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Screening for Anxiety in Patients With Inflammatory Arthritis Using the Multidimensional Health Assessment Questionnaire

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ABSTRACT. ***Objective.*** To analyze the Multidimensional Health Assessment Questionnaire (MDHAQ) in screening for anxiety in patients with rheumatoid arthritis (RA) and psoriatic arthritis (PsA), compared to the Hospital Anxiety and Depression Scale (HADS) as the reference standard.

Methods. Patients with a physician diagnosis of RA or PsA were invited to complete the MDHAQ and HADS at their routine rheumatology clinic visit. Sensitivity, specificity, percent agreement, and κ statistics were used to evaluate agreement between 2 MDHAQ items for anxiety and HADS subscale for Anxiety (HADS-A) score of ≥ 8. The first item is a question asked on a 4-point scale (0–3.3), and the second is a yes or no (blank) question asked within a 60-item review of symptoms (ROS) checklist.

Results. The study included 183 participants, of whom 126 (68.9%) had RA and 57 (31.1%) had PsA. The mean age was 57.3 years and 66.7% were female. Positive screening for anxiety according to a HADS-A score of ≥ 8 was seen in 39.3% of patients. Compared to those with a HADS-A score of ≥ 8, patients with an MDHAQ score of ≥ 2.2 or a positive on ROS had a sensitivity of 69.9%, specificity of 73.6% and substantial agreement (agreement 80.9%, κ 0.59).

Conclusion. The MDHAQ provides information similar to the HADS in screening for anxiety in patients with RA and PsA. The use of this single questionnaire, which can also be used to monitor clinical status and to screen for fibromyalgia and depression without requiring multiple questionnaires, may prove a valuable tool in routine clinical practice.

Key Indexing Terms: anxiety, patient-reported outcome measures, psoriatic arthritis, rheumatoid arthritis

Rheumatoid arthritis (RA) and psoriatic arthritis (PsA) are chronic inflammatory disorders that can result in chronic pain, functional disability, and systemic complications. Depression and anxiety are more prevalent in patients with RA and PsA compared with the general population. The prevalence of depression and anxiety varies widely between studies, owing to heterogeneous assessment methods and case definitions. The prevalence of depression has been estimated at 17.6% to 66.2% in RA[1,2] and 9% to 22% in PsA.[3] The prevalence of anxiety has been reported at 21% to 70% in RA[2] and 15% to 30% in PsA.[3] These figures are considerably higher than the general population, where rates of depression and anxiety have been reported as 12.9%[4] and 7.3%,[5] respectively.

Comorbid depression and anxiety can influence components in composite measures of disease activity used in rheumatology practice, such as the Disease Activity Score in 28 joints (DAS28),[6-8] and Routine Assessment of Patient Index Data 3 (RAPID3).[9-11] Anxiety is often described in the literature in combination with depression; however, in individuals with anxiety, up to 40% do not have comorbid depression.[12]

The use of patient-reported outcome measures (PROMs) is proposed to improve patient-clinician communication and the detection of unrecognized comorbidities.[13,14] However, the completion and evaluation of multiple patient questionnaires is not readily feasible in most clinical settings. The Multidimensional Health Assessment Questionnaire (MDHAQ) is a double-sided, single-page questionnaire that has been developed for use in routine rheumatology care, and has demonstrated utility in many inflammatory and noninflammatory rheumatic diseases, including RA and PsA.[15,16] The MDHAQ includes a number of indices that contribute to clinical assessment, including the RAPID3; a composite measure of physical function, pain, and patient global assessment (PtGA); the Rheumatoid Arthritis Disease Activity Index (RADAI; self-reported painful joint

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count); a 60-symptom review of symptoms (ROS) checklist; a fatigue visual numeric scale (VNS), MDHAQ Depression scale[17]; and the Fibromyalgia Assessment Screening Tools (FAST), FAST3 and FAST4.[18]

The MDHAQ also contains 2 items each related to depression and anxiety. Recently, Morlà et al demonstrated that the MDHAQ could be used effectively to screen for depression in patients with RA and spondyloarthropathy.[17] However, the utility of the MDHAQ in screening for anxiety has not yet been described.

We evaluated the MDHAQ items for anxiety in comparison with the Hospital Anxiety and Depression Scale subscale for Anxiety (HADS-A) as a reference standard to screen for anxiety in patients with RA and PsA, which may provide a more feasible screening tool for anxiety in a single questionnaire used in routine clinical care.

METHODS

Study participants. All patients with all diagnoses attending the Rheumatology Outpatient Department at Liverpool Hospital in Australia were asked to complete the MDHAQ (version R873AU-NP2E) and HADS questionnaires 24 hours before their routine clinical visit. Patients with a clinical diagnosis of RA or PsA, as assessed by their treating physician, were included in this study. All participants provided written informed consent, and ethics approval was gained from the South Western Sydney Local Health District Human Research Ethics Committee (approval no. LNR/13/LPOOL/370, originally approved in 2013, amendment in 2019). All participants were seen between May 2019 and December 2019. Both questionnaires were completed in English.

PROMs and questionnaires. The MDHAQ includes 2 items related to anxiety. The first item is a question regarding a patient's current state on a 4-point scale, with the potential responses being 0 ("without any difficulty"), 1.1 ("with some difficulty"), 2.2 ("with much difficulty") and 3.3 ("unable to do"). This item will henceforth be referred to as the "MDHAQ score" for anxiety for the purposes of this study. The second is a yes or no (blank) item within the ROS checklist to identify feelings of anxiety experienced within the past month.

The HADS is a single-sided, widely used, validated PROM to screen for depression and anxiety. It consists of 2 subscales, with 7 items each for depression and anxiety. Each item is scored from 0 to 3, with a total possible score of 21 for each subscale. A score of ≥ 8 in each subscale indicates a possible case of depression or anxiety, whereas a score of ≥ 11 indicates a probable case.[19] A score of ≥ 8 on the HADS-A was used to indicate a positive screen for anxiety in this study.

Other variables. Demographic data for participants were obtained from patient medical records. C-reactive protein (CRP; mg/L, reference range < 5 mg/L) and erythrocyte sedimentation rate (ESR; mm/h, reference range: male 0-15 mm/h, female 0-20 mm/h) were also recorded at the time of the visit.

Data analysis. Patient characteristics and patient-reported variables are shown as descriptive statistics. Continuous variables are reported as means and SD and categorical variables as frequencies and percentages. MDHAQ variables, including the RAPID3 score, RADAI, total score on the ROS, fatigue VNS, pain VNS, PtGA, CRP, ESR, MDHAQ scores for anxiety, and individual ROS items were compared between participants with a positive (HADS-A ≥ 8) and negative (HADS-A < 8) screen for anxiety using *t* tests for continuous variables and chi-square tests for categorical variables. Sensitivity, specificity, percent correctly classified, and κ statistics were used to evaluate the agreement between each MDHAQ item for anxiety and a HADS-A score of ≥ 8.

RESULTS

Patient characteristics. A total of 183 participants were included in the study, of whom 126 (68.9%) had a diagnosis of RA and 57 (31.1%) had a diagnosis of PsA. The mean age was 57.3 years across the cohort. The mean age in the RA cohort was higher than the PsA cohort (59.6 vs 52.3 yrs, $P < 0.01$). There was a higher proportion of female patients in the RA cohort compared with the PsA cohort (77% vs 43.9%, $P < 0.001$). There were no significant differences in years of education or BMI (calculated as weight in kilograms divided by height in meters squared) between RA and PsA cohorts (Table 1).

A total of 73 participants (39.3%) screened positive for anxiety according to a HADS-A score of ≥ 8, of whom 43 participants (23.5%) had a HADS-A score of ≥ 11. There was no statistically significant difference between the RA and PsA cohorts. Fifty-one participants (27.9%) scored ≥ 8 on the HADS for both depression and anxiety.

There was no significant difference in MDHAQ variables between the RA and PsA cohorts. The mean (SD) RAPID3 score was 11.6 (7.2), indicating moderate disease severity. The mean RADAI was 12.3 (10.9) and mean total score on the 60-symptom ROS was 11.7 (10.2). The mean CRP in the cohort was 6.5 (9.1) mg/L and the mean ESR was 19.1 (14.2) mm/h, with no difference between RA and PsA groups (Table 1).

Analysis of demographic, MDHAQ, and other variables in participants with and without self-reported anxiety. There was no significant difference in sex, age, years of education, or BMI between participants who screened negative or positive for anxiety according to a score of ≥ 8 on the HADS scale. MDHAQ variables, including the RAPID3 ($P < 0.001$) and its components pain VNS ($P = 0.01$) and PtGA ($P < 0.001$), RADAI ($P < 0.001$), total score on the 60-symptom ROS ($P < 0.001$) and fatigue VNS ($P < 0.001$) were all significantly higher in participants who screened positive for anxiety according to a HADS score of ≥ 8. There was no significant difference in CRP or ESR between participants who screened negative or positive according to the HADS (Table 2).

With regard to the MDHAQ anxiety score, there was a significantly lower proportion of participants who scored 0 on the MDHAQ anxiety score in those who screened positive for anxiety according to HADS-A compared to those who screened negative ($P < 0.001$). There was a significantly higher proportion of participants who scored ≥ 1.1 ($P < 0.001$) or ≥ 2.2 ($P < 0.001$) in those who screened positive for anxiety according to HADS-A compared to those who screened negative. The proportion of patients with an MDHAQ anxiety score of ≥ 3.3 did not differ between those with and without a positive HADS-A screen for anxiety. A significantly higher proportion of participants scored positive on the ROS for anxiety, if they had a positive HADS-A screen for anxiety ($P < 0.001$; Table 2).

Comparison of MDHAQ variables for anxiety and the HADS-A in screening for anxiety. MDHAQ variables for anxiety were compared with a HADS-A score of ≥ 8 as the reference standard for screening for anxiety. A positive screen for anxiety according to a composite of MDHAQ anxiety score of ≥ 2.2 or positive on ROS for anxiety was seen in 35% of the cohort, compared to

Table 1. Patient characteristics of the whole cohort and by diagnosis.

	All	RA	PsA	*P*, RA vs PsA
n	183	126	57	
Demographics				
Female sex, n (%)	122 (66.7)	97 (77)	25 (43.9)	< 0.001
Mean age, yrs	57.3 (15.0)	59.6 (14.7)	52.3 (14.8)	< 0.01
BMI	30.1 (8.1)	29.6 (8.2)	31.0 (7.8)	0.34
Education, yrs	11.4 (4.0)	11.1 (4.3)	12.2 (3.2)	0.10
HADS score, n. (%)				
HADS-A ≥ 8	73 (39.3)	52 (41.3)	21 (36.8)	0.63
HADS-A ≥ 11	43 (23.5)	30 (23.8)	13 (22.8)	> 0.99
HADS-D ≥ 8	65 (35.5)	45 (35.7)	20 (35.1)	> 0.99
HADS-D ≥ 11	34 (18.6)	23 (18.3)	11 (19.3)	0.84
MDHAQ				
MDHAQ anxiety, n (%)				
0	87 (47.5)	57 (45.2)	30 (52.6)	0.42
≥ 1.1	96 (52.5)	69 (54.8)	27 (47.4)	0.42
≥ 2.2	35 (19.1)	22 (17.5)	13 (22.8)	0.42
3.3	4 (2.2)	3 (2.4)	1 (1.8)	> 0.99
MDHAQ depression, n (%)				
0	88 (48.1)	59 (46.8)	29 (50.9)	0.63
≥ 1.1	95 (51.9)	67 (53.2)	28 (49.1)	0.63
≥ 2.2	34 (18.6)	23 (18.3)	11 (19.3)	0.84
3.3	4 (2.2)	3 (2.4)	1 (1.8)	> 0.99
ROS anxiety, n (%)	49 (26.2)	33 (26.2)	16 (28.1)	0.86
ROS depression, n (%)	41 (22.4)	27 (24.6)	14 (21.4)	0.70
Mean RAPID3	11.6 (7.2)	11.7 (6.9)	11.4 (8.0)	0.83
Mean RADAI	12.3 (10.9)	12.6 (11.2)	11.8 (10.4)	0.65
ROS total	11.7 (10.2)	11.4 (9.8)	12.4 (11.2)	0.55
Fatigue VNS	4.5 (3.0)	4.5 (3.0)	4.7 (3.3)	0.69
Pain VNS	4.6 (3.0)	4.6 (2.9)	4.7 (3.1)	0.79
PtGA	4.5 (2.8)	4.6 (2.6)	4.4 (3.2)	0.65
Other measures				
CRP mean, mg/L	6.5 (9.1)	7.1 (10.4)	5.0 (4.6)	0.10
ESR mean, mm/h	19.1 (14.2)	19.1 (14.4)	19.1 (13.8)	0.99

Values are expressed as mean (SD) unless otherwise indicated. CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; HADS: Hospital Anxiety and Depression Scale; HADS-A: Hospital Anxiety and Depression Scale for Anxiety; HADS-D: Hospital Anxiety and Depression Scale for Depression; MDHAQ: Multidimensional Health Assessment Questionnaire; PsA: psoriatic arthritis; PtGA: patient global assessment; RA: rheumatoid arthritis; RADAI: Rheumatoid Arthritis Disease Activity Index; RAPID3: Routine Assessment of Patient Index Data 3; ROS: review of symptoms checklist; VNS: visual numeric scale.

39.3% according to HADS-A. This composite measure provided a sensitivity of 69.9% (95% CI 59.3-80.4), specificity of 88.2% (95% CI 82.2-94.2), with substantial agreement (80.9% agreement, κ 0.59). Whereas a composite of MDHAQ anxiety score of ≥ 1.1 or positive on ROS for anxiety provided a higher sensitivity (93.2%, 95% CI 87.4-99), specificity dropped to 73.6% (95% CI 65.4-81.9), suggesting a higher false positive rate on screening (Table 3).

When compared to a HADS-A score of ≥ 11, an MDHAQ anxiety score of ≥ 2.2 had the highest percent agreement of 83.6%, but low sensitivity of 55.8% (95% CI 41.0-70.7). A composite of MDHAQ anxiety score of ≥ 2.2 or positive on ROS for anxiety raised sensitivity to 81.4% (95% CI 69.8-93.0), while maintaining adequate specificity (79.3%, 95% CI 72.6-86.0) and good agreement (79.8% agreement, κ 0.52; Table 3).

DISCUSSION

To our knowledge, our study is the first to examine the criterion validity of the MDHAQ in screening for anxiety in patients with inflammatory disorders. We demonstrated that an MDHAQ score of ≥ 2.2 or positive on the ROS provided excellent sensitivity and specificity for screening for anxiety (69.9% and 88.2%, respectively), with substantial agreement (80.9% agreement, κ 0.59). The MDHAQ includes a number of useful scales for clinical assessment during routine care, including the RAPID3, RADAI, and FAST4. Our study presents an additional tool within the MDHAQ for multidimensional clinical assessment through the use of a single questionnaire that encompasses both psychological screening and measures of disease activity. This is more feasible in routine practice than completing multiple disease-specific questionnaires, such as the HADS-D

Table 2. Demographic, MDHAQ and other variables in patients with and without self-reported anxiety.

	HADS-A < 8	HADS-A ≥ 8	*P*
n	110	73	
Female sex, n (%)	70 (63.6)	52 (71.2)	0.34
Age, yrs	56.7 (16.2)	58.2 (13.2)	0.50
BMI	30.4 (8.5)	29.6 (7.5)	0.52
Education, yrs	11.6 (3.8)	11.2 (4.4)	0.61
Mean RAPID-3	9.1 (6.7)	15.3 (6.4)	< 0.001
Mean RADAI	8.2 (8.1)	18.6 (11.6)	< 0.001
ROS total	8.2 (7.8)	17.1 (11.2)	< 0.001
Fatigue VNS	3.6 (3.0)	6 (2.5)	< 0.001
Pain VNS	4.7 (2.8)	5.9 (2.7)	0.01
PtGA	3.6 (2.7)	6.0 (2.5)	< 0.001
CRP, mean, mg/L	6.4 (8.7)	6.6 (9.7)	0.68
ESR, mean, mm/h	19.6 (15.5)	18.3 (12.1)	0.79
MDHAQ = 0, n (%)	81 (73.6)	6 (8.2)	< 0.001
MDHAQ ≥ 1.1, n (%)	29 (26.4)	67 (91.8)	< 0.001
MDHAQ ≥ 2.2, n (%)	3 (2.7)	32 (43.8)	< 0.001
MDHAQ = 3.3, n (%)	1 (0.9)	3 (4.1)	0.30
ROS anxiety positive, n (%)	10 (9.1)	39 (53.4)	< 0.001

Values are expressed as mean (SD) unless otherwise indicated. CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; HADS-A: Hospital Anxiety and Depression Scale for Anxiety; MDHAQ: Multidimensional Health Assessment Questionnaire; PtGA: patient global assessment; RAPID3: Routine Assessment of Patient Index Data 3; RADAI: Rheumatoid Arthritis Disease Activity Index; ROS: review of symptoms checklist; VNS: visual numeric scale.

Table 3. MDHAQ variables for anxiety in comparison to a HADS-A score of ≥ 8 as the gold standard, and a HADS-A score of ≥ 11.

	n (%)	Sensitivity, % (95% CI)	Specificity, % (95% CI)	Agreement	κ
HADS-A ≥ 8					
MDHAQ ≥ 1.1	96.0 (52.5)	91.8 (85.5-98.1)	73.6 (65.4-81.8)	80.9	0.62
MDHAQ ≥ 2.2	35.0 (19.1)	43.8 (32.5-55.2)	97.3 (94.2-100)	76.0	0.45
MDHAQ = 3.3	4.0 (2.2)	4.1 (0.0-8.7)	99.1 (97.3-100)	61.2	0.04
ROS anxiety positive	49.0 (26.2)	53.4 (42.0-64.9)	90.9 (85.5-96.3)	76.0	0.47
MDHAQ ≥ 1.1 or ROS positive	97.0 (53.0)	93.2 (87.4-99.0)	73.6 (65.4-81.9)	81.4	0.63
MDHAQ ≥ 2.2 or ROS positive	64.0 (35.0)	69.9 (59.3-80.4)	88.2 (82.2-94.2)	80.9	0.59
MDHAQ = 3.3 or ROS positive	51.0 (27.9)	54.8 (42.7-65.7)	90.0 (84.4-95.6)	76.0	0.47
HADS-A ≥ 11					
MDHAQ ≥ 1.1	96.0 (52.5)	97.67 (93.1-100)	61.4 (53.4-69.5)	69.9	0.41
MDHAQ ≥ 2.2	35.0 (19.1)	55.8 (41.0-70.7)	92.1 (87.7-96.6)	83.6	0.51
MDHAQ = 3.3	4.0 (2.2)	2.3 (0.0-6.8)	97.9 (95.5-100)	75.4	0.003
ROS anxiety positive	49.0 (26.2)	65.1 (50.9-79.4)	85.0 (79.1-90.9)	80.3	0.48
MDHAQ ≥ 1.1 or ROS positive	97.0 (53.0)	100.0 (100.0-100.0)	61.4 (53.4-69.5)	70.5	0.43
MDHAQ ≥ 2.2 or ROS positive	64.0 (35.0)	81.4 (69.8-93.0)	79.3 (72.6-86.0)	79.8	0.52
MDHAQ = 3.3 or ROS positive	51.0 (27.9)	65.1 (50.9-79.4)	83.6 (77.4-89.7)	79.2	0.46

HADS-A: Hospital Anxiety and Depression Scale for anxiety; MDHAQ: Multidimensional Health Assessment Questionnaire; ROS: review of symptoms checklist.

and HADS-A in addition to the MDHAQ, DAS28, Simplified Disease Activity Index, Clinical Disease Activity Index (CDAI), or the PsA Disease Activity Score.[20]

Depression and anxiety are often examined together as mental health disorders, yet they do not always coexist.[12] In our cohort, 22 (12%) participants screened positive for anxiety only according to HADS-A, 14 (7.7%) participants screened positive for depression only according to HADS-D, and 51 (27.9%) participants scored ≥ 8 on both the HADS-D and HADS-A. It is important to recognize anxiety as a separate entity as there are key differences in the management of anxiety, which do not overlap with depression.[21] Morlà et al examined the use of the MDHAQ in screening for depression, and demonstrated a 79.4% agreement and κ statistic of 0.52 in those who had an MDHAQ depression score of ≥ 2.2 or were ROS positive for depression.[17] We have demonstrated that the MDHAQ may also be a valuable tool in routine rheumatology care to identify these patients who may require further evaluation for anxiety.

Mental health comorbidities are not routinely screened for in routine rheumatology practice. It has been shown that screening for physical comorbidities, such as cardiovascular and osteoporosis risk assessments, are conducted more frequently.[22] The National Institute for Health and Care Excellence includes in their recommendations for the management of RA an annual assessment for depression.[23] Nevertheless, mood disorders are underrecognized and undertreated by nonpsychiatric physicians.[24] A number of patient, clinician, and systemic barriers have been identified. Clinician and systemic factors include inadequate knowledge regarding screening, diagnosis and treatment options; cultural barriers; and time and productivity requirements.[24] Further, patients may not seek help due to the associated stigma and perception of psychological problems as a sign of weakness.[25] Thus, alternative avenues and opportunities for communication are necessary to facilitate ease of disclosure of mental health concerns.

A bidirectional relationship has been described between mental health and physical well-being, as psychological comorbidities have been correlated with increased disease activity, reduced remission rates, and increased mortality in patients with inflammatory arthritis.[8,10,26] The proposed factors for this include socioeconomic, patient, and disease considerations.[27,28] We have confirmed, in our population, that a positive screen for anxiety is correlated with higher scores on PROMs used for clinical assessment in patients with inflammatory arthritis, including the RAPID3, RADAI, fatigue VNS, pain VNS and PtGA. This is particularly important for measures such as the CDAI or RAPID3, which are indices of disease activity that include PtGA. This can lead to overestimation and overtreatment of inflammatory disease activity. We demonstrated that patients with a positive screen for anxiety had mean RAPID3 scores in the high disease severity category, whereas patients who screened negative for anxiety had mean RAPID3 scores in the moderate disease severity category, despite no difference in inflammatory markers between these groups. This carries significant implications for treatment, since these measures are often used in the treat-to-target approach for the management of inflammatory arthritis[29,30] to monitor treatment response and guide titration of antirheumatic medications. Recognition of underlying psychological comorbidities is crucial to assist in the interpretation of these measures and avoid possible overtreatment. Further, our study supports the notion that psychological comorbidity may affect patient perceptions and cognitions,[7] and reveals additional therapeutic targets for patients with rheumatic disease, such as addressing stigmatism, barriers to communication, and health-related behaviors.

There are limitations to our study. First, the study participants included patients from a single center in Australia. Further examination in larger and more diverse cohorts of patients will be necessary to support our findings of agreement between the MDHAQ and HADS and the potential effects on clinical practice. Second, data on axial involvement in patients with PsA was not available, thus the use of the MDHAQ as a screening tool for depression and anxiety in patients with axial spondyloarthropathy needs further examination. Self-reported anxiety according to a HADS score was not correlated with a clinical diagnosis in this study. Though the HADS has been extensively validated in the outpatient setting, clinical assessment remains the gold standard for a diagnosis of anxiety, whereas questionnaires such as the HADS and MDHAQ are only screening tools. Participants were not excluded based on non-English–speaking background, though the proportion of these patients is unknown. Thus, the potential effect of patients who may have completed the questionnaires with external assistance is unknown. Finally, available data on pharmacological and nonpharmacological management of inflammatory arthritis and psychological comorbidity were not reliable; thus, analysis of the effect of treatment on the relationship between disease activity and management of psychological comorbidities was beyond the scope of this study.

In conclusion, we have demonstrated the criterion validity of the MDHAQ as a tool to screen for anxiety in patients with inflammatory arthritis during routine rheumatology care. We emphasize that this tool is concerned with screening rather than a clinical diagnosis of anxiety. Completion of a single multidimensional questionnaire may assist patients and clinicians to bridge communication barriers and detect unrecognized comorbidities. Our study supports the MDHAQ as a screening tool that may help overcome some of these barriers during routine rheumatology care for patients with inflammatory disorders. Further investigation is required to formally assess the feasibility of the MDHAQ as a screening tool for psychological comorbidity in clinical practice, and to evaluate the effect of routine detection of these comorbidities on patient treatment and outcomes in rheumatology care.

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