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Depression: a common comorbidity in women with rheumatoid arthritis—results from an Austrian cross-sectional study

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ABSTRACT

Objectives Previous research showed that depression is common in rheumatoid arthritis (RA). However, the prevalence very much depends on different assessment tools and sociocultural differences, respectively. The main study aim and research question was to investigate the proportion of depressive symptoms in Austrian female patients with RA.

Setting A nationwide multicentre study with seven secondary care centres all over Austria (hospital-based rheumatological outpatient clinics and private practices).

Participants 319 patients with RA and 306 healthy controls (HCO), all female Caucasians, were asked to complete a Beck's Depression Inventory–Fast Screen (BDI-FS). Patients and HCO were ≥18 years. Patients had to fulfil the 2010 classification criteria for RA. In addition, disease activity, disability, medication, drinking of alcoholic beverages, smoking and occupational status were evaluated.

Primary and secondary outcome measures A BDI-FS cut-off value of ≥4, per definition, indicates the presence of a depressive symptomatology.

Results The return rate of questionnaires was high: 235/319 (73.7%) in patients with RA and 180/306 (58.8%), ending up with 392 complete questionnaires from 223 patients with RA (69.9%) and 169 HCO (55.2%). The BDI-FS was significantly higher in patients with RA (median BDI-FS 2 (IQR 0–4) vs median 1 (IQR 0–2) in HCO, p<0.001). BDI-FS scores from ≥4, which by definition indicate depression, were found in 29.6% of patients with RA and 12.4% of HCO (p<0.001). Depressive symptoms were strongly associated with disease activity (Clinical Disease Activity Index, p<0.001) and disability (Health Assessment Questionnaire, p<0.005). No association of depressive symptoms with age, alcohol consumption, smoking, occupational status or use of medication was found.

Conclusions One-third of female patients with RA showed depressive symptoms. Depression was significantly higher in female patients with RA than in female HCO and was strongly associated with disease activity and disability. It would be of interest to address the same question in male participants.

Strengths and limitations of this study

- ► This is the first study on the rate of depressive symptoms in female patients with rheumatoid arthritis in Austria, comparing high numbers of patients with healthy control subjects.
- ► In this multicentre study setting, nationwide data from primary, secondary and tertiary rheumatological centres were gathered.
- ► The return rate of questionnaires was remarkably high, especially for a delicate topic like depression.
- ► Together with the assessment of depressive symptoms, data on disease activity, disability, medication, alcohol consumption, smoking and occupational status were collected.
- ► Missing explicit pain evaluation is a main limitation of this study.

INTRODUCTION

Rheumatoid arthritis (RA) is one of a number of immune-mediated diseases being recognised as being associated with depression. It is well known that both conditions, RA as such, as well as depression, essentially contribute to disability and are, apart from their negative impact on the individual, potential contributors to increasing direct and indirect economic costs for the affected patients.[1] Depression is most strongly associated with RA among all mental health disorders.[2] However, estimates of the prevalence range significantly between 14% and 48%, which are affected by a multitude of factors, including differences in measurement methods, diagnostic thresholds, and course and recurrence of depressive symptoms.[3] Today, a clinically and statistically significant association between RA and depression is suggested by evidence.[4 5] Considering the impact of personality traits, some data are challenging the historic assumption of an association between personality and RA.[6] However, recent research has revealed that

personality characteristics, to some extent, may have an influence on the patient's adjustment to RA, promoting either the vulnerability or resilience to depression.[7]

Up to this day, the traditional explanatory causation model asserts that pain and disability caused by physical illness are leading to mental health problems.[8] However, this hypothesis is questionable since we are achieving growing knowledge about the pathophysiology of RA and the introduction of molecular-targeted immune therapeutics. However, over the last decades, we have developed an understanding that the essential therapeutic advances in clinical rheumatology may comprise RA, as chronic joint disease, and also comorbidities, such as management of cardiovascular risk and also depression.[9]

The aim of the present study was to estimate the proportion of depression in female patients with RA in Austria and to investigate potential relationships with patient-specific characteristics, including age, disease activity, disability and sexual dysfunction.

METHODS

Study design and ethics

This cross-sectional study is in compliance with the Declaration of Helsinki.

Setting

Patients were recruited from four hospital-based outpatient clinics and three office-based rheumatologists, between October 2015 and October 2016. Patients with RA aged ≥18 years were included as cases. Patients were eligible for the study when they fulfilled the European League Against Rheumatismclassification criteria.[10] Women ≥18 years of age, without an inflammatory rheumatic condition, many of them attending the practice for a health check, were included as a healthy control group (HCO). HCO saw a general practitioner or a specialist in internal medicine. All participants were Caucasians. Patients and HCO received detailed information about the study and were instructed on how to fill in the questionnaire. All participants received a self-addressed return envelope. To ensure absolute anonymity, all study participants were instructed to strictly avoid any personal notes on envelopes and questionnaires. During the patient visit, medical information regarding the disease, disease activity and medication were filled in by the treating physician. Then, the form was handed over to the patient, who was asked to fill in all the other information at home. The patient was further asked to use the enclosed envelope to anonymously send the form to the Centre of Excellence in Medicine in Linz, Austria, a sub-organisation of the Austrian Medical Association that has been involved in processing numerous questionnaires in healthcare for over 20 years. All questionnaires were collected there. Alternatively, patients could choose to fill in the forms during their visit, at the hospital or in the office waiting area, and then put the questionnaire into the envelope and the envelope into the locked box provided. This box was finally sent to the Centre of Excellence in Medicine. A total of 625 questionnaires were distributed to 319 patients with RA and 306 HCO. In total, 415 questionnaires were sent back: 235/319 (73.7%) handed out to patients with RA and 180/306 (58.8%) given to HCO. For statistical analysis concerning the Beck's Depression Inventory Fast Screen (BDI–FS), we excluded patients with incomplete BDI-FS questionnaires (12 patients with RA and 11 HCO) and used only data from complete BDI-FS questionnaires: 392 in total, 223 patients with RA (69.9%) and 169 HCO (55.2%).

Variables and data sources

The main exposure variable was RA. Physicians were instructed to register age and current medication on the questionnaire. For patients with RA, physicians also recorded the date of RA diagnosis, presence of rheumatoid factor and anti-citrullinated proteins/peptides, tender joint count (TJC) in 28 joints, swollen joint count (SJC) in 28 joints, patient's global assessment (PGA) and physician's global assessment (PhGA). The last four variables were used to calculate the Clinical Disease Activity Index (CDAI).[11] In addition, medication was registered, particularly disease-modifying antirheumatic drugs (DMARDs) and glucocorticoids. The DMARDs were grouped: csDMARDs (conventional synthetic DMARDs: methotrexate, sulfasalazine, leflunomide, hydroxychloroquine) as well as bDMARDs (biological DMARDs: adalimumab, etanercept, infliximab, golimumab, certolizumab pegol, rituximab, abatacept, tocilizumab). All patients and HCO self-reported their comorbidities (diabetes mellitus, hypertension, coronary artery disease, chronic heart failure, peripheral artery disease) as well as weight and height to calculate the body mass index (BMI), alcohol consumption and smoking status. In addition, the questionnaire contained questions regarding marital and employment status.

The questionnaire contained the validated German version of the BDI-FS and the validated German version of the Changes in Sexual Functioning Questionnaire (CSFQ-14).[12–14]

The BDI-FS, a shortened and simplified version of its predecessors, the BDI and the BDI-II, is a self-report instrument for the detection of the extent of depressive symptoms in adults as well as in youths.[12] It has been designed for healthcare professionals and has been studied in various patient groups. Having been translated into different languages, it is, meanwhile, used worldwide. The BDI-FS measures depressive symptoms as well as the severity of depression, corresponding to psychological and non-somatic criteria for the diagnosis of a major depression. It has shown both good reliability, as well as discriminative and convergent validity, in various patient groups (patients presenting with mixed comorbidities, specific diseases such as oncological or neurological disorders, geriatric and paediatric patients, as well as chronic pain disorders). It has also proven that it is unidimensional. Especially in chronic somatic disorders like RA, it

Table 1 Grade of depression according to the BDI-FS sum score (BDI-FS: Beck Depression Inventory–Fast Screen[12])

BDI-FS sum score	Grade of depression
0–3	Minimal (normal)
4–8	Mild
9–12	Moderate
13–21	Severe

is beneficial that somatic and vegetative symptoms are left out. In addition, during its development, no statistically significant differences of means were to be detected when regarding single items. Comparing different questionnaires for the assessment of depressive symptoms in RA, the BDI-II performed best concerning convergent validity criteria, also being the only questionnaire meeting the predefined retest reliability criterion.[13] Apart from its application in diseases previously mentioned, it is also suitable for screening the general population for depressive symptoms, therefore, being the perfect tool for both the patients with RA and the HCO in our study. The questionnaire consists of seven questions (A–G), being answered on a 4-point Likert scale from 0 to 3. The results of the single questions are added up, leading to a total score between 0 (minimum) and 21 (maximum). A score between 0 and 3 is defined as minimal depression, by definition being within the normal range. BDI-FS scores ≥4, by definition, indicate depression.

The grading of the severity of the depressive symptoms represented by the BDI-FS score, applying the predefined categories, is given in table 1.

In addition, patients with RA also filled in the Health Assessment Questionnaire–Disability Index (HAQ-DI) to assess the grade of disability.[15]

Statistical methods

The primary endpoint was the proportion of women with positive depressive symptomatology, according to the BDI-FS, in the RA group as compared with HCO. All further tests were exploratory, not confirmatory. We tested categorical data with the χ^2 test and calculated, where appropriate, a test for trend. In addition, we calculated ORs and 95% CI. For comparison of continuous data with a symmetric distribution, we used unpaired Student t-tests. If continuous data departed from a near-normal distribution, we used the Wilcoxon rank-sum test as a non-parametric test. For correlation of parameters with non-normal distribution, we used Spearman rank correlation.

A p value <0.05 was accepted as statistically significant. We performed all analyses with Stata Statistical Software (Release 13 IC; StataCorp LP) or ALMO statistics system (www.almo-statistik.de).[16]

Patient and public involvement

No patient involved.

Table 2 Characteristics and comorbidities of patients with RA and HCO (multiple comorbidities per individual possible)

Characteristics	RA, n=223	HCO, n=169	P value
Age, years	54.9±11.3	47.5±11.9	<0.001
BMI	26.2+5.2	23.6+3.5	<0.001
Smoking (%)	44 (19.7)	43 (25.4)	0.19
Alcohol consumption (%)	161 (72.2)	159 (94.1)	<0.001
Living in a partnership (%)	172 (77.1)	143 (84.6)	0.062
Level of education			<0.001
Compulsory education (%)	46 (20.6)	7 (4.1)	
Professional diploma (%)	106 (47.5)	23 (13.6)	
Higher level (college/ university) (%)	71 (31.8)	139 (82.2)	
Employment status (%)	98 (43.9)	131 (77.5)	<0.001
RF-positive (%)	160 (71.7)		
ACPA-positive (%)	141 (63.2)		
csDMARD (%)	179 (80.3)		
bDMARD (%)	98 (43.9)		
Both csDMARD and bDMARD (%)	72 (32.3)		
No DMARD at all (%)	20 (8.9)		
CDAI categories			
<2.8 (remission) (%)	65 (29.1)		
>2.8–10.0 (LDA) (%)	99 (44.4)		
>10.0–22.0 (MDA) (%)	43 (19.3)		
>22.0 (HDA) (%)	16 (7.2)		
Individuals with comorbidities	54 (24.2)	29 (17.2)	0.09
Diabetes mellitus (%)	5 (2.2)	2 (1.2)	0.43
Hypertension (%)	45 (20.2)	23 (13.6)	0.046
CAD (%)	2 (0.9)	1 (0.6)	0.63
CHF (%)	3 (1.3)	0	0.11
PAD (%)	11 (4.9)	7 (4.1)	0.51

Data are given in mean±SD for continuous variables or n (%) for binary variables, unless otherwise specified.
ACPA, anti-citrullinated protein antibodies; bDMARD, biological DMARD; BMI, body mass index; CAD, coronary artery disease; CDAI, Clinical Disease Activity Index; CHF, chronic heart failure; csDMARD, conventional synthetic DMARD; DMARD, disease-modifying antirheumatic drug; HCO, healthy controls; HDA, high disease activity; LDA, Low disease activity; MDA, moderate disease activity; PAD, peripheral artery disease; RA, rheumatoid arthritis; RF, rheumatoid factor.

RESULTS

Mean RA disease duration was 12.0±10.1 years. Characteristics of patients with RA and HCO are shown in table 2.

Some of the patient characteristics were distributed unequally between the two groups analysed. The mean age in the RA patient group was 54.9±11.3 years, being significantly higher than in HCO (47.5±11.9 years), p<0.001. Disease activity in patients with RA was generally low, with a median CDAI of 5 (IQR 2–10.5); 65 patients (29.1%) had a CDAI ≤2.8, 99 patients (44.4%) had a

Table 3 Single items of the BDI-FS of patients with RA and HCO

BDI item	Overall (RA+HCO)	RA	HCO	P value
Sadness	0.29±0.5	0.35±0.55	0.20±0.42	0.004
Pessimism	0.26±0.57	0.36±0.66	0.12±0.38	<0.001
Failure	0.31±0.62	0.40±0.71	0.18±0.43	0.004
Ability to enjoy oneself	0.50±0.66	0.66±0.71	0.30±0.52	<0.001
Self-confidence	0.19±0.5	0.24±0.55	0.12±0.42	0.006
Self-criticism	0.47±0.66	0.52±0.74	0.40±0.53	0.35
Suicidal ideation	0.12±0.35	0.15±0.4	0.08±0.27	0.04

Data are given in mean±SD and p values for the differences between RA and HCO. Higher scores indicate a higher grade of dysfunction.
BDI-FS, Beck Depression Inventory–Fast Screen; HCO, healthy controls; RA, rheumatoid arthritis.

CDAI between >2.8 and 10.0, 43 patients (19.3%) had a CDAI between >10.0 and 22.0, and 16 patients (7.2%) had a high disease activity according to the CDAI (≥22.0).

Among the comorbidities reported, except for hypertension (p=0.046), there was no statistically significant difference between the RA patient group and HCO (table 2).

Patients with RA had a significantly higher risk of depression, as expressed by the BDI-FS. In patients with RA, the median BDI-FS was 2 (IQR 0–4) and in HCO the median BDI-FS was 1 (IQR 0–2; p<0.001). The results of the seven single items of the BDI-FS were significantly different between patients with RA and HCO except for self-criticism (table 3).

Using a binary definition of depression (BDI-FS score < or ≥4), a significant difference between the groups was also evident: in the RA group, 66/223 (29.6%) had a BDI-FS score ≥4 (indicating the presence of at least mild depression). In the HCO group, 21/169 (12.4%) had a BDI-FS score ≥4 (p<0.001) (table 4).

The highest BDI-FS score was 20 (severe) in patients with RA versus 10 (moderate) in HCO.

Suicide risk can be estimated by the BDI-FS using the items displaying pessimism and suicidal ideation. This specific risk could be revealed in 13 (6%) of the patients with RA and in 3 (2%) of HCO.

A significant correlation between depression (BDI-FS score) and disease activity (CDAI) was found (Spearman's rho=0.30; p<0.001). This correlation with BDI-FS is also given for each single component of the CDAI: for TJC (Spearman's rho=0.22; p=0.002), for SJC (Spearman's rho=0.18; p=0.008), for PGA (Spearman's rho=0.31; p<0.001) and for PhGA (Spearman's rho=0.29; p<0.001).

A significant correlation between depression (BDI-FS score) and disability (HAQ) was also found (Spearman's rho=0.32; p<0.005).

There was a strong association between BDI-FS and female sexual dysfunction (FSD). Increasing BDI category is strongly associated with the presence of FSD (see table 5).

The percentage of women with FSD was higher in the RA group (106/223, 47.5%) when compared with HCO (24/169, 14.2%). Detailed data on the association between FSD and RA have already been reported elsewhere.[17]

Depression was also significantly associated with obesity, expressed by the BMI (Spearman's rho=0.14; p=0.006). There was no association between depression and the number of comorbidities collected (p=0.48). Among the single comorbidities reported, there was neither an association with diabetes mellitus (p=0.4), coronary artery disease (p=0.36) nor with peripheral artery disease

Table 4 Rate of depression in patients with RA and HCO

	RA, n=223	HCO, n=169	P value
Depression, n	66/223 (29.6%)	21/169 (12.4%)	<0.001
BDI-FS categories			
Minimal (0–3)	157 (70.4)	148 (87.6)	
Mild (4–8)	53 (23.8)	19 (11.2)	
Moderate (9–12)	10 (4.5)	2 (1.2)	
Severe (13–21)	3 (1.3)	0 (0.0)	

BDI-FS, Beck Depression Inventory–Fast Screen; HCO, healthy controls; RA, rheumatoid arthritis.

Table 5 Probability of FSD depending on the grade of depression according to the BDI-FS

BDI-FS	n^1 (RA+HCO)	n^2 (FSD)	OR for FSD (95% CI)	P value
0–3	278	75 (27.0%)	1 (ref)	
4–8	67	33 (49.3%)	2.63 (1.50 to 4.59)	0.0004
>8	12	8 (66.7%)	5.4 (1.10 to 15.00)	0.003

BDI categories >8 have been combined due to the low number of cases in the highest BDI category.
Test for trend of odds: p<0.0001; n^1=number of individuals (patients with RA and HCO) and n^2=number of individuals (%) with FSD in the respective BDI-FS category (only individuals having completed both CSFQ and BDI-FS questionnaires were included).
BDI-FS, Beck Depression Inventory–Fast Screen; CSFQ, Changes in Sexual Functioning Questionnaire; FSD, female sexual dysfunction; HCO, healthy controls; RA, rheumatoid arthritis; ref, reference.

(p=0.26). However, both hypertension as well as chronic heart failure were significantly associated with depression (p<0.04 for both).

Smoking was not associated with depression. In total, 241/303 (79.5%) of non-smokers and 62/87 (71.3%) of smokers were in the lowest BDI-FS category (0–3) (p=0.409).

Patients with RA were significantly more often abstinent from alcohol: 62/223 (27.8%) patients with RA never drank alcohol versus 10/169 (5.9%) of the HCO (p<0.001). There was no significant association between depression and alcohol consumption (p=0.55).

There was no significant correlation between age and depression (BDI-FS) (Spearman's rho=0.039; p=0.46). We found no association between depression and living in a partnership (p=0.874). However, patients with RA showed a trend towards being more likely to live alone than HCO (p=0.062).

There was a borderline association between depression and employment status (OR 0.62; 95% CI 0.38 to 1.01; p=0.051); this was virtually unchanged after adjustment for age (OR 0.47; 95% CI 0.21 to 1.04; p=0.055).

RA was associated with a significantly lower OR of being employed (OR 0.21; 95% CI 0.13 to 0.33; p<0.0001). This association was also existent after adjustment for age (OR 0.15; 95% CI 0.07 to 0.36; p<0.0001).

Regarding medication, there was neither association with the use of csDMARDs (p=0.99), bDMARDs (p=0.55) nor glucocorticoids (p=0.45).

DISCUSSION

Of all mental health disorders, depression is most strongly associated with RA.[3]

Getting more and more insights into the reciprocity between depression and RA, current literature links depression with an increased risk for RA.[18] A recent retrospective population-based cohort study covering data for 26 years, from 1986 to 2012, identified that depression even increases the risk for developing RA by 38%. Antidepressants may decrease this risk in these patients, which is an interesting finding that requires further research.[19] Of note, particularly this disorder can reduce the likelihood of achieving remission in patients with RA.[20 21] Referring to data from biologic registries, depression at baseline contributes to approximately a 30% reduction in the odds of a positive response to biologic treatment in RA.[22] Last but not least, depression in RA is associated with increased mortality, from both suicide and non-suicide.[23 24] Lacking data on the proportion of depression in RA for Austria, one aim of our study was to address this dimension in female patients with RA. Both conditions—RA and depression—are partly sharing the same symptoms, for example, fatigue or sleep disturbances. In the assessment of both, the choice of the research scale—either including or excluding these shared symptoms—makes a decisive difference. The BDI-FS was chosen due to its aforementioned specific ability to discriminate between depressive and somatic symptoms in establishing the diagnosis of depression, its good performance in comparison with other tools and its availability in German.[12]

In line with the literature, we found a significantly higher percentage of depression in patients with RA compared with HCO. This also holds true after exclusion of confounders like age so that the age difference between HCO and RA group does not interfere with our results. In our study population, almost one-third of patients with RA showed a BDI-FS >4, indicative of depression.

We found a strong correlation of depression and disease activity (p<0.001) as well as disability (p<0.005). Moreover, 73.5% of our patients with RA were in remission or in low disease activity, representing an extremely well disease controlled patient group, with a high rate of bDMARDs (44%). However, neither for the use of csDMARDs, bDMARDs nor glucocorticoids, an association with depression was found. Meanwhile, there is profound evidence for an association between depression severity and inflammation, each of them having independent effects on perceived pain, which has been discussed for quite some time. Linear increases of severe pain, by the levels of C reactive protein and depression severity, show that obviously both factors contribute to perceived pain.[25] A limitation of our study is the lack of a concise question on pain, apart from assessing the PGA (in terms of the CDAI), which showed a significant association with the BDI-FS.

Among environmental factors being responsible for developing RA, cigarette smoking is the one with the strongest evidence.[26] Smoking can lead to a smouldering inflammation and nicotine potentially decreases levels of serotonin and monoamine oxidase, leading to depression.[27 28] In our patients with RA, we did not find an association between cigarette smoking and depression. The proportion of smokers in our study was relatively small (22.2%). There was also no association between depression and alcohol consumption. This is quite surprising in a high-income country like Austria, considered as permissively consuming alcohol, also rated this way by WHO.[29] Generally, alcohol consumption was quite low in both groups but significantly lower in the RA group compared with HCO. This may be due to two factors. First, we investigated female patients, expecting that they drank less than men. Second, patients with RA suffering from a chronic disease may be reluctant to drink alcohol and may try to avoid alcohol while being on a continuous medication like methotrexate. Of note, given the low level of alcohol consumption in our study, it is difficult to detect any potential association between depression and alcohol consumption.

Although depression frequently co-occurs with multiple chronic diseases, in our study there was no association of the BDI-FS with the total number of comorbidities.[30] Among the single comorbidities reported, only hypertension and chronic heart failure showed an association with depressive symptoms. According to several studies, depression rises the risk for hypertension and is even

considered an independent risk issue for hypertension, with an ongoing discussion about possible shared pathophysiological mechanisms.[31] However, data evaluating the prevalence of depression in hypertensive patients vary considerably depending on the method of evaluation.[32] It is well known that in patients with heart failure, depression as well as anxiety disorders are common. Like in rheumatology, this is the reason for adverse outcomes such as reduced adherence to treatment, impaired quality of life, and elevated morbidity and mortality.[33 34] Although specific guidelines for depression screening in patients who had a heart failure are lacking, the 2016 European guidelines for heart failure suggest the early use of the BDI in order to screen for depressive symptoms.[35] The association of depression with the BMI as a marker for overall adiposity in our study replicates former findings on a positive association between BMI and depressive mood.[36]

One strength of our study is the high number of investigated patients in this field. This multicentre study delivers data on depression in Austrian female patients with RA, from all over the country, for the first time. It bears comparison with a recently published German study, which our findings are in line with. In this VADERA II study including both male and female patients with RA and using the BDI II, a predecessor of the BDI-FS, the prevalence of mild and moderate depressive symptoms was also common: 55.4% (mild or worse) and 22.8% (moderate or worse).[37]

Another strength is the remarkably high return rate of questionnaires, even more pronounced considering the intimate issues prompted, such as symptoms of depression and sexual dysfunction. This is probably due to an obviously good and trusting relationship between patients and physicians. Our major effort was to ensure complete anonymity. Given the high return rate of questionnaires, we have obviously succeeded this task. However, this process is also associated with the risk that patient characteristics may be distributed unequally between the two groups, which is the case in our study. As mentioned, this is a result of the study design. Weighing up pros and cons, we feel that our approach was the best way to ensure a pursued high return rate.

In daily clinical routine, the mere assessment of clinical disease activity in patients with RA is obviously not able to reflect the prevalence of depressive symptoms. In order to support and amend clinical care, patients with RA should be routinely screened for depressive symptoms as for other comorbidities.[38] Missing depression, an obviously frequent comorbidity in RA, could have negative implications on the course of the rheumatic disease, the quality of life and also the response to therapies.[39] Apart from the great advances in RA treatment, one must be aware that successful therapy of inflammation alone may sometimes not be sufficient for the individual patient. Patients with RA with concomitant depression may present with severe pain without clinical signs of disease activity and elevation of inflammatory indices. Further therapeutic steps like psychotropic medication or psychotherapy that are beneficial in depression should be considered and not be detained from these patients.

Incorporating findings and growing knowledge, both on depression and depressive symptoms in daily clinical practice, could clear the way for a multidisciplinary approach, which is a promising treatment strategy, both for RA and pain in association with depression.[40 41]

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