Depression in Rheumatoid Arthritis

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Abstract. **Operationalized diagnostic criteria for depression were used to assess 137 (76% male, 24% female) patients with rheumatoid arthritis (RA). Forty-two percent met criteria for some form of depression. Discriminant function analysis revealed a significant relationship between the presence or history of depression and higher levels of pain, but not between current depression and common indicators of RA activity or severity. These results suggest that depression is a frequent disorder among persons with RA. The importance of patient appraisal of disease and assessment of repeated depressive episodes is discussed. Attention to specific interventions for depression in conjunction with the treatment of the RA is suggested. (*J Rheumatol 1988;***15:920–925)**

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DEPRESSION PAIN RHEUMATOID ARTHRITIS

Depression[1–4] and depressive symptoms[5] have been shown to be common in persons with rheumatoid arthritis (RA). The use of operational criteria that specify the "necessary and sufficient" grounds for a depressive diagnosis has increased sensitivity and specificity for the diagnosis of depression[6]. The diagnostic criteria for a major depressive disorder (MDD) require the presence, for more than 2 weeks, of hopelessness, depressed mood, loss of interest, and the daily presence of at least 4 of the following symptoms: change in weight or appetite, sleep disturbance, psychomotor agitation or retardation, loss of interest in usual activities or decrease in sexual drive, loss of energy, feelings of worthlessness, diminished concentration, or suicidal ideation. Dysthymic disorder (DD), the other primary category of depressive disorders, is a less severe, chronic form of depression (symptoms must be present for at least 2 years). Thus, a diagnosis of depression can be obtained only when depressive symptomatology are present in several systems (i.e., mood, cognition, somatic functioning).

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To date, only one study[7] has applied operationalized criteria to the diagnosis of depression in RA. Hudson and his colleagues[7] administered the Diagnostic Interview Schedule to 14 outpatients with RA. None of the 14 patients evaluated in the study met the criteria for MDD although 2 (14%) of the patients had a history of MDD. The authors did not report the prevalence of dysthymia in their sample.

Rimon and his colleagues[2] followed a sample of 100 patients with RA for 15 years. Using unstructured psychiatric interviews, they found that 20% of the sample were depressed and that 8% of the sample had recurrent depressions over the 15-year period. Research Diagnostic Criteria (RDC)[8], which are similar to DSM-III criteria, have been used to diagnose depression in chronic pain patients. Lindsay and Wyckoff[9] reported that 87% of a sample of 300 pain clinic patients met the RDC for depression. However, it is not clear whether this figure included only major depressions or also included minor depression.

Researchers who did not use operationalized criteria[1–3] or RDC[9] in patients with chronic pain have found much higher rates of MDD. It is unclear if previous reports have greatly overestimated depression in RA or if applying operationalized criteria, as used in DSM-III, demonstrates that while depressive symptoms are common in RA, true depressive disorders are not. Moreover, little attention has been directed to the presence of DD. Our study applied DSM-III diagnostic criteria for depressive disorders to a large sample of persons with classic or definite RA. Evaluation of depression in a disease such as RA that frequently includes significant pain would be inadequate without attempting some understanding of the interrelationship of depression and pain. To that end, our study also examined the relationship between ratings of pain and disease activity measures and the presence of both current depressive symptoms and history of depressive disorders.

MATERIALS AND METHODS

Subjects. The subjects of this study were 137 patients with definite or classic RA from 2 outpatient rheumatology clinic populations (H.S. Truman Memorial Veterans Hospital and University of Missouri Hospital and Clinics). All patients receiving care in these clinics between August, 1984 and February, 1986 who met ARA criteria for definite or classic RA and who did not have dementia, psychosis, major communicative disorder, major cardiovascular disease, or any other major contraindicating problem were solicited for study participation. The presence or absence of depressive symptomatology was not considered in subject selection.

Ninety-eight percent of the patients were Caucasian. Mean duration of disease was 134.8 months (SD = 111.0, range 8 - 567.7 months). The total sample consisted of 104 males and 33 females (Table 1). The university sample tended to be younger ($p < 0.04$) and had significantly more female subjects ($\chi^2 = 9.92$, df = 1, N = 137, $p < 0.001$) and higher levels of education ($p < 0.005$). The 2 sample populations were comparable in disease variables, including type of disease onset, disease duration, anatomic stage, and functional class.

Procedure. All subjects were interviewed using the portion of the National Institute of Mental Health Diagnostic Interview Schedule (DIS)[11] pertaining to MDD, single episode, and dysthymia[6]. Additional questions, assessing history of depressive disorders, were added to the DIS for this study. Before beginning the study, 3 interviewers were trained to administer and rate the DIS. Interrater agreement on diagnoses was high (98.9% for MDD, 100% for past MDD, 83% for DD, and 94% across all diagnoses).

After obtaining informed consent, subjects were administered the abbreviated DIS, a pain assessment questionnaire including the McGill Pain Questionnaire (MPQ)[12], a visual analog (pain) scale (VAS)[13], and a pain questionnaire derived from one used in a reported study[14]. Subjects rated their pain and mood on 7 likert scales anchored with opposite descriptors at each end of a continuum (e.g., totally satisfied vs totally dissatisfied) addressing variables such as satisfaction with current life situation, physical activity, self-esteem, changes in "nerves" because of pain, perception about the future, mood, and degree of social isolation. The items rating mood, isolation, and nerves were highly correlated with the depressive diagnosis and therefore were excluded from analysis. Each subject also provided demographic and medical history data. A clinical nurse practitioner with extensive experience in rheumatology examined each subject and assessed the extent and activity of his or her RA by objective evaluation of joints (including joint circumference), grip strength (using a dynamometer), walking time, and gait. Erythrocyte sedimentation rates (ESR) were performed on blood from each subject using the Westergren method[15]. Subjects were assessed within the same 4-h period during each visit.

Data analysis. Comparisons between disorders on discontinuous data (sex, race, anatomic stage) were made using nonparametric procedures (Wilcoxon 2-sample test, χ^2, Fisher's exact test, or Kruskal-Wallis test[16]). One-way ANOVA were performed to compare diagnostic and nondepressed groups on continuous variables (joint circumference, pain ratings). *Post hoc* analyses were performed with the Waller-Duncan K-ratio[17] test, which applies more conservative criteria for decreasing F-ratios. To examine the relationships between diagnoses of depression and other disease related characteristics of patients with RA, discriminant function analyses[18-20] were performed, which employed demographic, disease course and pain variables to predict current and recurrent depression.

Two criterion variables were developed from the DIS for use in the discriminant function analyses[20]. The first criterion variable ("current depression") categorized subjects into 2 groups. Group membership was determined by the presence or absence of depressive disorder at the time of admission to the study (Group 1 = not currently depressed; Group 2 = currently depressed). Depression was defined as a diagnosis of MDD and/or DD. The second criterion variable used in the discriminant function analyses ("current or past depression") also categorized subjects into 2 groups. Group membership was determined by absence of both current depression and history of depression (Group 1) or presence of either history of depression or current depression (Group 2). Depression was again defined as a diagnosis of MDD and/or DD.

Twenty predictor variables were used for both discriminant function analyses including: ESR, disease stage and duration, functional class, total number of swollen joints and total joint count (derived from the joint exam), demographic variables including age, education, and socioeconomic status[10], pain measures from the MPQ including number of words chosen and the body area affected by the numbness, aching, pin-like, burning, and stabbing pain sensations, and rating on the VAS.

Table 1. *Characteristics of study patients with rheumatoid arthritis*

	Combined Sample	VA Hospital Sample	University Hospital Sample
Total n	137	95	42
Males	104	94	10
Females	33	1	32*
Mean age (yr)	58.3 (SD=9.6)	59.8 (SD=7.8)	54.8 (SD=12.0)
Mean (yr) education	11.0 (SD=2.7)	10.5 (SD=2.9)	12.02 (SD=2.7)
Males	10.7 (SD=2.9)	10.5 (SD=2.8)	12.4 (SD=2.2)
Females	11.9 (SD=2.2)	9.0	12.0 (SD=2.2)
Index of Social Position (Occupation × Education)**[10]			
II Males	5	4	1
Females	3	0	3
III Males	21	20	1
Females	8	0	8
IV Males	51	48	3
Females	12	0	12
V Males	10	10	0
Females	2	1	1

* Group differences significant at $p < 0.01$

** Social position classification was unavailable for 24 subjects.

RESULTS

Prevalence of depressive diagnosis and symptoms. Overall, 42.3% of the sample met criteria for MDD or DD. Twenty-three of the subjects (17.0%) met criteria for a MDD, while 55 subjects (40.7%) met criteria for DD. Significantly more females than males (34.4 and 11.7%, respectively) met criteria for MDD ($\chi^2 = 8.92$, $p < 0.003$). Prevalence rate for DD was 46% for females and 38% for males. The diagnostic criteria for MDD and DD are not mutually exclusive and 20 (14.6%) met criteria for both MDD and DD (double depression)[21]. Significantly more females than males (31.3 and 9.7%, respectively) met criteria for double depression ($\chi^2 = 8.98$, $p < 0.003$). Slightly more than half the subjects, 73, (53.3%) were not depressed. Prevalence rates for depression (MDD or DD) did not differ between the university and VA sample (42.1% for VA, 43.9% for UMCHC).

Subjects with MDD or DD did not differ significantly from subjects who did not meet criteria for either diagnosis with regard to age, socioeconomic status, disease duration, education level, sex, anatomic stage, functional class, race, type of disease onset, or disease course. Patients with histories of MDD did not differ significantly from subjects without histories of MDD on any variables.

Pain and disease activity correlates of depression diagnosis. All depressed patients, regardless of specific depression diagnosis, reported significantly more pain than nondepressed patients (Table 2). As would be predicted, currently depressed patients reported significantly more pain than either nondepressed patients or subjects who had been depressed in the past. Specifically, currently depressed subjects gave significantly higher ratings even for "pain at its least" than patients who had histories of depression. Patients with MDD reported significantly more pain by VAS than nondepressed patients or those with other types of depression. Similarly, using the Present Pain Intensity measure derived from the MPQ, currently depressed patients indicated greater pain intensity than subjects with histories of depression. Finally, using the Number of Words Chosen on the MPQ (generally thought to be one of the best measures of overall levels of pain), all subjects with depression or histories of depression chose significantly more words on a pain adjective checklist than nondepressed subjects.

Only 2 objective measures of RA disease extent or severity differed significantly with depression. The 6 patients with a history of depression had higher mean ESR ($p < 0.05$) and paradoxically, smaller mean joint size ($p < 0.05$) than currently depressed or nondepressed subjects (Table 3). When analyzed separately by gender, these group differences were not significant.

The discriminant analysis which used "current or past depression" as the criterion variable (Table 4) resulted in the identification of 4 variables that made significant ($p < 0.05$) contributions to the predictive equation: number of words chosen, ESR, percent of body marked "numb" on the body map, and satisfaction with current life situation. Together, these variables accounted for 19% of the variance and produced a correct classification rate of 66.4% which significantly exceeded the chance rate of classification ($z = 3.53$, $p < 0.01$)[15].

In contrast, none of the disease activity variables emerged as significant predictors in the discriminant analysis using "current depression" as the criterion variable. The pain variable, number of words chosen, which accounted for 8% of the variance, resulted in the correct classification of current depression for 64% of the patients, but this rate of classification did not significantly exceed chance at the 0.05 level ($z = 1.37$, $p > 0.05$)[16].

Table 2. *Mean ratings of pain variables by depression diagnosis*†

Variables	Diagnosis				
	MDD	DD	Past MDD	MDD or DD	Nondepressed
Average pain (0–5 scale)	3.1**	3.1***	3.2**	3.1***	2.4
Pain now	2.6**	2.4*	2.4	2.4**	1.8
Pain at least	1.5**	1.4*	1.3	1.3*	1.0
Pain at worst	4.5**	4.6***	4.6*	4.5***	3.8
VAS (10 cm)	4.6**	4.3	4.7	4.3	3.4
MPQ					
Present pain intensity	2.6**	2.4*	2.4	2.4**	1.8
Number words chosen	11.5**	11.6**	12.9***	10.9***	7.9

† One-way ANOVA performed to compare diagnostic groups to nondepressed group

* Significant at $p < 0.05$

** Significant at $p < 0.01$

*** Significant at $p < 0.001$

Table 3. *Mean scores on measures of RA activity by depression diagnosis*

	Depression Diagnosis								
	Group 1			Group 2			Group 3		
	Currently Depressed‡			History of Depression††			No Depression		
	Total (n=58)	Male (n=42)	Female (n=16)	Total (n=6)	Male (n=3)	Female (n=3)	Total (n=73)	Male (n=59)	Female (n=14)
Joint Circumference									
Right index	2.6	2.7	2.3	2.5*	2.9	2.2	2.7	2.7	2.4†
Right little	2.3	2.3	1.9	2.1*	2.5	1.9	2.3	2.4	1.9
Left index	2.6	2.6	2.2	2.4*	2.9	2.2	2.7	2.7	2.4†
Left little	2.2	2.2	1.8	2.0**	2.4	1.8	2.3	2.3	2.0
Measures									
ESR	30.6	27.2	45.9	40.7**	52.0	21.5	22.9	22.7	31.7
Total joint score#	25.7	26.5	30.8	22.0	31.3	14.0	25.9	25.3	22.7
50′ walk time (sec)	13.7	13.2	17.0	14.5	10.0	10.2	13.0	12.3	11.2
Right hand grip strength (mm Hg)	18.2	19.5	11.2	14.0	19.2	12.8	20.7	22.7	8.8
Morning stiffness (h)	1.4	1.2	2.1	1.7	1.3	0.8	1.3	1.2	2.2

* Groups differ $p<0.05$, post hoc analysis indicated Group 2 differed significantly from Groups 1 and 3

**Groups differ $p<0.05$, post hoc analysis indicated Group 2 differed significantly from Group 3

†Groups differ $p<0.05$, post hoc analysis indicated Group 3 females differed significantly from Groups 1 and 2 females

‡Includes all currently depressed (MDD or DD) subjects and takes precedence over history of MDD

††Past history of major depressive episode but not currently depressed

#Total number painful, tender, swollen joints

Table 4. *Variables predicting current or past depression (discriminant function equation)*

Order of Entry	Variable	Cumulative Variance Accounted For	F Value (df)
1	Number words chosen (MPQ)	0.09	9.70 (1, 93)
2	ESR	0.13	7.08 (2, 92)
3	Numbness (MPQ)	0.16	5.73 (3, 91)
4	Satisfaction with current lifestyle	0.19	5.20 (4, 90)

DISCUSSION

Using a structured interview with operational criteria, 42% of this sample of outpatients with RA met criteria for a depressive disorder. Most patients with RA exhibiting depression met criteria for DD (41%); however, many (17%) met criteria for MDD. The overall rate of depressive disorders noted in this sample was similar to that reported by Rimon and his colleagues[2] who used unstructured interviews to obtain their data. These researchers did not differentiate between MDD and DD.

Several unique characteristics of our sample warrant caution in the generalization of our results to the general population of persons with RA. Our sample, unlike the general population of persons with RA, had more males than females. In addition, our sample was skewed toward lower educational achievement and lower income levels.

The depression rate found in our sample exceeds depression rates in community samples (5.6%)[22], but approximates the rate found in other types of serious chronic illnesses (e.g., 44% in a spinal cord injured sample[23]; 35% in an amputee sample[24]). Studies of medical in- and outpatients have yielded variable estimates of depression ranging from 12 – 56% in primary care outpatients and 20 – 24% of medical inpatients reporting at least some symptoms of depres-

sion[25]. Self-report measures have produced lower rates[26]. The high level of depression found in this sample of patients with RA emphasizes the importance of assessment for depression in persons with RA and the need to develop appropriate treatment regimens for depression associated with RA.

Several factors may have affected the prevalence of depressive disorders in our sample. It can be argued that the rate of depressive disorders reported in our study may underestimate the true prevalence because our sample included more males than females. Females have been shown to have a higher rate of depressive disorders[27]. Alternatively, it can be argued that our reliance upon DSM-III criteria inflated the level of depressive disorders because several symptoms of depression and RA overlap. In DSM-III, fatigue and insomnia are used as criteria for depression yet both symptoms are also hallmarks of RA. Newer criteria, recently published in DSM-IIIR[28], have narrowed the criteria for somatic symptoms of depression, requiring that symptoms be distinct from any accompanying illness. Also, in contrast to DSM-III, in order to meet the DSM-IIIR criteria for MDD, a person's daily functioning must be impaired. Although it is not possible to reclassify our patients using DSM-IIIR criteria, 80% of our subjects positively endorsed insomnia and/or fatigue items; 21% of this group met criteria for MDD. Thus endorsement of symptoms common to RA and depression may have inflated our estimate of depression. If these criteria had been applied to our sample the prevalence of MDD would have been lower.

Our results differ substantially from Hudson, *et al*[7] who administered the DIS to a small group of outpatients with RA and found no current cases of major depression. There were several limitations in this study which may account for the difference in outcome. Hudson, *et al* used a small sample recruited from the practice of a participating rheumatologist. It is possible that a selection factor operated resulting in the choice of the 14 subjects who were less impaired and more tractable — in short, less depressed. Further, the sample may not have been representative due to its small size. Although Hudson, *et al* reported using an interviewer who was blind to the patient's diagnosis, it was noted that obvious joint deformities in 3 (21%) of the subjects alerted the interviewer to the rheumatic diagnosis. Raters in our study were not blind to rheumatic diagnosis and consequently may have been biased in their ratings. It is possible that raters may have been aware of the hypothesis as the interview has high face validity. The frequent assessment of interrater reliability in our study suggests that rater bias is an unlikely explanation for the differences. The size of our sample, the concurrence of depression rates with other chronic conditions, and the concurrence with earlier estimates of depression in RA suggest that the levels of depression found in our study are valid.

The discriminant function analyses revealed that the best predictor of depression diagnosis was the number of words chosen from the pain adjective checklist on the MPQ, ESR, the use of numbness in the description of RA pain, and satisfaction with current lifestyle. These 4 variables accounted for only 20% of variance leaving the largest portion of the variance unexplained. Nonetheless, this finding suggests elaborate descriptions of pain or dissatisfaction may serve as a cue or "red flag" indicating the need for a thorough assessment of depression. It is interesting that the 4 variables predicting depression represent 3 distinct domains: pain, disease activity, and current satisfaction. The correlation of variables from different domains with depression supports earlier work indicating that depression is an end product resulting from a number of vulnerability factors including early experiences, biological factors, level and perception of life stress, and perceived resources[29]. An additional, well established vulnerability factor for persons with chronic illness is the depletion of social resources which may lead to divorce and financial difficulties[4]. Clinicians should recognize that depression is predicted by the patient's appraisal of his or her disease, including pain and satisfaction.

Our results indicate the existence of a small group of persons with RA who have a history of depressive episodes. Exclusion of currently depressed persons from this group undoubtedly resulted in a low estimate of the number of subjects experiencing recurrent depressions. A similar group was reported by Rimon and Laakso[2]. Our methodology prevents determination of depression before the existence of RA. Further examination of this subgroup is needed to explore the boundaries of the relationship between recurrent depression and RA.

In a relevant study examining pain, mood and disease activity, Moldofsky and Chester[30] found 2 distinct pain-mood patterns associated with RA activity in 16 randomly selected patients. Half the patients exhibited a synchronous pain-mood association wherein mood changes were associated with increased pain. In the other half, a paradoxical or inverse relationship between intensity of mood disturbance and measured pain was found. These patients reported more confidence during RA flares and were pessimistic and hopeless when their disease was less active. Moldofsky and Chester did not assess depression; our findings suggest that their paradoxical group, which was characterized by pessimism, hopelessness and rigidity, may have been composed of persons prone to repeated depressive episodes or dysthymia.

In summary, 42% of a large outpatient sample of patients with classic or definite RA were found to be depressed, meeting criteria for either MDD or DD. The majority of depressed subjects were dysthymic, showing chronic depressions. Four variables were found that predicted depression although the amount of variance predicted was moderate. Although the population studied does not reflect a representative sample of patients with RA, the high prevalence of depression among this sample indicates the need for further evaluation of depression in RA using a sample with more female subjects and applying operational criteria from DSM-IIIR.

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