Clinically suspect arthralgia and early rheumatoid arthritis: advances in imaging and impact on daily life

Boer, A.C.

8

Depression and anxiety associate with less remission after 1 year in rheumatoid arthritis

Aleid Boer
Tom Huizinga
Annette van der Helm - van Mil

Annals of the Rheumatic Diseases (2018) Jan 8. doi: 10.1136/annrheumdis-2017-212867

Depression and anxiety have been considered to influence disease activity, and with great interest we read the recently published report by Michelsen *et al.*[1] In this large, prospective, multicentre observational study, depression and anxiety reduced the likelihood of joint remission based on composite scores, in rheumatoid arthritis (RA) after 3 and 6 months. Differences were predominantly caused by subjective markers of disease activity rather than by C reactive protein or erythrocyte sedimentation rate. The study cannot prove causality; however, their findings imply that baseline depression/anxiety can impair the fulfilment of remission criteria during follow-up, influencing important treatment decisions.

As replication is a keystone in research, we aimed to validate their findings in an independent cohort, the Leiden Early Arthritis Clinic (EAC), to assess generalisability of the results. The EAC is a population-based inception cohort of patients with newly diagnosed arthritis that started in 1993; from 2010 onwards patients completed the Short Form-36 (SF-36) at baseline.[2]

We studied patients included between 2010 and 2014 who fulfilled the 2010 criteria for RA (n=343) and selected patients who completed the SF-36 (n=293). Patients with RA were treated according to the insight of the treating rheumatologist: standard therapy regimen consists of early initiation with methotrexate; in case of failure a second

Table 8.1: Baseline characteristics of patients with rheumatoid arthritis with versus without baseline depression/anxiety according to the MCS ≤38 or MH ≤56

	All patients (n=293)	Depressed/ anxious (n=81)	Not depressed/ anxious (n=212)	P value
Age, mean (SD)	57 (15)	54 (15)	58 (14)	0.02
Female, n (%)	193 (66)	58 (72)	135 (64)	0.20
Symptom duration in months, median (IQR)	3 (1-8)	3 (1-7)	3 (1-8)	0.72
Currently smoking, n (%)	65 (23)	25 (33)	40 (20)	0.08
ACPA positive, n (%)	162 (55)	43 (53)	119 (56)	0.64
ESR (mm/h) median (IQR)	28 (14-41)	28 (14-42)	28 (14-41)	0.85
CRP (mg/L), median (IQR)	10 (3-22)	7 (3-26)	10 (3-20)	0.76
EGA, mean (SD)	49 (20)	49 (24)	49 (19)	0.44
PGA, mean (SD)	45 (27)	54 (27)	42 (26)	0.001
Pain, mean (SD)	60 (25)	63 (24)	58 (25)	0.92
68-TJC, median (IQR)	10 (5-17)	11 (6-19)	10 (5-16)	0.18
66-SJC, median (IQR)	5 (2-11)	5 (2-10)	6 (2-11)	0.14
DAS44, mean (SD)	2.9 (0.8)	3.0 (0.8)	2.9 (0.8)	0.45

Pain measured by a 0-100 Visual Analogue Scale (VAS). 68-TJC, 68 tender joint counts; 66-SJC, 66 swollen joint counts; ACPA, anticitrullinated peptide antibody; CRP, C reactive protein; DAS44, 44-joint Disease Activity Score; EGA, evaluator's global assessment by a 0–100 VAS; ESR, erythrocyte sedimentation rate; MCS, mental component summary; MH, mental health subscale; PGA, patient's global assessment by a 0–100 VAS; VAS, Visual Analogue Scale.

synthetic disease-modifying antirheumatic drug (DMARD) was prescribed and in case of failure a biologic DMARD was allowed.[3] Outcome of joint remission was 44-joint Disease Activity Score (DAS44 ≤2.4) after 1-year.[4, 5] Similar as Michelsen *et al.* we identified depression/anxiety by the SF-36 mental health subscale (MH ≤56) and SF-36 Mental Component Summary (MCS ≤38).

Baseline characteristics are shown in Table 8.1. The percentage of depressed/anxious RA-patients was 20% according to the SF-36MCS ≤ 38, and 23% according to the SF-36MH ≤56. Anxious/depressed patients were significantly younger and had a higher patient global assessment (Table 18.1). Anxiety and depression were negatively associated with achieving DAS remission after 1 year, analysed with logistic regression models corrected for age, gender and symptom duration (OR=0.21, 95% CI 0.09 to 0.46 for MCS; OR=0.24, 95% CI 0.11 to 0.51 for MH; p<0.001; Figure 8.1). Analyses with additional correction for baseline DAS showed similar results (MCS p<0.001; MH p=0.001). Further analyses on features of disease activity at year 1 showed that anxiety/depression was associated with more pain (β=12.1, p< 0.001 for MCS; β=11.1, p=0.03 for MH) and a trend for a higher patient's global assessment (β=9.0, p=0.07 for MCS).

Thus, our study on the association of baseline anxiety and depression with remission after 1 year validated the findings from Michelsen *et al.*. We observed higher percentages of patients with RA in DAS remission, which could be caused by the longer duration of treatment (evaluation of remission at 1 year, instead of 3 and 6 months by Michelsen *et al.*).

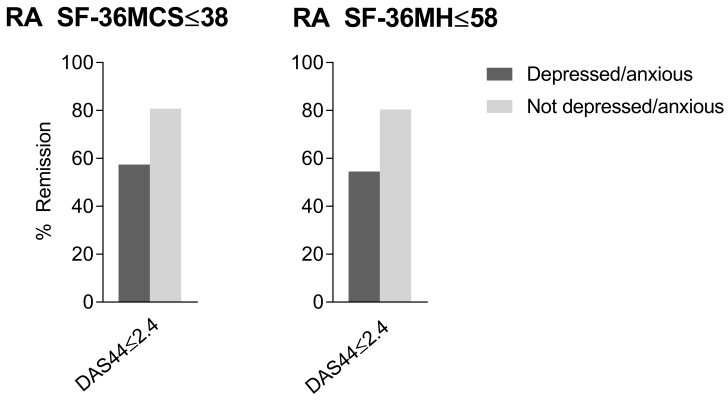

Figure 8.1: Percentages of patients with RA in remission at 1 year (DAS44 ≤2.4) for RA patients that did or did not have depression/anxiety at the time of diagnosis. DAS44, 44-joint Disease Activity Score; RA, rheumatoid arthritis; SF-36 MCS, Medical Outcomes Survey Short Form-36 mental component summary; SF-36 MH, Medical Outcomes Survey Short Form-36 mental health subscale.

Concluding, baseline depression and anxiety are associated with a lower chance to achieve DAS remission, which was mostly reflected by associations with subjective features of disease activity. Also our study cannot prove causality, although the association between the mental state and DAS components suggests that efforts to improve the psychological well-being early in the disease course may prevent higher DAS scores later on. This could potentially prevent increased medical costs due to more intensified treatment strategies.

References

[1] Michelsen B, Kristianslund EK, Sexton J, Hammer HB, Fagerli KM, Lie E, 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;76:1906–1910.

[2] de Rooy DP, van der Linden MP, Knevel R, Huizinga TW, van der Helm-van Mil AH. Predicting arthritis outcomes–what can be learned from the Leiden Early Arthritis Clinic? Rheumatology (Oxford). 2011;50:93–100.

[3] Ajeganova S, van Steenbergen HW, van Nies JA, Burgers LE, Huizinga TW, van der Helm-van Mil AH. Disease-modifying antirheumatic drug-free sustained remission in rheumatoid arthritis: an increasingly achievable outcome with subsidence of disease symptoms. Ann Rheum Dis. 2016;75:867–73.

[4] Combe B, Landewe R, Lukas C, Bolosiu HD, Breedveld F, Dougados M, et al. EULAR recommendations for the management of early arthritis: report of a task force of the European Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT). Ann Rheum Dis. 2007;66:34–45.

[5] Goekoop-Ruiterman YP, de Vries-Bouwstra JK, Allaart CF, van Zeben D, Kerstens PJ, Hazes JM, et al. Clinical and radiographic outcomes of four different treatment strategies in patients with early rheumatoid arthritis (the BeSt study): a randomized, controlled trial. Arthritis Rheum. 2005;52:3381–90.