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Anxiety and depression in rheumatoid arthritis patients: prevalence, risk factors and consistency between the Hospital Anxiety and Depression Scale and Zung's Self-rating Anxiety Scale/Depression Scale

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Abstract

Objectives: The aim was to explore the prevalence and independent risk factors for anxiety and depression in RA patients and to assess the consistency between the hospital anxiety and depression scale (HADS) and Zung's self-rating anxiety scale/depression scale (SAS/SDS).

Methods: In total, 160 RA patients and 60 healthy controls (HCs) were enrolled consecutively, and HADS and SAS/SDS were completed.

Results: The HADS-defined anxiety rate, HADS-defined depression rate, SAS-defined anxiety rate and SDS-defined depression rate were 36.9, 36.3, 29.4 and 29.4%, respectively, in RA patients, all of which were much higher in RA patients than in HCs (all $P < 0.001$). A relatively high consistency was observed between HADS-defined anxiety and SAS-defined anxiety ($\kappa = 0.551$, $P < 0.001$) and between HADS-defined depression and SDS-defined depression ($\kappa = 0.563$, $P < 0.001$) in RA patients. Interestingly, screened by multivariate logistic regression analyses, single/divorced/widowed marital status, swollen joint count, disease duration, ESR, physician's global assessment (PhGA) and DAS28 were independently correlated with HADS-defined or SAS-defined anxiety risk in RA patients; meanwhile, female biological sex, single/divorced/widowed marital status, rural location, disease duration, PhGA and DAS28 were independently associated with HADS-defined or SDS-defined depression risk in RA patients.

Conclusion: Anxiety and depression are highly prevalent in RA patients and are independently correlated with single/divorced/widowed marital status and higher disease activity. In addition, the HADS presents a high consistency with the SAS/SDS with many fewer questions, which might be more suitable for long-term assessment of RA.

Lay Summary

What does this mean for patients?

People with RA also frequently have mental health conditions, such as anxiety and depression. We wanted to see what percentage of people with RA have mental health conditions and which aspects of RA affect the occurrence of these mental health conditions. We also wanted to compare two questionnaires used to diagnose mental health conditions, namely the hospital anxiety and depression scale and Zung's self-rating anxiety scale/depression scale. In this study, we investigated 160 people with RA and 60 healthy people. We found that mental health conditions are common in people with RA; between 29.4 and 36.9% of people in our study had anxiety, and between 29.4 and 36.3% had depression. These rates are higher than those seen in healthy people. Many factors could affect the occurrence of mental health conditions, including marital status, joint status, disease duration and inflammation status. The two questionnaires produced consistent results when evaluating mental health conditions of patients. However, the hospital anxiety and depression scale has fewer questions and might therefore be more suitable for long-term assessment of RA.

Keywords: rheumatoid arthritis, anxiety, depression, consistency, risk factors.

Key messages

- The anxiety and depression rates were higher in RA patients than in healthy controls.
- High consistency between HADS-defined anxiety/depression and SAS/SDS-defined anxiety/depression was observed in RA patients.
- Some independent risk factors for anxiety or depression in RA patients were observed.

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Introduction

RA is a chronic autoimmune disease characterized by affected joints and systemic inflammation that impacts 0.24% of the worldwide population and has a higher prevalence in females than in males [1, 2]. Although encouraging advancements have been made in RA management, such as the introduction of novel biologics and small-molecule drugs [3–5] and the deep exploration of treatment strategies (treat-to-target, tapering, etc.), RA remains an incurable disease with a high risk of flares and a threat of disability [6]. Furthermore, RA patients commonly have extra-articular diseases, such as cardiovascular injuries and interstitial pneumonia [7]. The above issues greatly aggravate the psychological pressure on RA patients, leading to a high prevalence of mental disorders [8, 9].

Previous papers have reported that anxiety and depression are highly prevalent in RA patients, indicating that the anxiety rate might even be as high as 69.6% and the depression rate as high as 14–58.3% [10–15]. Meanwhile, other studies have observed that anxiety or depression is related to pain degree, quality of life, and sleep disturbance in RA patients [16, 17]. However, previous studies have applied only a single scale to evaluate anxiety and depression, and the independent risk factors related to their occurrence have seldom been investigated; moreover, the consistency between different scales in RA patients has also not been reported sufficiently.

Therefore, in the present study we applied two types of anxiety and depression scales, namely the hospital anxiety and depression scale (HADS) and Zung's self-rating anxiety scale/depression scale (SAS/SDS), aiming to investigate the prevalence and independent risk factors for anxiety and depression in RA patients and to evaluate the consistency between the two scales.

Methods

Subjects

In this study, 160 RA patients who came to our hospital from December 2022 to February 2023 were enrolled. The inclusion criteria were as follows: diagnosed with RA based on the ACR/EULAR (2010) or ARA (1987) classification criteria of RA [18, 19]; aged >18 years; and participating in this study voluntarily. The exclusion criteria were as follows: a history of malignant tumour; a history of psychosis or mental disorder; a history of major surgery; moderate or severe cognitive impairment and could not complete the study questionnaire normally; and pregnant or lactating women. Additionally, a total of 60 healthy people were recruited as healthy controls. The eligibility criteria were as follows: without abnormality in a physical examination and biochemical indexes; age- and biological sex-matched with RA patients; without moderate or severe cognitive impairment; without a history of malignant tumour, psychosis or mental disorder, major surgery or autoimmune diseases; and understood the study protocol. In addition, ethical approval was obtained from the Ethics Committee of the Affiliated Suqian First People's Hospital with approval number 2023-SL-0005. Informed consent was signed by each subject.

Data collection

Clinical features of RA patients were collected, including demographics, medical histories, disease features and medications. In addition, questionnaires for the HADS for anxiety (HADS-A), HADS for depression (HADS-D), SAS and SDS were completed by all subjects.

Assessment

The anxiety and depression of all subjects were assessed. Anxiety was defined as a HADS-A score ≥8 or a SAS score ≥50, and depression was defined as a HADS-D score ≥8 or an SDS score ≥50 [20, 21]. Anxiety and depression rates were both calculated. Additionally, the severity of anxiety was divided into none (<8 on the HADS-A or <50 on the SAS), mild (HADS-A score = 8–10 or SAS score = 50–59), moderate (HADS-A score = 11–14 or SAS score = 60–69) and severe (HADS-A score ≥ 5 or on SAS score ≥ 70). Likewise, the severity of depression was classified as none (HADS-D score < 8 or SDS score < 50), mild (HADS-D score = 8–10 or SDS score = 50–59), moderate (11–14 on HADS-D score or 60–69 SDS score) and severe HADS-D score ≥ 15 or SDS score ≥ 70) [22, 23].

Statistics

SPSS v.22.0 (IBM, USA) and GraphPad Prism v.7.0 (GraphPad Software, USA) were applied for data analysis and figure construction, respectively. The normality of the data was checked by the Kolmogorov–Smirnov test. Data were normally distributed are presented as the mean ± SD, whereas data that were not normally distributed are presented as the median (range). Categorical variables are presented as a number (percentage). Unpaired student's *t*-test, the χ^2 test or Fisher's exact test was used for analysis of comparisons. Univariate and stepwise multivariate logistic regression models were built, in which all continuous variates were divided into high and low (cut by the median value). Pearson's test was used for analysis of correlations. Cohen's κ was used for evaluation of consistency. A value of $P < 0.05$ indicated statistical significance.

Results

Characteristics of RA patients

A total of 160 RA patients were enrolled, with a median age of 59.0 (interquartile range: 51.0–66.8) years, consisting of 72.5% females and 27.5% males. The median disease duration was 8.0 (interquartile range: 2.0–18.0) years, the median DAS28 score was 5.1 (interquartile range: 4.3–5.5), and the median clinical disease activity index (CDAI) was 18.0 (interquartile range: 14.3–22.0). The other detailed characteristics of RA patients regarding demographics, medical histories, disease features and medications are presented in Table 1.

Anxiety and depression status in RA patients

The HADS-A score (6.9 ± 3.6 *vs* 2.9 ± 2.2, $P < 0.001$; Fig. 1A), SAS score (43.7 ± 11.8 *vs* 30.5 ± 4.7, $P < 0.001$; Fig. 1B), HADS-defined anxiety rate (36.9 *vs* 5.0%, $P < 0.001$; Fig. 1C) and SAS-defined anxiety rate (29.4 *vs* 0.0%, $P < 0.001$; Fig. 1D) were all elevated in RA patients compared with HCs, respectively. The HADS-D score (6.7 ± 3.6 *vs* 2.0 ± 1.6, $P < 0.001$; Fig. 2A), SDS score (45.2 ± 12.7 *vs* 31.1 ± 4.9, $P < 0.001$; Fig. 2B), HADS-defined depression rate (36.3 *vs* 0.0%, $P < 0.001$; Fig. 2C) and SDS-defined depression rate (29.4 *vs* 0.0%, $P < 0.001$; Fig. 2D) were also all elevated in RA patients compared with HCs, respectively. In addition, the severities of HADS-defined or SAS/SDS-defined

Table 1. Features of RA patients

Item	RA patients ($n = 160$)
Demographics	
Age, median (IQR), years	59.0 (51.0–66.8)
Biological sex, *n* (%)	
Male	44 (27.5)
Female	116 (72.5)
BMI, median (IQR), kg/m^2	23.3 (20.7–25.6)
Education level, *n* (%)	
Primary school or below	79 (49.4)
Middle or high school	63 (39.4)
Undergraduate or above	18 (11.3)
Marital status, *n* (%)	
Married	136 (85.0)
Single/divorced/widowed	24 (15.0)
Employment status, *n* (%)	
Employed	82 (51.2)
Unemployed	78 (48.8)
Location, *n* (%)	
Urban	52 (32.5)
Rural	108 (67.5)
Medical history	
Hypertension, *n* (%)	
No	118 (73.2)
Yes	42 (26.3)
Hyperlipidaemia, *n* (%)	
No	133 (83.1)
Yes	27 (16.9)
Diabetes, *n* (%)	
No	137 (85.6)
Yes	23 (14.4)
Disease features	
Disease duration, median (IQR), years	8.0 (2.0–18.0)
RF positive, *n* (%)	
No	18 (11.2)
Yes	142 (88.8)
ACPA positive, *n* (%)	
No	14 (8.8)
Yes	146 (91.3)
TJC, median (IQR)	4.0 (3.0–6.0)
SJC, median (IQR)	3.0 (2.0–5.0)
ESR, median (IQR), mm/h	51.9 (32.2–100.0)
CRP, median (IQR), mg/l	24.1 (8.2–49.7)
DAS28 score (ESR), median (IQR)	5.1 (4.3–5.5)
PGA score, median (IQR)	5.0 (4.0–6.0)
PhGA score, median (IQR)	5.0 (4.0–6.0)
CDAI score, median (IQR)	18.0 (14.3–22.0)
Medications	
NSAID, *n* (%)	
No	51 (31.9)
Yes	109 (68.1)
GC, *n* (%)	
No	110 (68.7)
Yes	50 (31.3)
csDMARD, *n* (%)	
No	12 (7.5)
Yes	148 (92.5)
tsDMARD, *n* (%)	
No	130 (81.2)
Yes	30 (18.8)
bDMARD, *n* (%)	
No	125 (78.1)
Yes	35 (21.9)

The Kolmogorov–Smirnov test was used as the normality test. Variates without a normal distribution are displayed as the median (IQR). bDMARD: biologic DMARD; CDAI: clinical disease activity index; csDMARD: conventional synthetic DMARD; DAS28: DAS in 28 joints; GC: glucocorticoid; IQR: interquartile range; PGA: patient's global assessment; PhGA: physician's global assessment; SJC: swollen joint count; TJC: tender joint count; tsDMARD: targeted synthetic DMARD.

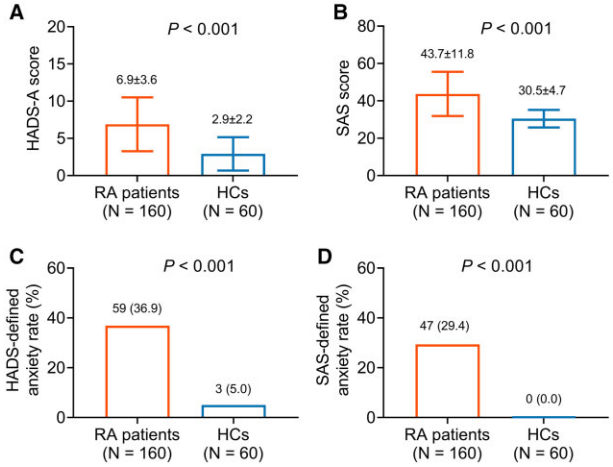

Figure 1. Anxiety score and rate were elevated in RA patients Comparison of HADS-A score (**A**), SAS score (**B**), HADS-defined anxiety (**C**) and SAS-defined anxiety (**D**) between the RA patients and the HCs. Student's unpaired *t*-test and Fisher's exact test were used for comparison analysis. HADS: hospital anxiety and depression scale; HADS-A: hospital anxiety and depression scale for anxiety; HCs: healthy controls; SAS: Zung's self-rating anxiety scale

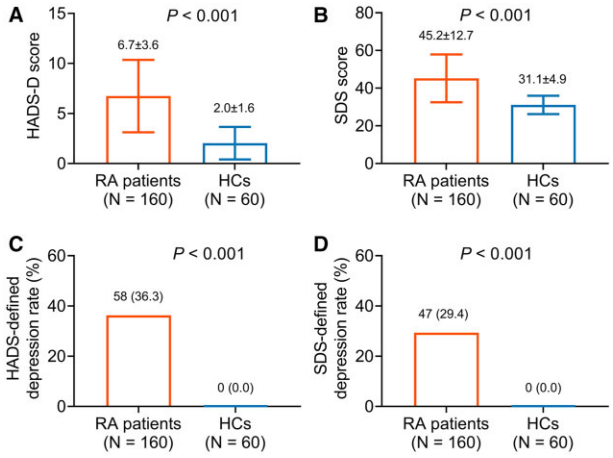

Figure 2. Depression score and rate were increased in RA patients Comparison of HADS-D score (**A**), SDS score (**B**), HADS-defined depression (**C**) and SDS-defined depression (**D**) rates between the RA patients and the HCs. Student's unpaired *t*-test and Fisher's exact test were used for comparison analysis. HADS: hospital anxiety and depression scale; HADS-D: hospital anxiety and depression scale for depression; HCs: healthy controls; SDS: Zung's self-rating depression scale

anxiety and depression were higher in RA patients than in HCs (all $P < 0.001$; Supplementary Table S1, available at *Rheumatology Advances in Practice* online).

Independent risk factors for anxiety in RA patients

Univariate logistic regression analyses revealed several factors that might be related to HADS-defined or SAS-defined anxiety in RA patients, including education level, disease duration, tender joint count (TJC), swollen joint count (SJC), ESR, DAS28 score and physician's global assessment (PhGA) (Supplementary Table S2, available at *Rheumatology Advances in Practice* online). However, the above factors might interact with each other to affect the analyses; therefore, multivariate confirmation was needed.

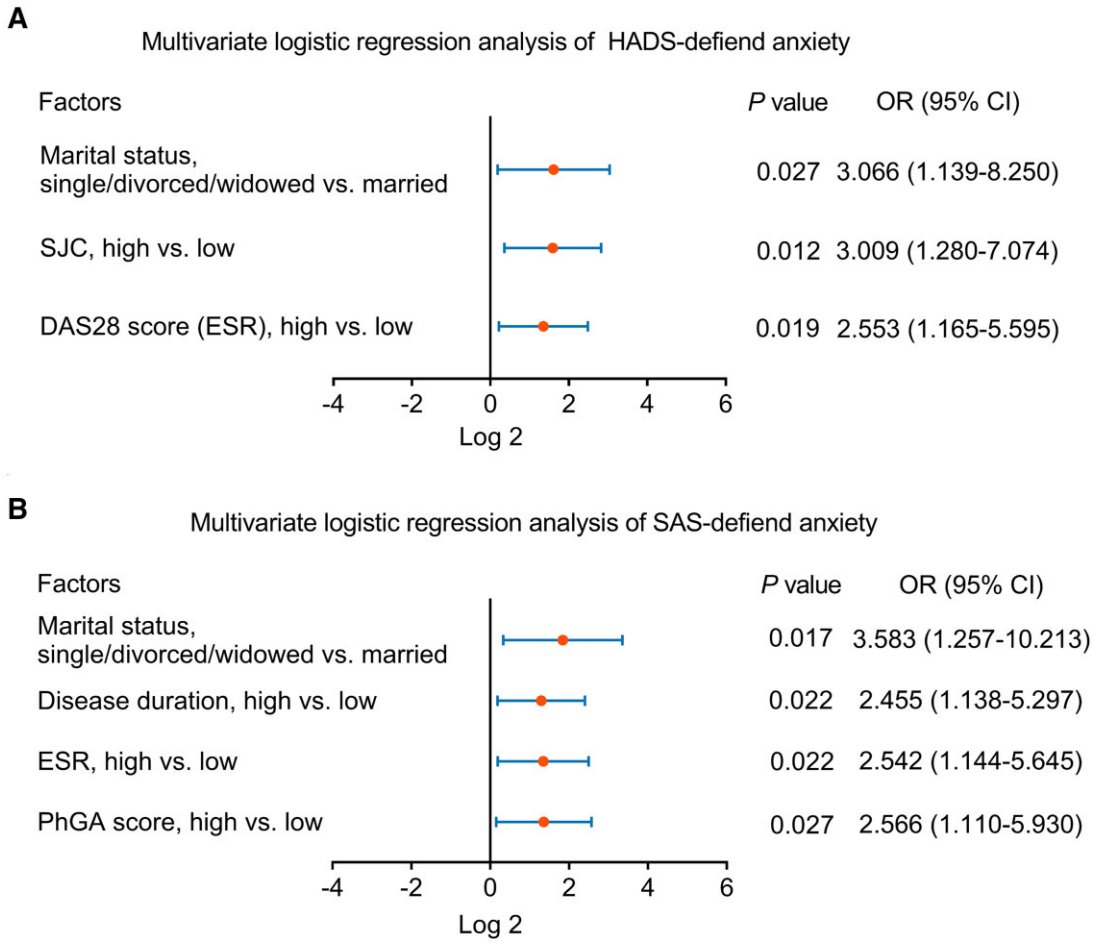

Figure 3. Multivariate analyses of factors related to anxiety risk in RA patients Multivariate logistic regression analyses of factors that were independently correlated with HADS-defined anxiety (**A**) and SAS-defined anxiety (**B**) in RA patients. Univariate and stepwise multivariate logistic regression analysis were applied. DAS28: DAS in 28 joints; HADS: hospital anxiety and depression scale; OR: odds ratio; PhGA: physician's global assessment; SAS: Zung's self-rating anxiety scale; SJC: swollen joint count

Multivariate logistic regression analyses were performed, which revealed that marital status [single/divorced/widowed *vs* married, odds ratio (OR) = 3.066, $P = 0.027$], SJC (high *vs* low, OR = 3.009, $P = 0.012$) and DAS28 score (high *vs* low, OR = 2.553, $P = 0.019$) were independently correlated with HADS-defined anxiety risk in RA patients (Fig. 3A); meanwhile, marital status (single/divorced/widowed *vs* married, OR = 3.583, $P = 0.017$), disease duration (high *vs* low, OR = 2.455, $P = 0.022$), ESR (high *vs* low, OR = 2.542, $P = 0.022$) and PhGA score (high *vs* low, OR = 2.566, $P = 0.027$) were independently associated with SAS-defined anxiety risk in RA patients (Fig. 3B).

Independent risk factors for depression in RA patients

Univariate logistic regression analyses revealed some factors that might be linked with HADS-defined or SDS-defined depression in RA patients, including female biological sex, education level, location, disease duration, TJC, SJC, ESR, CRP, DAS28 score and CDAI score (Supplementary Table S3, available at *Rheumatology Advances in Practice* online). Similar to anxiety-related factors, the above factors linked with depression might interact with each other to affect the findings; thus, multivariate confirmation is also warranted.

Multivariate logistic regression analyses were performed, which revealed that marital status (single/divorced/widowed *vs* married, OR = 8.527, $P < 0.001$), location (rural *vs* urban, OR = 2.877, $P = 0.029$) and DAS28 score (high *vs* low, OR = 7.751, $P < 0.001$) were independently related to HADS-defined depression risk in RA patients (Fig. 4A); at the same time, sex (female *vs* male, OR = 6.447, $P = 0.002$), marital status (single/divorced/widowed *vs* married, OR = 5.474, $P = 0.002$), disease duration (high *vs* low, OR = 2.742, $P = 0.017$), DAS28 score (high *vs* low, OR = 2.566, $P = 0.025$) and PhGA score (high *vs* low, OR = 2.580, $P = 0.029$) were independently linked with SDS-defined depression risk in RA patients (Fig. 4B).

Consistency between the HADS and SAS/SDS in RA patients

The HADS-A score showed a high correlation with the SAS score ($r = 0.669$, $P < 0.001$; Fig. 5A) in RA patients, as did the HADS-D score and SDS score ($r = 0.672$, $P < 0.001$; Fig. 5B). Importantly, Cohen's κ tests were performed, which showed that HADS-defined anxiety had a relatively high consistency with SAS-defined anxiety ($\kappa = 0.551$, $P < 0.001$), and HADS-defined depression had a similar consistency with SDS-defined depression ($\kappa = 0.563$, $P < 0.001$) in RA patients

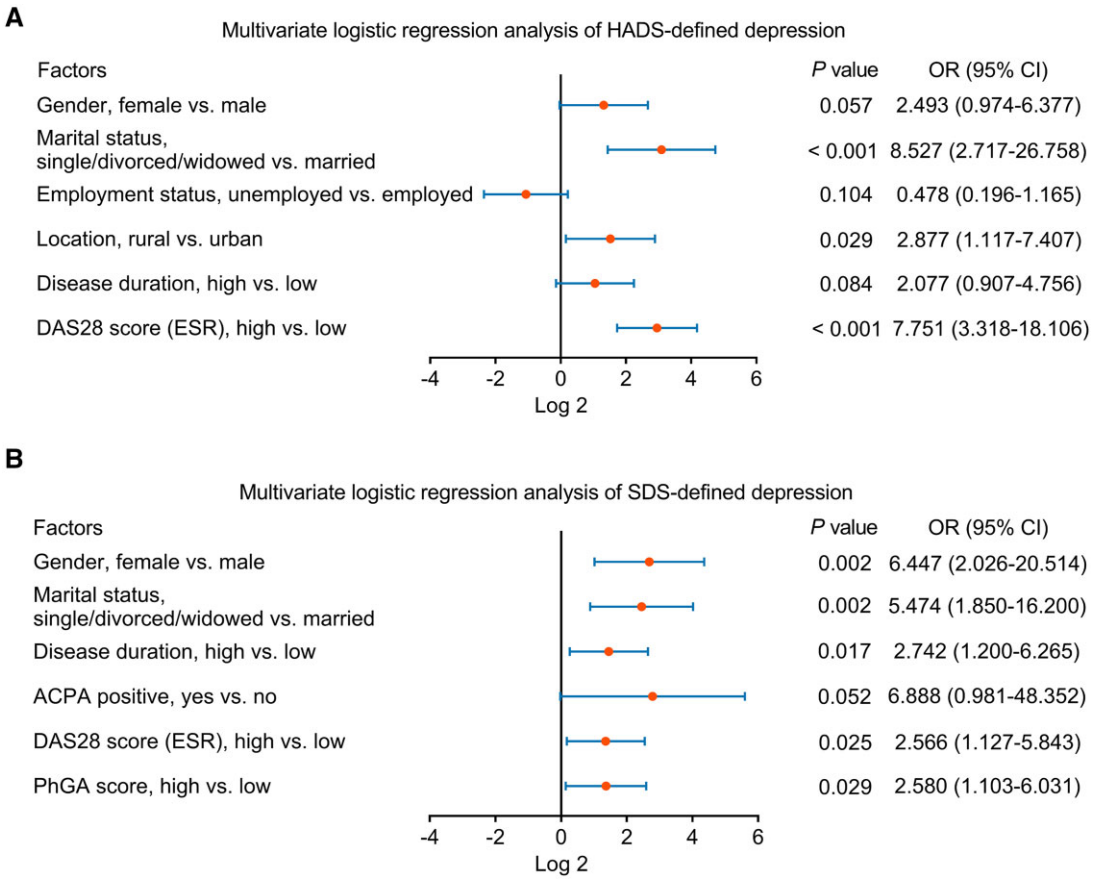

Figure 4. Multivariate analyses of factors related to depression risk in RA patients Multivariate logistic regression analyses of factors that were independently correlated with HADS-defined depression (**A**) and SDS-defined depression (**B**) in RA patients. Univariate and stepwise multivariate logistic regression analysis were applied. DAS28: DAS in 28 joints; HADS: hospital anxiety and depression scale; OR: odds ratio; PhGA: physician's global assessment; SDS: Zung's self-rating depression scale

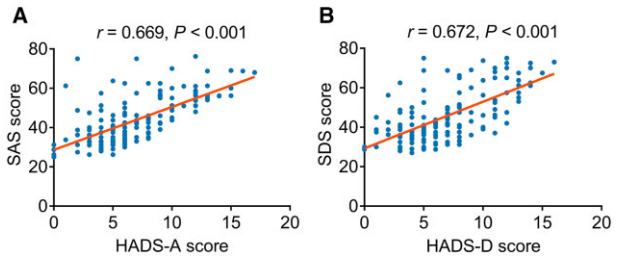

Figure 5. The hospital anxiety and depression scale is closely correlated with Zung's self-rating anxiety scale/depression scale in RA patients The correlation between HADS-A score and SAS score (**A**) and between HADS-D score and SDS score (**B**) in RA patients. Pearson's test was used for correlation analysis. HADS-A: hospital anxiety and depression scale for anxiety; HADS-D: hospital anxiety and depression scale for depression; SAS: Zung's self-rating anxiety scale; SDS: Zung's self-rating depression scale

(Supplementary Table S4, available at *Rheumatology Advances in Practice* online).

Discussion

A bidirectional association between RA and mood disorders (including anxiety and depression) was reported in a previous study [24]. In detail, RA patients have to face many obstacles during routine daily life owing to unbearable pain, joint deformity, fatigue, diet, etc. Owing to the incurability of RA, these RA patients are always under high psychological pressure, which vastly increases their risk of anxiety and depression [12, 16, 25]. The increased financial disbursement for anxiety and depression could, in turn, aggravate RA by reducing the expense for RA treatment. Hence, it is essential to focus on anxiety and depression in RA patients. One previous study indicated that depression and anxiety rates are 50.3 and 25.3% in RA patients, respectively [12]. In another study, 17.6% of RA patients had anxiety and 27.7% of RA patients had depression [26]. Partly in line with these studies, we reported that the anxiety and depression rates were 29.4 and 29.4% according to the SAS/SDS questionnaire and 36.9% and 36.3% according to the HADS questionnaire, respectively, which were notably higher than those in HCs. These findings remind the rheumatologist to pay attention to the mental health of RA patients and consult with a psychiatrist if necessary.

As self-report questionnaires, both the SAS/SDS and HADS are convenient in evaluating anxiety and depression compared with professional scales that need evaluation by psychiatrists (such as the Hamilton scale). However, application of the SAS/SDS questionnaire consistently exhibits a relatively low adherence because it consists of 40 questions, whereas the HADS questionnaire is more acceptable to the patients, because it has only 14 questions [27]. In the present study, it was shown that the internal consistency between the HADS and SAS/SDS was high. These findings indicated that

the HADS and SAS/SDS were interchangeable in evaluating anxiety and depression in RA patients. From this aspect, the HADS appears to be a better choice. Another interesting finding was that the anxiety and depression rates evaluated by the HADS were generally higher than those evaluated by the SAS/SDS in RA patients; moreover, an anxiety rate of 5% could be found in the HCs. These findings suggest that the HADS might present a false-positive rate, limited by its relatively short questionnaire [28]. Combining these two abovementioned results, it is revealed that the rheumatologist needs to balance precision and convenience when evaluating anxiety and depression in RA patients and, accordingly, choose the SAS/SDS or HADS. In addition, given the large number of patients and the huge outpatient pressure in China, the scale with higher convenience (HADS) seems to be a better option than scales with lower convenience (SAS/SDS questionnaire) in evaluating anxiety and depression.

It is crucial to find some risk factors related to anxiety and depression, which might help to realize better management of these mood disorders in RA patients. One previous study indicated that disease severity, pain and inflammation status are associated with the risk of depression [29]. Another study found that TJC28, female sex and patient's global assessment are correlated with anxiety and depression risk [30]. Similar to these findings, we found that marital status (single/divorced/widowed) and higher disease activity indexes were independently correlated with higher anxiety and depression rates. The possible reasons might be as follows. First, unmarried RA patients would face more inconvenience in daily life and lack of daily chatting compared with married RA patients, which would increase their risk of developing anxiety and depression [31]. Second, RA patients with a more severe disease situation (high SJC, disease activity, inflammation, etc.) suffer from a higher risk of developing disability, more expense for disease treatment and more feelings of discomfort caused by the disease (pain, fatigue, etc.), which cause a higher risk of developing anxiety and depression [32]. These independent risk factors might be used to identify those patients who have a higher risk of developing the mental disorder, and those patients at high risk should receive early screening or medical intervention if needed.

Some limitations in the present study should be noted. First, RA is a chronic disease with a long duration; hence, it was difficult to understand fully the variation in anxiety and depression in RA patients and the long-term disease burden that was caused by anxiety and depression in this case–control study. Hence, a further study with a longer follow-up and with more visits is needed. Second, given that it is difficult to collect economic factors, these aspects were not included in the multivariate model, which should be detected in the future. Third, owing to the limited medical resources, these RA patients did not receive a diagnosis of anxiety or depression by a professional psychiatrist, and further study could be conducted in a multidisciplinary manner. Fourth, the sample size was not large enough to draw a firm conclusion, hence further study with a larger sample size is needed.

Conclusion

In conclusion, anxiety and depression occur commonly in RA patients and are independently related to marital status (single/divorced/widowed) and higher disease activity. In addition, the HADS presents a high consistency with the SAS/SDS but with many fewer questions, which might make it a more suitable option for the common routine assessment in RA patients.

Supplementary material

Supplementary material is available at *Rheumatology Advances in Practice* online.

Data availability

The datasets used and/or analysed during the present study are available from the corresponding author upon reasonable request.

Author contributions

Lu Cheng (Conceptualization, Methodology, Formal Analysis, Writing—original draft, Writing—review & editing), Wenjia Gao (Conceptualization, Methodology, Formal Analysis, Writing—original draft, Writing—review & editing), Yan Xu (Data curation, Resources, Investigation, Writing—review & editing), Zhe Yu (Data curation, Resources, Investigation, Writing—review & editing), Wen Wang (Data curation, Resources, Investigation, Writing—review & editing), Jun Zhou (Formal Analysis, Resources, Investigation, Writing—original draft), and Yinshan Zang (Conceptualization, Project administration, Formal Analysis, Supervision, Writing—original draft, Writing—review & editing)

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