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Ultrasound evaluation contrasts clinical disease activity evaluation in rheumatoid arthritis patients with concomitant anxiety or depression

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ABSTRACT

Objectives: To compare disease activity as assessed by ultrasonography (US) between rheumatoid arthritis (RA) patients with and without anxiety or depression, and to compare clinical disease activity and sociodemographic measures between these patient groups.

Methods: Anxious or depressed patients were identified by EuroQoL-5D-3L question "I am not/moderately/extremely anxious or depressed." US assessments of 36 joints and 4 tendons were performed and power Doppler (PD) and grey scale (GS) sum scores calculated (both range 0–120). Comparisons between anxious/depressed and not anxious/depressed patients were performed in unadjusted analyses, adjusted logistic regression, and sensitivity analyses.

Results: A total of 201 RA patients starting biological disease-modifying antirheumatic drugs were included (82 % women, mean age 52 years, disease duration 10 years). Hundred-and-nine patients (54.2 %) were moderately or extremely anxious/depressed. Median (IQR) PD (13 (4, 21) vs. 10 (3, 20), $p = 0.53$) and GS (28 (18, 42) vs. 25 (14, 41), $p = 0.51$) sum scores were similar between anxious/depressed and not anxious/depressed patients, respectively, whereas composite scores of disease activity were significantly worse in the anxious/depressed patients ($p < 0.001$), as were also patient-reported outcomes, ESR, CRP and plasma calprotectin (all $p \leq 0.02$). Sensitivity analyses confirmed these findings, except for CRP. Self-reported economy and sleep difficulties were also worse in the anxious/depressed patients and a higher proportion were not working (all $p < 0.001$).

Conclusion: This study highlights the negative impact of anxiety and depression on RA patients in standard care, and underscores the challenges in disease activity assessment. US examination may be a valuable objective tool in the evaluation of these patients.

Introduction

Anxiety and depression is by far more common in patients with rheumatoid arthritis (RA) than in the general population, with a prevalence ranging from 10 to 50 %, depending on assessment metods [1]. Concomitant anxiety and depression in patients with RA may be challenging for treatment adherence and follow-up, and for achievement of remission [2,3]. Anxiety and depression may also challenge evaluation of disease activity, as these conditions may influence disease perception and patient-reported outcomes (PROs) [2-5].

Ultrasonography (US) is a valuable tool in the assessment of disease activity in patients with RA, and may be of particular value when the assessment of disease activity by clinical examination is challenging [6].

As anxious or depressed patients may have higher disease activity than patients without anxiety or depression as measured by clinical composite scores of disease activity, there is a need to investigate whether such differences are also reflected in imaging modalities, such as US [7].

Hence, the aim of this study was to compare disease activity as assessed by a comprehensive US evaluation in RA patients with and

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without anxiety or depression. Secondary aim was to compare clinical disease activity and sociodemographic measures between these patient groups.

Patients and methods

Patients

RA patients who fulfilled the American College of Rheumatology 1987 criteria and started or switched biological disease-modifying antirheumatic drug (bDMARD) treatment in 2010–2013, as well as responded to the EuroQol-5 Dimensions-3 Levels (EQ-5D-3L) questionnaire [8], were included in the study. The patients were part of a previously described cohort [6]. All patients gave their written informed consent before inclusion. The study was approved by the Norwegian Regional Committee for Medical and Health Research Ethics South East (2009/1254; ref. 12217; ref. 21658).

Assessments

The following information was assessed at the start or switch of bDMARD: age, sex, disease duration, type of bDMARD (infliximab, etanercept, adalimumab, golimumab, certolizumab pegol, rituximab, abatacept, tocilizumab), concomitant csDMARDs (methotrexate, sulphasalazine, leflunomide, azathioprine), concomitant prednisolone (mg), anti-CCP (positive/negative), any children (yes/no), highest level of education college or university (yes/no), any sleep difficulties (yes/no), some or severe sleep difficulties (yes/no), current work status and self-evaluation of economy (good, medium, poor).

Depression and anxiety

Anxious or depressed patients were identified by the EQ-5D-3L questionnaire, question 5: "I am not anxious or depressed/I am moderately anxious or depressed/I am extremely anxious or depressed, and then categorized into not and moderately/extremely anxious or depressed" [8].

Patient-reported outcome measures

The following PROs were assessed on a 0 (best) to 100 (worst) visual analogue scale (VAS): Patient's global assessment of disease activity, pain, joint pain, back pain and fatigue. Patients also self-reported the modified Stanford Health Assessment Questionnaire (MHAQ, range 0 (best) – 3 (worst)) [9], the Short-Form 36 (SF-36) [10], presented as mental health scale score and mental and physical component summaries, and the Rheumatoid Arthritis Impact of Disease (RAID, range 0 (best) - 10 (worst)), including pain, physical functioning, fatigue, sleep disturbance, physical wellbeing, emotional wellbeing and coping (all on a 0–10 numeric rating scale) [11]. Pain catastrophizing (range 0 (best) – 6 (worst)) was self-reported using the mean of the following two questions from the Coping Strategies Questionnaire (CSQ): "When I have pain, it's terrible and I think it's never going to get any better" and "When I have pain, I feel I can't stand it anymore" [12].

Other disease activity measures

Erythrocyte sedimentation rate (mm/h), C-reactive protein (mg/l) and plasma calprotectin (µg/L, ELISA, CALPRO AS [13]) were measured. Counts of 32 swollen/tender joints (28 joint count with addition of ankles and the five metatarsophalangeal joints scored as one joint bilaterally) together with evaluator's global assessment of disease activity were assessed by one of two experienced nurses blinded to the US results. The following composite scores of disease activity were calculated: 28-joint Disease Activity Score with ESR (DAS28ESR) [14], DAS28 with CRP (DAS28CRP) [14], Simplified Disease Activity Index (SDAI) [14] and Clinical Disease Activity Index (CDAI) [14].

Ultrasonography assessments

US assessments were performed by an experienced physician (HBH) blinded to the clinical and PRO results, using a Siemens Antares Excellence version, with 5–13 MHz probe with PD frequency 7.3 MHz and PRF 391 Hz. We used the OMERACT approved definitions of US elementary lesions, with the Norwegian US atlas as a reference, including a semi-quantitative 0–3 power Doppler (PD) and grey scale (GS) scoring of 36 joints (bilateral wrist (radiocarpal, midcarpal, radioulnar joints scored separately), metacarpophalangeal joints 1–5, proximal interphalangeal joints 2–3, elbow, knee, ankle (tibiotalar joint), metatarsophalangeal joints 1–5), and four tendon sheaths (bilateral extensor carpi ulnaris and tibialis posterior) [15,16]. PD (range 0–120) and GS (range 0–120) sum scores were calculated. Examples of US verified synovitis and tenosynovitis are shown in the supplementary figures file.

Statistics

Demographics and disease activity measures were compared across patients with and without anxiety/depression as identified through EQ-5D-3L in unadjusted analyses with independent *t*-test, Mann-Whitney U-test or Chi-square test, as appropriate, as well as in logistic regression analyses adjusted for age and sex. The standardized effect size Cohen's d was calculated by dividing the mean difference by the pooled standard deviation, presented as absolute values, and interpreted as small ($\leq$0.2), moderate (>0.2 and $\leq$0.5), large (>0.5 and $\leq$0.8) and very large (>0.8). Sensitivity analyses with comparison of disease activity measures across patients with and without anxiety/depression adjusted for factors known to impact inflammation were performed in logistic regression analyses, with a) additional adjustment for concomitant csDMARD and prednisolone dose, in addition to age and sex, and b) with additional adjustment for concomitant csDMARD, prednisolone dose and number of previous bDMARDs, in addition to age and sex. A p-value <0.05 was considered statistically significant. The analyses were performed as complete case analyses. IBM SPSS Statistics version 26.0.0.1 was used for all analyses.

Results

Patients

A total of 201 RA patients were included in the study when they started or switched bDMARD treatment (81.6 % women, mean (SD) age 52.2 (12.7) years, disease duration 10.0 (9.0) years). According to EQ-5D-3L, 109 patients (54.2 %) were moderately or extremely anxious/depressed at inclusion (Table 1).

The anxious/depressed patients had worse self-evaluated economy and a lower proportion was currently working. Additionally, a lower proportion of the anxious/depressed patients had children and a higher proportion experienced sleep disturbances. The anxious/depressed patients also used more prednisolone. Apart from this, demographical characteristics were similar between patients with and without anxiety or depression (Table 1).

Clinical disease activity measures according to EQ-5D-3L anxiety/depression status

All clinical disease activity measures were significantly worse in the anxious/depressed patients, including composite scores of disease activity ($p < 0.001$), PROs ($p < 0.001$), swollen and tender joint counts ($p \leq 0.04$), ESR, CRP and plasma calprotectin ($p \leq 0.02$, Table 2 (number of available cases is shown in Supplementary Table 1).

The anxious/depressed patients also had significantly worse pain

Table 1
Demographics according to EQ-5D-3L anxiety/depression status.

	Anxious or depressed patients ($n = 109$)	Not anxious or depressed patients ($n = 92$)	p, unadjusted[1]	p, adjusted[2]
Age, mean (SD) years	53.0 (13.1)	51.3 (12.2)	0.36	0.36
Women, *n* (%)	87 (79.8)	75 (81.5)	0.76	0.76
Disease duration, mean (SD) years	10.2 (9.2)	9.8 (8.8)	0.76	0.83
bDMARD, *n* (%)			0.27	0.30
Infliximab	12 (11.0)	13 (14.1)		
Etanercept	40 (36.7)	34 (37.0)		
Adalimumab	15 (13.8)	4 (4.3)		
Golimumab	7 (6.4)	5 (5.4)		
Certolizumab pegol	7 (6.4)	12 (13.0)		
Rituximab	18 (16.5)	17 (18.5)		
Abatacept	2 (1.8)	3 (3.3)		
Tocilizumab	8 (7.3)	4 (4.3)		
bDMARD naïve, *n* (%)	53 (51.0)	49 (57.0)	0.41	0.36
Concomitant csDMARD, *n* (%)	90 (83)	78 (85)	0.67	0.68
Using prednisolone, *n* (%)	64 (59.8)	48 (52.7)	0.32	0.34
Prednisolone (mg), median (IQR)	5 (0, 10)	2.5 (0, 5)	0.07	0.02
Anti-CCP positive, *n* (%)	85 (79.4)	67 (75.3)	0.49	0.48
BMI, mean (SD)	25.0 (4.0)	24.8 (4.5)	0.80	0.93
Any children, *n* (%)	74 (67.9)	74 (80.4)	0.04	0.008
College or university, *n* (%)	50 (45.9)	56 (60.9)	0.03	0.06
Any sleep difficulties, *n* (%)	101 (92.7)	64 (69.6)	<0.001	<0.001
Some or very much sleep difficulties, *n* (%)	69 (63.3)	33 (35.9)	<0.001	<0.001
Currently working, *n* (%)	48 (46)	67 (75)	<0.001	<0.001
Self-evaluated economy, *n* (%)			<0.001	0.03
Good	40 (36.7)	57 (62.6)		
Medium	53 (48.6)	34 (37.4)		
Poor	16 (14.7)	0 (0.0)		

[1] Independent *t*-test, Mann-Whitney U-test or Chi-square test, as appropriate.
[2] Logistic regression analyses, adjusted for age and sex; bDMARD, biological disease-modifying antirheumatic drug; BMI, body mass index, kg/m^2; csDMARDs, including methotrexate, sulphasalazine, leflunomide and azathioprine; EQ-5D-3L; EuroQol 5-Dimensions 3-Levels.

catastrophizing ($p < 0.001$), coping ($p < 0.001$) and SF-36 mental health subscale and mental and physical component summaries ($p \leq 0.03$), than the patients without anxiety/depression.

The standardized effect size Cohen's d was very large for patient's global, pain, joint pain, fatigue, MHAQ, RAID, coping, SF-36 mental health scale score, SF-36 physical component summary, DAS28ESR, DAS28CRP, CDAI and SDAI (Table 2). Furthermore, according to clinical composite scores, significantly more patients with anxiety/depression were in a state of high disease activity ($p < 0.001$, Fig. 1).

Disease activity according to ultrasound measures

A total of 181/201 patients (90 %) had PD sum score of one or more, whereas all patients had GS sum score of one or more. Median (IQR) PD and GS sum scores were similar in patients with vs. without anxiety/depression (Table 2). Similar proportions of patients with vs. without anxiety/depression had PD sum score above the 75 percentile, that is, PD sum score >20 (Fig. 1).

Sensitivity analyses

In sensitivity analyses adjusting for concomitant csDMARD and prednisolone treatment in addition to age and sex, we found consistent findings as in the main analyses (Table 2), with similar US findings across anxious/depressed and not anxious/depressed patients, but worse clinical disease activity measures in the anxious/depressed patients. The only exception was 32 swollen joint count which no longer was significantly different across the two groups ($p = 0.05$). Additional sensitivity analyses with adjustment for number of previous bDMARDs in addition to age, sex, csDMARD and prednisolone, also showed consistent findings, except for 32 swollen joint count ($p = 0.09$) and CRP ($p = 0.11$) which no longer were significantly different across the two groups.

Discussion

In this observational study of 201 patients with RA starting or switching bDMARDs, the anxious or depressed patients had similar levels of disease activity as assessed by a comprehensive US evaluation as the patients without anxiety or depression, but significantly worse clinical composite scores of disease activity, patient-reported outcomes, ESR and plasma calprotectin. The anxious or depressed patients also had worse self-evaluated economy, lower proportions had children and were currently working, and a higher proportion had sleep difficulties. The standardized mean difference (Cohen's d) between anxious/depressed and not anxious/depressed patients was larger for disease activity measures that included subjective assessments.

About half of the patients reported to be moderately or extremely anxious or depressed according to EQ-5D-3L, which is in line with previous studies [2,17,18]. In general, the proportion of patients identified as anxious/depressed varies according to measurement tool used [1].

To our knowledge, this is the first study to compare US findings in RA patients with vs. without anxiety/depression. Previously, discordance between clinical and US assessment of disease activity in patients with RA is described [19]. Still, clinical examination is the standard approach in every-day follow-up of RA patients. This may be challenging when patients have concomitant anxiety or depression, as these conditions are known to impact patient-reported outcomes and hence also composite scores of disease activity [2]. Future studies should explore if anxious/depressed patients who have inadequate response to treatment as assessed by clinical composite scores of disease activity also have more US verified arthritis than patients without anxiety/depression during follow-up.

In this study, patients with anxiety or depression had significantly higher 32 swollen joint count in unadjusted analyses and when adjusted for age and sex. However, this difference was no longer significant when also adjusting for concomitant csDMARDs, prednisolone and number of previous bDMARDs, which all may impact joint swelling/inflammation. Calprotectin was significantly higher in the anxious/depressed patients,

Table 2
Disease activity and PROs according to EQ-5D-3L anxiety/depression status.

	Anxious or depressed (n = 109)	Not anxious or depressed (n = 92)	p unadj.[1]	Cohen's d[2]	p adj.[3]
Patient's global, median (IQR)	66 (50, 77)	38 (16, 56)	<0.001	1.20	<0.001[a,b,c]
Evaluator's global, median (IQR)	35 (25, 45)	25 (17, 35)	<0.001	0.57	<0.001[a,b,c]
Pain, median (IQR)	62 (42, 72)	30 (15, 53)	<0.001	1.08	<0.001 [a,b,c]
Joint pain, median (IQR)	61 (39, 75)	30 (13, 42)	<0.001	1.13	<0.001[a,b,c]
Back pain, median (IQR)	46 (14, 68)	12 (0, 38)	<0.001	0.74	<0.001[a,b,c]
Fatigue, median (IQR)	65 (42, 83)	35 (12, 62)	<0.001	0.84	<0.001[a,b,c]
MHAQ, median (IQR)	0.9 (0.6, 1.1)	0.3 (0.0, 0.6)	<0.001	1.25	<0.001[a,b,c]
RAID, mean (SD)	5.7 (1.8)	3.3 (1.9)	<0.001	1.31	<0.001[a,b,c]
Coping, mean (SD)	4.4 (2.3)	2.5 (2.0)	<0.001	0.90	<0.001[a,b,c]
SF-36 mental health scale score, mean (SD)	62.4 (20.1)	78.5 (12.9)	<0.001	0.94	<0.001[a,b,c]
SF-36 MCS, mean (SD)	42.2 (12.6)	47.6 (11.2)	0.03	0.45	0.05[a], 0.04[b], 0.03[c]
SF-36 PCS, mean (SD)	29.3 (8.5)	38.7 (8.1)	<0.001	1.14	<0.001[a,b,c]
Pain catastrophizing, median (IQR)	3.0 (2.0, 3.5)	1.5 (1.0, 2.5)	<0.001	0.69	<0.001[a,b,c]
32 SJC, median (IQR)	7 (4, 12)	5 (3, 10)	0.02	0.31	0.04[a], 0.05[b], 0.09[c]
32 TJC, median (IQR)	8 (4, 13)	4 (1, 8)	<0.001	0.75	<0.001[a,b,c]
ESR, median (IQR) mm/h	29 (17,45)	20 (10, 31)	<0.001	0.48	0.002[a], 0.005[b], 0.02[c]
CRP, median (IQR) mg/L	8 (3, 24)	4 (1, 9)	<0.001	0.38	0.02[a], 0.006[b], 0.11[c]
Plasma calprotectin, median (IQR) µg/L	1482 (815, 2950)	910 (576, 1582)	<0.001	0.59	<0.001[a,b], 0.003[c]
DAS28ESR, mean (SD)	5.2 (1.3)	3.9 (1.3)	<0.001	1.02	<0.001[a,b,c]
DAS28CRP, mean (SD)	4.8 (1.2)	3.5 (1.1)	<0.001	1.09	<0.001[a,b,c]
CDAI, mean (SD)	24.4 (12.2)	15.5 (9.2)	<0.001	0.82	<0.001[a,b,c]
SDAI, mean (SD)	26.2 (13.1)	16.4 (9.7)	<0.001	0.84	<0.001[a,b,c]
PD sum score, median (IQR)	13 (4, 21)	10 (3, 20)	0.21	0.11	0.53[a,b], 0.69[c]
GS sum score, median (IQR)	28 (18, 42)	25 (14, 41)	0.18	0.11	0.51[a], 0.52[b], 0.78[c]
PD sum score, *n* (%)					
0–3	23 (21.1)	28 (30.4)			
4–11	28 (25.7)	23 (25.0)	0.41	NA	0.45[a],0.27[b], 0.37[c]
12–21	32 (29.4)	20 (21.7)			
>22	26 (23.9)	21 (22.8)			

[1] Independent *t*-test, Mann-Whitney U-test or Chi-square test, as appropriate.
[2] Cohen's d values are presented as absolute values.
[3] Logistic regression analyses.
[a] adjusted for age and sex.
[b] adjusted for age, sex, csDMARD (yes/no) and prednisolone (mg).
[c] adjusted for age, sex, csDMARD (yes/no), prednisolone (mg) and number of previous bDMARDs; CDAI, clinical disease activity index; CRP, C-reactive protein; DAS28ESR, disease activity score with 28 joints and ESR; DAS28CRP, DAS28 with CRP; ESR, erythrocyte sedimentation rate; EQ-5D-3L; EuroQol 5-Dimensions 3-Levels; GS, grey scale; MHAQ, modified health assessment questionnaire; RAID, rheumatoid arthritis impact of disease; SDAI, simplified disease activity index; SF-36, MCS, Short form-36 mental component summary; SF-36 PCS, SF-36 physical component summary; SJC, swollen joint count; TJC, tender joint count; PD, power Doppler.

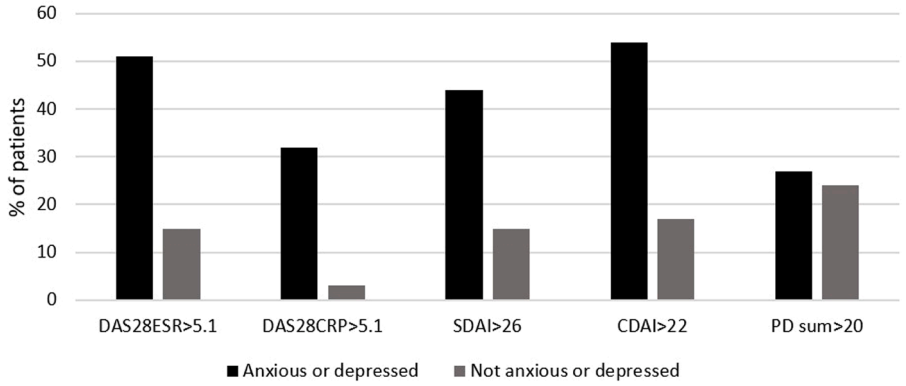

Fig. 1. Proportion of patients in high disease activity according to anxiety/depression status (DAS28ESR, disease activity score with 28 joints and ESR; DAS28CRP, DAS28 with CRP; CDAI, clinical disease activity index; PD, power Doppler; SDAI, simplified disease activity index).

as were also ESR and CRP, although CRP was not significantly different in sensitivity analyses. Plasma calprotectin is known to reflect both clinically and US verified inflammatory activity in RA patients [20,21] Furthermore, in a study of seventy patients with early undifferentiated arthritis, calprotectin was associated with anxiety [22]. This is the first study to compare calprotectin between anxious/depressed vs. not anxious/depressed RA patients. Previously, CRP and proinflammatory cytokines like IL-6 and IL-17 have been associated with depression in RA patients [5,23]. It would be of interest to explore in future studies whether RA and anxiety and depression share common inflammatory pathways including calprotectin.

Apart from this, we could also hypothesize that the higher inflammatory markers in the anxious/depressed group of patients could be related to arthritis or tenosynovitis in other locations than those examined. To gain a better understanding of the disparity between composite scores of disease activity and US evaluation, further investigation, including US evaluation of more than the thirty-six joints and four tendon sheet in this study is warranted.

Our findings of worse self-reported economy and more unemployment in the anxious or depressed patients are in line with a recent Chinese cross-sectional study of 215 RA patients, according to which depressed RA patients were more likely to have lower income and no employment than the non-depressed RA patients [24]. In the same study patient-reported outcomes and composite scores of disease activity were significantly higher in the anxious/depressed patients, like in this study.

Limitations of our study include that both patients starting a first bDMARD as well as patients switching bDMARDs were included. However, consistent results were found when also adjusting for line of bDMARD treatment. Furthermore, diagnostic codes for anxiety and depression were not assessed, and we assessed anxiety and depression in one combined variable. However, by using a simple patient-reported question on anxiety/depression, the results may be relevant for the average patient in routine care follow-up. Also, anxiety and depression are known to often overlap [25]. Previously, it is shown that RA patients who self-report anxiety or depression have less probability of achieving remission as assessed by clinical composite scores [2]. Given that replication is a cornerstone in research and this is the first study to compare both clinical and US verified inflammatory activity in RA patients with and without anxiety or depression, it would be of interest to try to replicate the findings in a larger cohort of patients.

In conclusion, the anxious/depressed patients with RA had significantly worse clinical composite scores of disease activity, patient-reported outcomes, ESR and plasma calprotectin than the patients without anxiety/depression, in spite of similar levels of US verified disease activity. Furthermore, self-evaluated economy, unemployment, and sleep difficulties were worse in the anxious/depressed patients. This study highlights the negative impact of anxiety and depression on RA patients in standard care, and the need for more studies including objective assessments of joint inflammation in these patients.

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Data availability

The research data is available upon reasonable request and following necessary approvals.

CRediT authorship contribution statement

Brigitte Michelsen: Conceptualization, Methodology, Software, Formal analysis, Resources, Data curation, Writing – original draft, Visualization, Project administration, Funding acquisition, Validation, Investigation, Writing – review & editing. **Joseph Sexton:** Methodology, Formal analysis, Resources, Visualization, Data curation, Validation, Investigation, Writing – review & editing. **Tore K Kvien:** Validation, Investigation, Formal analysis, Resources, Visualization, Writing – review & editing. **Sella Aarestad Provan:** Validation, Investigation, Formal analysis, Resources, Visualization, Writing – review & editing. **Hilde Berner Hammer:** Conceptualization, Methodology, Resources, Data curation, Formal analysis, Visualization, Project administration, Funding acquisition, Validation, Investigation, Writing – review & editing.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Brigitte Michelsen reports financial support was provided by South-Eastern Norway Regional Health Authority. Diakonhjemmet Hospital reports financial support was provided by Research Council of Norway. Brigitte Michelsen reports a relationship with Novartis AG that includes: funding grants and speaking and lecture fees. Tore K Kvien reports a relationship with Grünenthal Ltd that includes: speaking and lecture fees. Tore K Kvien reports a relationship with Janssen Pharmaceuticals Inc that includes: consulting or advisory and speaking and lecture fees. Tore K Kvien reports a relationship with Sandoz Inc that includes: consulting or advisory and speaking and lecture fees. Tore K Kvien reports a relationship with AbbVie Inc that includes: consulting or advisory and funding grants. Tore K Kvien reports a relationship with Gilead Sciences that includes: consulting or advisory. Tore K Kvien reports a relationship with Novartis that includes: consulting or advisory and funding grants. Tore K Kvien reports a relationship with Pfizer that includes: consulting or advisory and funding grants. Tore K Kvien reports a relationship with UCB that includes: consulting or advisory and funding grants. Sella Aarestad Provan reports a relationship with Pfizer and Boehringer Ingelheim that includes: consulting or advisory. Hilde Berner Hammer reports a relationship with AbbVie that includes: consulting or advisory and speaking and lecture fees. Hilde Berner Hammer reports a relationship with Novartis that includes: consulting or advisory and speaking and lecture fees. Hilde Berner Hammer reports a relationship with UCB that includes: consulting or advisory. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.semarthrit.2024.152502.

References

[1] Matcham F, Rayner L, Steer S, Hotopf M. The prevalence of depression in rheumatoid arthritis: a systematic review and meta-analysis. Rheumatology 2013; 52:2136–48. https://doi.org/10.1093/rheumatology/ket169.
[2] Michelsen B, Kristianslund EK, Sexton J, et al. Do depression and anxiety reduce the likelihood of remission in rheumatoid arthritis and psoriatic arthritis? Data from the prospective multicentre NOR-DMARD study. Ann Rheum Dis 2017;76: 1906–10. https://doi.org/10.1136/annrheumdis-2017-211284.
[3] Rathbun AM, Reed GW, Harrold LR. The temporal relationship between depression and rheumatoid arthritis disease activity, treatment persistence and response: a systematic review. Rheumatology 2013;52:1785–94. https://doi.org/10.1093/rheumatology/kes356.
[4] Barton JL, Imboden J, Graf J, Glidden D, Yelin EH, Schillinger D. Patient-physician discordance in assessments of global disease severity in rheumatoid arthritis. Arthritis Care Res 2010;62:857–64. https://doi.org/10.1002/acr.20132.
[5] Fragoulis GE, Cavanagh J, Tindell A, et al. Depression and anxiety in an early rheumatoid arthritis inception cohort. associations with demographic, socioeconomic and disease features. RMD Open 2020;6:e001376. https://doi.org/10.1136/rmdopen-2020-001376.
[6] Hammer HB, Uhlig T, Kvien TK, Lampa J. Pain catastrophizing, subjective outcomes, and inflammatory assessments including ultrasound: results from a longitudinal study of rheumatoid arthritis patients. Arthritis Care Res 2018;70: 703–12. https://doi.org/10.1002/acr.23339.
[7] Geng Y, Gao T, Zhang X, Wang Y, Zhang Z. The association between disease duration and mood disorders in rheumatoid arthritis patients. Clin Rheumatol 2022;41:661–8. https://doi.org/10.1007/s10067-021-05967-2.
[8] EuroQol–a new facility for the measurement of health-related quality of life. Health Policy 1990;16:199–208.
[9] Pincus T, Summey JA, Soraci Jr SA, Wallston KA, Hummon NP. Assessment of patient satisfaction in activities of daily living using a modified Stanford Health Assessment Questionnaire. Arthritis Rheum 1983;26:1346–53.
[10] Kvien TK, Kaasa S, Smedstad LM. Performance of the Norwegian SF-36 Health Survey in patients with rheumatoid arthritis. II. A comparison of the SF-36 with disease-specific measures. J Clin Epidemiol 1998;51:1077–86.
[11] Gossec L, Paternotte S, Aanerud GJ, et al. Finalisation and validation of the rheumatoid arthritis impact of disease score, a patient-derived composite measure

of impact of rheumatoid arthritis: a EULAR initiative. Ann Rheum Dis 2011;70:935–42. https://doi.org/10.1136/ard.2010.142901.
[12] Jensen MP, Keefe FJ, Lefebvre JC, Romano JM, Turner JA. One- and two-item measures of pain beliefs and coping strategies. Pain 2003;104:453–69. https://doi.org/10.1016/s0304-3959(03)00076-9.
[13] Hammer HB, Fagerhol MK, Wien TN, Kvien TK. The soluble biomarker calprotectin (an S100 protein) is associated to ultrasonographic synovitis scores and is sensitive to change in patients with rheumatoid arthritis treated with adalimumab. Arthritis Res Ther 2011;13:R178. https://doi.org/10.1186/ar3503.
[14] Smolen JS, Aletaha D, McInnes IB. Rheumatoid arthritis. Lancet 2016;388:2023–38. https://doi.org/10.1016/s0140-6736(16)30173-8.
[15] Hammer HB, Bolton-King P, Bakkeheim V, et al. Examination of intra and interrater reliability with a new ultrasonographic reference atlas for scoring of synovitis in patients with rheumatoid arthritis. Ann Rheum Dis 2011;70:1995–8. https://doi.org/10.1136/ard.2011.152926.
[16] Wakefield RJ, Balint PV, Szkudlarek M, et al. Musculoskeletal ultrasound including definitions for ultrasonographic pathology. J Rheumatol 2005;32:2485–7.
[17] Matcham F, Norton S, Scott DL, Steer S, Hotopf M. Symptoms of depression and anxiety predict treatment response and long-term physical health outcomes in rheumatoid arthritis: secondary analysis of a randomized controlled trial. Rheumatology 2016;55:268–78. https://doi.org/10.1093/rheumatology/kev306.
[18] Matcham F, Davies R, Hotopf M, et al. The relationship between depression and biologic treatment response in rheumatoid arthritis: an analysis of the British Society for Rheumatology Biologics Register. Rheumatology 2018;57:835–43. https://doi.org/10.1093/rheumatology/kex528.
[19] Hammer HB, Michelsen B, Sexton J, et al. Swollen, but not tender joints, are independently associated with ultrasound synovitis: results from a longitudinal observational study of patients with established rheumatoid arthritis. Ann Rheum Dis 2019;78:1179–85. https://doi.org/10.1136/annrheumdis-2019-215321.
[20] Jarlborg M, Courvoisier DS, Lamacchia C, et al. Serum calprotectin: a promising biomarker in rheumatoid arthritis and axial spondyloarthritis. Arthritis Res Ther 2020;22:105. https://doi.org/10.1186/s13075-020-02190-3.
[21] Nordal HH, Brokstad KA, Solheim M, Halse AK, Kvien TK, Hammer HB. Calprotectin (S100A8/A9) has the strongest association with ultrasound-detected synovitis and predicts response to biologic treatment: results from a longitudinal study of patients with established rheumatoid arthritis. Arthritis Res Ther 2017;19:3. https://doi.org/10.1186/s13075-016-1201-0.
[22] Bandinelli F, Benucci M, Salaffi F, et al. Do new and old biomarkers of early undifferentiated arthritis correlate with Arthritis Impact Measurement Scales? Clin Exp Rheumatol 2021;39:79–83. https://doi.org/10.55563/clinexprheumatol/nqqx5k.
[23] Albeltagy ES, Elaziz SYA, Abozaid SY, El Zomor HM, Elhamed SSA. Interleukin 6, interleukin 17, disease-related and contextual factor association with depression, and its severity in patients with rheumatoid arthritis. Clin Rheumatol 2021;40:895–904. https://doi.org/10.1007/s10067-020-05326-7.
[24] Li F, Ai W, Ye J, et al. Inflammatory markers and risk factors of RA patients with depression and application of different scales in judging depression. Clin Rheumatol 2022;41:2309–17. https://doi.org/10.1007/s10067-022-06174-3.
[25] Anyfanti P, Gavriilaki E, Pyrpasopoulou A, et al. Depression, anxiety, and quality of life in a large cohort of patients with rheumatic diseases: common, yet undertreated. Clin Rheumatol 2016;35:733–9. https://doi.org/10.1007/s10067-014-2677-0.