowed	25 (3.90)	
Family income per month, *n* (%)		617
<€610	25 (3.89)	
€610–1220	102 (15.88)	
€1220–1830	147 (23.01)	
€1830–2440	126 (19.61)	
€2440–2745	57 (8.91)	
€2745	184 (28.69)	
Disabled condition		641
Positive	14 (2.18)	
RA status		
Disease activity, mean (S.D.)		
Patient VAS	62 (24.6)	639
Physician VAS	54.06 (21.6)	638
TJC	9.85 (7.2)	641
SJC	8.19 (5.5)	641
DAS28-CRP	4.98 (1.2)	639
Functional status, mean (S.D.)		
HAQ score	1.05 (0.7)	641
Inflammatory variables, mean (S.D.)		
ESR	30.38 (24.8)	631
CRP, mg/l	20.90 (33.0)	641
Immunological status, mean (S.D.)		
RF	367 (57.2)	641
ACPA	313 (48.8)	641
Radiographic status, *n* (%)		
Erosion	110 (17.16)	641
Total van der Heijde modified Sharp score, mean (S.D.)	5.29 (7.5)	641

DAS28-CRP: 28-joint DAS with CRP; SJC: swollen joint count; TJC: tender joint count; VAS; visual analogue scale.

higher during the first year after diagnosis. In the Overman *et al*. study [15], close results were observed, with prevalence significantly higher in the first year, but time was not included in the multiple regression analysis.

The significant demographic and socio-economic factors associated with psychological distress in our study agreed with the mean risk factors observed in depression disorders in the general population and include female sex, low educational level (primary school), some professions (employee category) and low family income. In a worldwide health report, the prevalence of depression was higher in women than men [38]. As previously reported in the literature, age was not associated with increased risk of depression. Low socio-economic

FIG. 1 Percentage of patients testing positive for psychological distress (Mental Health Inventory 5 score <52/100) over 3 years

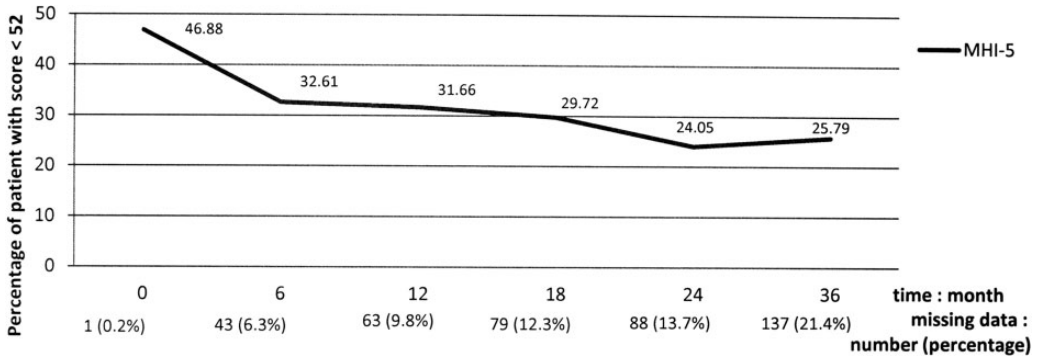

TABLE 2 Association between HAQ score over time (at each visit) and psychological distress in RA by multilevel regression analysis

HAQ variable	OR	95% CI	Incomplete medical report, *n* (%)	*P*-value
Model 1: at baseline	2.20	1.65, 2.92	29 (4.52)	<0.0001
Model 2: at 6 months	3.32	2.26, 4.86	72 (11.23)	<0.0001
Model 3: at 12 months	2.10	1.41, 3.14	135 (21.06	0.0003
Model 4: at 18 months	3.53	2.36, 5.27	128 (19.97	<0.0001
Model 5: at 24 months	3.59	2.29, 5.63	166 (25.90	0.0003
Model 6: at 36 months	2.50	1.52, 4.10	173 (26.99	0.0003

The six models are presented in supplementary Tables S1–S6, available at *Rheumatology* Online. HAQ co-variable linked to MHI-5 in a multivariate logistical unconditional model at each time point (model 1 = baseline, model 2 = month 6, model 3 = month 12, model 4 = month 18, model 5 = month 24 and model 6 = month 36). MHI-5: five-item Mental Health Inventory; OR: odds ratio.

status is a risk factor for depression in the general population by a variety of outcome measures [38, 39]. Very low family income (<€610/month) was not associated, but we observed a trend of association with low family income, and the small sample size in this group could explain this result. In RA, data are available in the literature only for established disease, with low educational level associated with depression in one study [40]. Female sex is a consistently associated variable and a risk factor for depression [41]. However, depression risk is also associated with co-morbid conditions such as cardiovascular diseases [42]. We found no association of marital status and psychological distress, perhaps because its association with depression is more complex, as is seen in the psychiatric literature. Other important variables include coping mechanisms [16], social support [43] and stress [11]. Thus psychological variables are also important in assessing the risk of depression in RA.

For specific disease criteria, high disease activity and poor functional status were significantly associated with risk of psychological distress in RA patients. Intensity of pain and functional impairment (HAQ-DI) have been associated with anxiety [10, 11, 43]. The HAQ was the most reliable variable predicting risk of psychological distress in our study, with consistency over time. In established RA, the HAQ score is also one of the most important factors associated with depression and psychological distress [11, 44]. HAQ disability has also been associated with depression in some studies of early RA [17, 20, 21]. However, our study is the first in early RA to show an association with risk of psychological distress over time. Our study investigated both single clinical parameters and global assessment of disease activity and showed that only subjective components of the DAS28 explain the increased risk of psychological distress. TJC and pain on a VAS were also associated, but only at some time point, and were not selected as baseline predictive factors. In early RA, a link between subjective clinical parameters such as pain intensity [17, 20, 21] or global composite criteria such as the DAS28 [16] and psychological distress has also been reported. In contrast, in the Overman *et al*. study [15], only the global activity score (Thompson articular index, a weighted score including both swollen and painful joints) in the clinical assessment of disease activity was evaluated. We found no synovitis or inflammatory markers associated with risk of psychological distress, as was reported previously [17]. Nor did we find any association of immunological status and

Table 3 Predictive baseline variables of psychological distress in early RA (Generalized Estimating Equation model)

Significant predictive variable	β	OR	95% CI	*P*-value
Female sex	0.41	1.51	1.06, 2.17	0.0237
Primary school	0.67	1.96	1.16, 3.32	0.0125
Occupation	0.48	1.62	1.08, 2.43	0.0196
High patient VAS score[a] >32	0.41	1.51	1.18, 1.92	0.0009
High physician VAS score[a] >23	0.28	1.33	1.05, 1.67	0.0158
HAQ score	0.80	2.23	1.81, 2.75	<0.0001

[a]High patient and physician global assessment of disease activity on a VAS > median. VAS: visual analogue scale.

baseline radiographic damage, perhaps because the early stage of disease has few consequences on joint damage. The literature contains no evaluation of the impact of immunological or radiological status on psychological distress.

Coping seems to be an important factor in psychological status. Ramjeet *et al*. [18] revealed that 39% and 38% of a range of depression scores (CES-D) and anxiety scores (State-Trait Anxiety Inventory), respectively, were explained by coping mechanisms.

The major strengths of our study are its longitudinal design and recruitment of a large number of patients with very early RA (3.4 months disease duration) as compared with other studies. Our sample is representative of patients in daily practice newly diagnosed with arthritis. Our database allowed us to investigate the relationship and the predictive value of psychological distress with a large and varied set of variables, including demographic and socio-economic factors; subjective and objective clinical evaluations; radiographic, biological and immunological factors and treatments.

However, some limitations include the assessment of psychological distress with a well-validated screening tool for depressive and anxiety disorders, but without diagnostic criteria or psychiatric medical history. However, our objective was not to make a psychiatric diagnosis of depression or anxiety but to detect patients at risk of psychological distress for further individual psychiatric evaluation and management. Also, we could not examine the role of personality characteristics, coping mechanisms and social support.

In conclusion, our results confirm that psychological distress, screened mainly for depression and anxiety, is common in patients with early RA. Psychological distress is associated and is predicted by some sociodemographic and disease-specific clinical variables such as subjective components of the DAS28 and especially functional status (HAQ-DI). The HAQ-DI was shown to be associated with other disease burdens in RA [45, 46]. Psychological evaluation should be an important part of RA care because of its major impact on disease course and burden.

Rheumatology key messages

- This study highlights the importance of psychological distress in early RA, which should be considered in disease management.
- HAQ disability is the major factor linked to psychological distress in early RA.
- This study identified predictive factors of psychological distress in a large early RA cohort.

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Supplementary data

Supplementary data are available at *Rheumatology* Online.

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