EJR European Journal of Rheumatology

DOI:10.5152/eurjrheum.2024.24014

Original Article

Diagnosis of Mental Disorders Complicated by Rheumatoid Arthritis: A Study of the Validity of a Questionnaire Method and Diagnosis by the Psychiatrist

Miwa Yusuke[1], Tomioka Hiroi[2], Miwa-Mitamura Yuko[3]

Abstract

Objective: Rheumatoid arthritis (RA) is associated with depression in approximately 15% of patients, most of whom have been studied using questionnaires. As the depression questionnaire includes questions about physical symptoms, caution should be exercised when interpreting the results due to an underlying disease. In addition, few studies have been conducted on other psychiatric disorders. Here, we examined the validity of diagnosing rheumatoid arthritis complicated by psychiatric disorders using a questionnaire.

Methods: Forty-nine outpatients with RA who consented to participate in this study were included. The patient background information included age, sex, type of anti-rheumatic drug, prednisolone use, presence of diabetes, hypertension, dyslipidemia, and C-reactive protein. The Patient Health Questionnaire-9 (PHQ-9) and Center for Epidemiologic Studies Depression Scale (CES-D) questionnaires were used; scores of ≥10 on the PHQ-9 and ≥16 on the CES-D were considered the cut-off. The psychiatrist was blinded to the questionnaire results and arrived at a diagnosis based on the Diagnostic and Statistical Manual of Mental Disorders-IV (DSM) in a separate room. Additionally, the specificity and sensitivity of the PHQ-9 and CES-D were examined.

Results: Eleven patients had abnormal psychiatric diagnoses. The PHQ-9 had a specificity of 0.98, a sensitivity of 0.36, a positive predictive value of 0.80, and a negative predictive value of 0.89. The CES-D had a specificity of 0.87, a sensitivity of 0.91, a positive predictive value of 0.51, and a negative predictive value of 0.98.

Conclusion: The PHQ-9 and CES-D may help screen for psychiatric disorders associated with RA.

Keywords: Rheumatoid arthritis, psychology, patient-reported outcome measures

ORCID iDs of the authors:
M.Y. 0000-0001-5956-7974;
T.H. 0009-0000-4501-3030;
M-M.Y. 0000-0002-0425-5145.

Cite this article as: Yusuke M, Hiroi T, Yuko M. Diagnosis of mental disorders complicated by rheumatoid arthritis: A study of the validity of a questionnaire method and diagnosis by the psychiatrist. *Eur J Rheumatol.* 2024;11(4):405-409.

[1] Division of Rheumatology, Department of Medicine, Showa University School of Medicine, Tokyo, Japan
[2] Department of Psychiatry, Showa University School of Medicine, Kanagawa, Japan
[3] Department of Nursing and Rehabilitation Sciences, Showa University, Tokyo, Japan

Corresponding author:
Miwa Yusuke
E-mail: y.miwa@mbf.ocn.ne.jp

Received: May 22, 2024
Revision requested: June 27, 2024
Last revision received: July 20, 2024
Accepted: August 14, 2024
Publication Date: November 27, 2024

Introduction

Various diseases complicate RA. Depression is the most common complication, accounting for approximately 15%.[1] The odds ratio is 1.42 (95% CI 1.3-1.5) compared with healthy controls.[2] Twenty-two percent of patients with RA reported mental symptoms such as depression, anxiety, panic, etc., as "symptoms other than joint symptoms" in the 2020 White Paper on Rheumatology, while 23.3% of RA patients stated "mental health care" as one of their "requests for medical care," indicating that patients' needs are not small.[3]

A study on the factors involved in joint pain in RA revealed that joint pain is associated with various factors, with depression being the common factor, rather than morning stiffness or disease activity.[4] However, anxiety and joint pain are not correlated and have been reported as features of psychological status in RA.[5] It has also been stated that when depression is complicated by RA, complication and hospitalization rates are higher, and survival rates are lower than in normal depression.[7] When depression is associated with rheumatoid arthritis, treatment of rheumatoid arthritis itself may improve the associated depression attributed to high disease activity.[7,8,9]

Regarding the diagnostic methods and condition assessment of depression associated with RA using the Diagnostic and Statistical Manual of Mental Disorders (DSM), the reporting years ranged from 1998-2010.[10-13] Furthermore, general judgment was arduous owing to the significant progress in treating RA during this period, such as biological drug therapy. On the contrary, the Hospital Anxiety and Depression Scale (HAD-S), The Center for Epidemiologic Studies Depression Scale (CES-D), Beck Depression Inventory (BDI), and Patient Health Questionnaire-9 (PHQ-9) calculated only the percentage of depression.[14] In previous

reports, the CES-D, BDI, and PHQ-9 have been commonly used as diagnostic indicators for RA and depression.[15] However, the Japanese version of the BDI is intended for people aged 13 to 80 years and was not used in this study because it included patients aged 80 years or older. In the presence of an underlying disease, diagnosing depression and other psychiatric disorders is challenging, and diagnosis by an experienced psychiatrist is required. Hence, in our novel study, we examined the validity of diagnosing RA complicated by psychiatric disorders using the CES-D and PHQ-9.

Material and Methods

Participants and Sampling Method

The target patients included 66 RA patients who visited the Department of Internal Medicine, Showa University Northern Yokohama Hospital. Additionally, they consented to this study and were available for investigation. The target age group was 18 years and older. The American college of rheumatology/European league against rheumatism (ACR/EULAR) (2010) criteria for the classification of RA were used.[16]

Study Period, Study Design, and Study Items

This cross-sectional study was conducted from August 1, 2020, to July 30, 2022, and included patients enrolled during the same period. Patients who did not consent to the study or could not schedule an interview with a psychiatrist were excluded. Study items included age, sex, disease duration, smoking history, body mass index (BMI), prednisolone use, methotrexate use, and other conventional antirheumatic drugs. Laboratory tests used erythrocyte sedimentation rate, C-reactive protein (CRP), rheumatoid factor, and serum matrix metalloproteinase-3 (MMP-3) levels, which are commonly used as indicators for the diagnosis of RA and the evaluation of disease activity. No additional laboratory tests were conducted. The Simplified Disease Activity Index (SDAI), a composite assessment index, was used to evaluate disease activity in RA.[17] Simplified Disease Activity Index (SDAI) is widely used as a disease activity assessment index for RA, with a score of ≤11 indicating low disease activity, a score ≥11 or less than 26 indicating moderate disease activity, and a score >26 points indicating high disease activity. The PHQ-9 and CES-D were employed as questionnaire tables.[18,19,20] A commercially available product was purchased and used; for the PHQ-9, a cutoff score of ≥10 and CES-D ≥16 points were used. Receiver operating characteristic (ROC) curves were plotted for each patient.

Psychiatric Diagnostic Methods

The psychiatrist (H.T.) was blinded to the results of the assessment of disease activity of RA, PHQ-9, and CES-D. Furthermore, they assessed the patient in a separate room from the examination room where RA was treated. Psychiatric diagnoses were made according to H.T. One psychiatrist (H.T.) was interviewed to prevent diagnostic bias among physician psychiatrists. The psychiatrist made the diagnosis based on DSM-IV as a method. Participants completed the PHQ-9 and CES-D, handed them over to Y.M., and were then interviewed by a psychiatrist on the same day.

Statistical Analyses

The specificity, sensitivity, positive predictive value, and negative predictive value of the PHQ-9 and CES-D were calculated using the diagnosis made by the psychiatrist as the gold standard. We used the EZR statistical software (ver. 2.5-1, Saitama Medical Center, Jichi Medical University, Saitama, Japan), a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria).[21]

Ethical Considerations

The ethical considerations were approved by the Clinical Trial Review Committee of Showa University Northern Yokohama Hospital (No. 20H029, approved on July 15, 2020). Written informed consent was obtained from all study participants.

Results

Seventy patients were included in the study. The mean age was 65.4 years, and 72.6% were female, which is a typical population for RA (Table 1). In addition, the mean SDAI was 5.1, indicating low disease activity, which is in line with the current standard population for RA in Japan. The study required a 30-minute interview with a psychiatrist, and 88 patients were enrolled, excluding 16 who could not participate in the study due to schedule or time constraints, 6 who disagreed with the survey, and 4 with other psychiatric diseases (one with neurosis, 1 with anxiety, and 2 with adjustment disorders) (Figure 1). Of 62 patients, the psychiatrists diagnosed 1 patient with major depression, 1 with moderate depression, and 5 with mild depression. The remaining 55 patients were found to be without a psychiatric diagnosis.

The mean patient age was 65.4 years, and 45 (72.6%) were female. The distribution of PHQ-9 scores indicated that 4 patients had a PHQ-9 score of 10 or higher, 3 patients had significant depression, and 1 was diagnosed as healthy by a psychiatrist (Table 2). The sensitivity was not high at 0.429; however, the specificity was 0.982, the positive predictive value (PPV) was 0.75, and the negative predictive value (NPV) was 0.931, which was relatively high. The ROC curve depicted an area under the curve (AUC) of 0.887 (95% CI 0.794-0.980), **which showed moderate diagnostic performance**.

The distribution of CES-D scores established that 12 patients had a CES-D score of ≥16; 7 patients had significant depression while 5 patients were diagnosed as healthy by a psychiatrist (Table 2). The sensitivity was high at 1.0. However, the specificity was 0.909. The PPV was 0.583, and the NPV was 1.0, which was relatively high. The ROC curve indicated an AUC of 0.943 (95% CI 0.886-1.0), which was judged to be a helpful indicator.

Discussion

In the present study, we examined the validity of psychiatrist diagnostic methods and questionnaire methods by semi-structured diagnostic interviews for diagnosing psychiatric disorders in patients with RA. A fully structured interview is characterized by asking all patients the same questions in a set order, and the patient's performance is judged based on predetermined evaluation criteria. A semi-structured interview is characterized by asking all patients the same questions, and then the interviewer asks individual questions, and the patient's performance is judged based on both the predetermined evaluation criteria and the interviewer's judgment.[22]

Studies on the sensitivity and specificity of the PHQ-9 and CES-D in the general population have been reported, and the results of analyses using the PHQ-9 vary depending on where the

Main Points

- Although psychiatric disorders are a frequent complication of rheumatoid arthritis (RA), affecting about 15%, a questionnaire is used for their diagnosis. There are no reports on the validity of psychiatrists' diagnoses and psychiatric disorder questionnaires in rheumatoid arthritis.
- The PHQ-9 and CES-D may help screen for psychiatric disorders associated with RA.
- The PHQ-9 and CES-D are useful as screeners for diagnosing psychiatric disorders associated with rheumatoid arthritis.

Table 1. Baseline Characteristics of RA Patients

Factors	
n	62
Age (year)	65.4 ± 15.3
Sex (female), n (%)	45 (72.6)
Disease duration (month)	81 ± 157
Class (1 : 2 : 3 : 4)	33 : 22 : 5 : 2
Body mass index (kg/m^2)	22.8 ± 4.3
Smoking history, yes (%)	24 (39.9)
Prednisolone use, yes (%)	25 (40.3)
Prednisolone dosage (mg/day) (user only)	5.6 ± 5.4
Methotrexate use, yes (%)	38 (61.3)
Methotrexate dosage (mg/week) (user only)	8.4 ± 2.8
csDMARDs use, yes (%)	27 (40.9)
bDMARDs use, yes (%)	10 (16.1)
NSAIDs use, yes (%)	15 (22.7)
Diabetes, yes (%)	6 (9.1)
Hypertension, yes (%)	24 (36.3)
Dyslipidemia, yes (%)	14 (21.2)
Tender joint count	1.24 ± 2.49
Swollen joint count	0.48 ± 1.05
Patient VAS (mm)	21.0 ± 26.9
Dr VAS (mm)	7.2 ± 12.3
SDAI	5.1 ± 5.5
CRP (mg/dL)	0.6 ± 1.1
Serum MMP-3 (ng/mL)	132.3 ± 163.2
RF (IU/mL)	87.8 ± 222.9

bDMARDs, biological disease-modifying anti-rheumatic drugs; csDMARDs, conventional synthetic disease-modifying anti-rheumatic drugs; MMP-3, matrix metalloproteinase-3; NSAIDs, non-steroidal anti-inflammatory drugs; RF, rheumatoid factor; SDAI, simplified disease activity index; VAS, visual analog scale.

gold standard is set; however, the semi-structured diagnostic interview had a sensitivity of 0.85, a specificity of 0.85, and a sensitivity of 0.64 for the fully structured diagnostic interview. The sensitivity and specificity of the semi-structured diagnostic interview were 0.85 and 0.85, respectively, while the sensitivity and specificity of the fully structured diagnostic interview

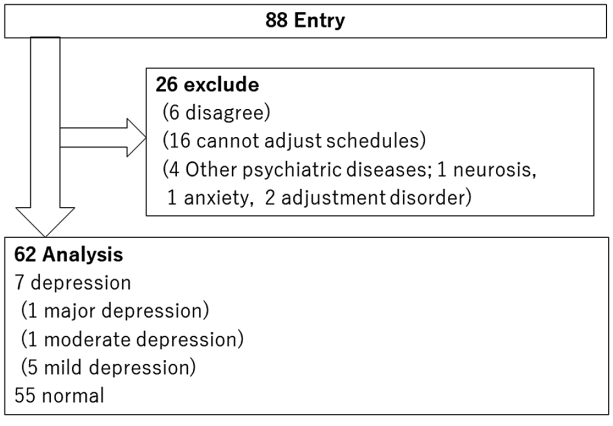

Figure 1. Flow chart of the study.

Table 2. Summary of the PHQ-9 and CES-D

		Depression	
	Score	Yes	No
PHQ-9	≥ 10	3	1
	< 9	4	54
CES-D	≥ 16	7	5
	>15	0	50

CES-D, The Center for Epidemiologic Studies Depression Scale; PHQ-9, Patient Health Questionnaire-9.

were 0.64 and 0.88, respectively. Furthermore, the sensitivity and specificity of the Mini International Neuropsychiatric Interview (MINI) were reported to be 0.74 and 0.89, respectively. In a study using the CES-D, the sensitivity was reported to be 1.0, the specificity was 0.909, the positive predictive value was 0.583, and the negative predictive value was 1.0.[23,24] Compared to the present study, the PHQ-9 had high specificity but low sensitivity. However, the sensitivity and specificity of CES-D were at the same level. Regarding the differences between the results of the CES-D and PHQ-9, the PHQ-9 has 9 items and the CES-D has 20 items. The CES-D focuses on identifying high-risk groups within the community. The items consist of 5 items about depressed mood, 8 about physical symptoms, 2 about interpersonal relationships, and 4 questions about positive emotions. The items about depressed mood and physical symptoms are not significantly different from other depression scales, but the CES-D is unique in that it asks about the extent to which people feel positive emotions and evaluations of others in interpersonal relationships daily. On the other hand, the PHQ-9 has questions that correspond one-to-one with the DSM-IV diagnostic criteria, and each question contains multiple questions. Differences in the questionnaire characteristics may be reflected in the results.

Compared with a previous report in patients with RA, the PHQ-9's sensitivity and positive predictive value were low.[15] In contrast, the present study's specificity and negative predictive value were similar. Although there were no significant differences in patient backgrounds, the cause was unclear due to regional factors.

The strengths of this study are as follows: (1) The interviewers who conducted psychiatric diagnoses were psychiatrists with extensive medical experience. Psychiatric diagnosis of patients with underlying diseases is considered challenging, especially for RA patients, whose main symptoms are joint pain and fatigue; however, there is an overlap with

Table 3. Sensitivity, Specificity, PPV, and NPV for PHQ-9 and CES-D

	Sensitivity	Specificity	PPV	NPV
PHQ-9	0.429	0.982	0.75	0.931
CES-D	1	0.909	0.583	1

CES-D, The Center for Epidemiologic Studies Depression Scale; NPV, negative predictive value; PHQ-9, Patient Health Questionnaire-9; PPV, positive predictive value.

symptoms seen in depression, and it is arduous to determine the cause. In a previous report, the diagnosis was made by a graduate student of clinical psychology, a nurse, and a research coordinator. However, with extensive clinical experience, the psychiatrist who conducted this study made a precise diagnosis. (2) The questionnaire results were blinded to factors influencing the psychiatric diagnosis, such as RA disease activity. (3) The questionnaires used for the comparative study included the PHQ-9 and HADS-D from previous reports; however, the PHQ-9 and CES-D were used in the present study. Although the PHQ-9 was used as a standard item and the CES-D, which had not been examined before, was used, the sensitivity and specificity of the CES-D were clarified. However, they cannot be compared because of differences in research participants and methods.

However, the study's limitations are as follows: 1) It is a medium-scale study at a limited number of institutions (university hospitals and Yokohama City), and these results have only been reported for a limited number of facilities in previous studies because it is difficult to standardize standards between facilities, such as standardizing diagnostic criteria among psychiatrists and evaluations by rheumatologists; 2) the disease activity of RA is low and is consistent with the current status of RA treatment and reflects the current evaluation; 3) 21 (30%) of 70 eligible patients were excluded, and there is a possibility that psychiatric patients may be latent in this group, which is a problematic issue; 4) there is only 1 psychiatrist who made the psychiatric diagnoses. Interviews for psychiatric diagnoses are the gold standard, and their evaluation needs to be consistent, which makes it difficult to conduct studies at multiple institutions. The number of people who could be studied was limited because of the time required for interviews in this type of research. Regarding this, it would be desirable to have 2 interviewers conduct each interview independently, but there is a limit when considering the time burden of interviewing patients.

Future studies should be conducted with-with an increased cases. This is because the percentage of patients with abnormalities in psychiatric diagnoses was small. This may be due to decreased disease activity with advances in the treatment of RA and a lower incidence of depression and other disorders.[8] Additionally, it is desirable to develop a questionnaire that is more sensitive and specific than the current one and to develop a composite evaluation index that includes disease activity and blood test findings of RA.

Conclusion

A study on the validity of the questionnaire and diagnostic methods of psychiatrists in diagnosing psychiatric disorders in patients with RA indicated that the sensitivity of the PHQ-9 and the sensitivity and specificity of the CES-D were relatively high. However, the specificity of the PHQ-9 was low. These results suggest that the PHQ-9 and CES-D may help screen for psychiatric disorders associated with RA.

Ethics Committee Approval: This study was approved by the Ethics Committee of Showa University Northern Yokohama Hospital (Approval No: 20H029 Date: July 15, 2020).

Informed Consent: Written informed consent was obtained from all study participants.

Peer-review: Externally peer reviewed.

Acknowledgments: Nobuyuki Yajima, Sakiko Isojima, Ryo Yanai, Nao Oguro, Sho Ishii, Shinichiro Nishimi, Noriko Konishi, Kazutaka Kawamori, Ryo Inoue, and Kosuke Sakurai at Division of Rheumatology, Department of Medicine, Showa University School of Medicine, Tokyo, Japan. We thank Editage (www.editage.jp) for editing the English language.

Author Contributions: Concept – M.Y., M-M. Y.,H.T.; Design – M.Y.H.T.; Supervision – M.Y.; Materials – M.Y. H.T.; Data Collection and Processing – M.Y., M-N. Y., H.T.; Analysis and Interpretation – M-M. Y., H.T.; Literature Review – M.Y; Writing Manuscript – M.Y.; Critical Review – M.Y., M-M. Y., H.T.

Declaration of Interests: The authors have no conflict of interest to declare.

Funding: The authors declared that this study has received no financial support.

References

1. Dougados M, Soubrier M, Antunez A, et al. Prevalence of comorbidities in rheumatoid arthritis and evaluation of their monitoring: results of an international, cross-sectional study (COMPRA). *Ann Rheum Dis*. 2014;73(1):62-68. [CrossRef]
2. Margaretten ME, Katz P, Schmajuk G, Yelin E. Missed opportunities for depression screening in patients with arthritis in the United States. *J Gen Intern Med*. 2013;28(12):1637-1642. [CrossRef]
3. Japan Rheumatism Friendship Foundation. 2020 White Paper on Rheumatism – the reality of rheumatoid arthritis patients. *Nagare*. 2021;16:356, Tokyo, Japan.
4. Hosaka M, Matsushima D, Saito N, et al. Research on factors influencing joint pain in patients with rheumatoid arthritis. *Japanese Society of Psychosomatic Medicine*. 1999;39:87.
5. Miwa Y, Yajima N, Shiozawa F, et al. Relationship between psychological factors and arthralgia in patients with rheumatoid arthritis. *Mod Rheumatol*. 2002;12(1):32-36. [CrossRef]
6. Nakada J, Nakamura A. Depression is closely associated with quality of life and the development of complications in patients with rheumatoid arthritis. *Clin Rheumatol*. 2008;20:284-290.
7. Miwa Y, Nishimi A, Nishimi S, et al. Combined infliximab and methotrexate treatment improves the depressive state in rheumatoid arthritis patients more effectively than methotrexate alone. *Eur J Rheumatol*. 2014;1(4):147-149. [CrossRef]
8. Miwa Y, Isojima S, Saito M, et al. Comparative study of infliximab therapy and methotrexate monotherapy to improve the clinical effect in rheumatoid arthritis patients. *Intern Med*. 2016;55(18):2581-2585. [CrossRef]
9. Miwa Y, Hosaka M, Ohtsuka K, et al. Depression is improved when low-dose tacrolimus is given to rheumatoid arthritis patients, showing an inadequate response to biological agents. *Mod Rheumatol*. 2013;23(5):920-924. [CrossRef]
10. Abdel-Nasser AM, Abd El-Azim SA, Taal E, El-Badawy SA, Rasker JJ, Valkenburg HA. Depression and depressive symptoms in rheumatoid arthritis patients: an analysis of their occurrence and determinants. *Br J Rheumatol*. 1998;37(4):391-397. [CrossRef]
11. Frank RG, Beck NC, Parker JC, et al. Depression in rheumatoid arthritis. *J Rheumatol*. 1988;15(6):920-925.
12. Lok EYC, Mok CC, Cheng CW, Cheng CW, Cheung EFC. Prevalence and determinants of psychiatric disorders in patients with rheumatoid arthritis. *Psychosomatics*. 2010;51(4):338-338.e8. [CrossRef]
13. Uguz F, Akman C, Kucuksarac S, Tufekci O. Anti-tumor Necrosis Factor-alpha therapy is associated with less frequent mood and anxiety disorders in patients with rheumatoid arthritis. *Psychiatry Clin Neurosci*. 2009;63(1):50-55. [CrossRef]

14. Matcham F, Rayner L, Steer S, Hotopf M. The prevalence of depression in rheumatoid arthritis: a systematic review and meta-analysis. *Rheumatology (Oxford)*. 2013;52(12):2136-2148. [CrossRef]
15. Hitchon CA, Zhang L, Peschken CA, et al. Validity and reliability of screening measures for depression and anxiety disorders in rheumatoid arthritis. *Arthritis Care Res*. 2020;72(8):1130-1139. [CrossRef]
16. Aletaha D, Neogi T, Silman AJ, et al. 2010 Rheumatoid arthritis classification criteria: an American College of Rheumatology/Europian League Against Rheumatism collaborative initiative. *Ann Rheum Dis*. 2010;69(9):1580-1588. [CrossRef]
17. Aletaha D, Ward MM, Machold KP, Nell VPK, Stamm T, Smolen JS. Remission and active disease in rheumatoid arthritis: defining criteria for disease activity states. *Arthritis Rheum*. 2005;52(9):2625-2636. [CrossRef]
18. Muramatsu K, Miyaoka H, Kamijima K, et al. Performance of the Japanese version of the Patient Health Questionnaire-9 (J-PHQ-9) for depression in primary care. *Gen Hosp Psychiatry*. 2018;52:64-69. [CrossRef]
19. Radloff LS. The CES-D Scale: a self-report depression scale for research in the general population. *Appl Psychol Meas*. 1977;1(3):385-401. [CrossRef]
20. Shima S, Shikano T, Kitamura T, et al. New self-rating scales for depression. *Clin Psychiatry*. 1985;27:717-723.
21. Kanda Y. Investigation of the freely available easy-to-use software 'EZR' for medical statistics. *Bone Marrow Transplant*. 2013;48(3):452-458. [CrossRef]
22. Brugha TS, Bebbington PE, Jenkins R. A difference that matters: comparisons of structured and semi-structured psychiatric diagnostic interviews in the general population. *Psychol Med*. 1999;29(5):1013-1020. [CrossRef]
23. Negeri ZF, Levis B, Sun Y, et al. Accuracy of the Patient Health Questionnaire-9 for screening to detect significant depression: updated systematic review and individual participant data meta-analysis. *BMJ*. 2021;374:n2183.
24. Vilagut G, Forero CG, Barbaglia G, Alonso J. Screening for depression in the general population with the center for epidemiologic studies depression (CES-D): a systematic review with meta-analysis. *PLoS One*. 2016;11(5):e0155431. [CrossRef]