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ORIGINAL RESEARCH

Diagnostic and Clinical Utility of the GAD-2 for Screening Anxiety Symptoms in Individuals With Multiple Sclerosis

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Abstract

Objective: To assess the diagnostic and clinical utility of the 2-item Generalized Anxiety Disorder Scale (GAD-2) for screening anxiety symptoms in individuals with multiple sclerosis (MS).

Design: Cross-sectional.

Setting: University-affiliated MS neurology and rehabilitation center.

Participants: The sample comprised adults (N=99) (ages 19-72; mean ± SD=46.2±13.0; 75% women) with a physician-confirmed MS diagnosis who were receiving care in a university-affiliated MS center. Disease durations ranged from 1 to 37 years (mean ± SD=10.7±8.4).

Interventions: Not applicable.

Main Outcome Measures: Participants completed the 7-item Generalized Anxiety Disorder Scale (GAD-7) and GAD-2. Internal consistency was calculated for both measures. Area under the receiver operating characteristics curve (AUC), the 95% confidence interval for the AUC, and Youden's *J* were calculated to determine the optimal GAD-2 cutoff score for identifying clinically significant anxiety symptoms, as defined by the previously validated GAD-7 cutoff score of ≥8.

Results: Internal consistency was excellent for the GAD-7 (Cronbach α=.91) and acceptable for the GAD-2 (α=.77), and the measures were highly correlated (*r*=.94). The GAD-2 had excellent overall accuracy for identifying clinically significant anxiety symptoms (AUC=0.97; 95% confidence interval, 0.94-1.00). A GAD-2 cutoff score of ≥3 provided an optimal balance of good sensitivity (0.87) and excellent specificity (0.92) for detecting clinically significant anxiety symptoms. Alternatively, a cutoff score of ≥2 provided excellent sensitivity (1.00) and fair specificity (0.76).

Conclusions: The GAD-2 is a clinically useful and psychometrically valid tool for screening anxiety symptoms in MS rehabilitation and neurology care settings. Importantly, this tool has the potential to identify individuals with MS who are at risk for anxiety disorders and who may benefit from rehabilitation psychology interventions to ultimately improve functioning and quality of life.

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Multiple sclerosis (MS) is a progressive neurodegenerative disease of the central nervous system that can profoundly interfere with individuals' physical and psychological functioning and well-being.[1-6] Individuals who are coping with a new MS diagnosis and those who have been living with the disease for many years often experience uncertainty and worry about the disease. Uncertainty about the pace and severity of disease progression can contribute to emotional distress in the form of depression and/or anxiety symptoms.[7-9] Rehabilitation health care providers (eg, physicians, psychologists, rehabilitation therapists) with a specialty in MS have long recognized the increased prevalence of depressive symptoms in this population (40%-60%) compared to the general population (15%-20%).[10] Research over the past few decades has increasingly focused on improving the detection, assessment, and

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treatment of depression in individuals with MS. Screening tools such as the 9-item Patient Health Questionnaire (PHQ-9), as well as the brief 2-item PHQ-2, have been validated for use in individuals with MS and are often used as part of routine care in rehabilitation and neurology clinics.[11]

In contrast to the wealth of research dedicated to understanding and treating depression in MS, research investigating anxiety and its treatment in this population is still in its infancy. One of the first studies in this area noted that individuals with MS are at increased risk of developing anxiety disorders (36%) relative to the general population (29%), and that a history of depression may place individuals with MS at greater risk for developing anxiety disorders.[10,12,13] Since that time, several additional studies have been published on anxiety in MS regarding prevalence rates, clinical correlates (eg, disability, MS subtype), psychiatric comorbidities, and overlapping physiologic symptoms (eg, pain, sleep disturbance). Importantly, the presence of anxiety is a risk factor for suicidal ideation in depressed individuals with MS.[14] However, despite evidence for increased risk of anxiety and its negative effects on functioning and morbidity, anxiety remains underdiagnosed in MS and is not routinely or systematically evaluated during medical appointments.[15]

One of the barriers, commonly cited by health care providers, to assessing mental health symptoms, including anxiety, is limited clinical time. With appointments typically lasting 30 minutes or less, assessment of emotional distress may be limited to a few qualitative interview questions about mood. As previously noted, however, use of brief, validated questionnaires like the PHQ-2 has the potential to more accurately screen for depressive symptoms and promote appropriate referrals to health or rehabilitation psychologists for further assessment and treatment. Recent efforts have been made to validate similar tools for the assessment of anxiety symptoms in MS, including the 7-item anxiety subscale from the Hospital Anxiety and Depression Scale (HADS) and the 7-item Generalized Anxiety Disorder Scale (GAD-7).[16,17]

The HADS anxiety subscale and the GAD-7 exhibit good to excellent psychometric properties and are especially effective for screening symptoms of generalized anxiety disorder, which is the most common anxiety disorder both in MS and the general population.[10,12] As noted by Terrill et al, the GAD-7 offers the specific advantage of being open source and having established cutoff scores for mild, moderate, and severe levels of anxiety.[17] However, because the GAD-7 includes items related to physical MS symptoms (eg, restlessness, feeling tense, trouble relaxing) that may be present even in the absence of anxiety, additional work is needed to assess and validate brief anxiety screening measures that do not include physiologic items. Analogous work has been performed on the PHQ-2, which focuses on cognitive and affective depressive symptoms (ie, depressed mood and anhedonia) and not the physiologic symptoms (ie, fatigue, poor sleep, appetite, psychomotor speed) included in the full PHQ-9. To address the issue of physiologic symptom overlap in the assessment of anxiety, a 2-item version of the Generalized Anxiety Disorder Scale (GAD-2) was developed, which specifically assesses anxiousness/nervousness and uncontrollable worry. The 2-item version does not include the physiologic symptoms noted above.[18] The GAD-2 also features a recommended cutoff score ($\geq$3), which has been validated against a criterion standard clinical interview for detecting generalized anxiety disorder in the general population.[18]

The GAD-2 offers great potential for accurately and efficiently detecting anxiety symptoms in individuals with MS; however, to date, the diagnostic and clinical utility of the measure, including its sensitivity and specificity for detecting clinically significant anxiety, has not been psychometrically tested in this population. Therefore, the goal of the present study is to establish the sensitivity and specificity of the GAD-2 with respect to the previously established cutoff score of the GAD-7. We hypothesize that the GAD-2 will provide an accurate and useful clinical measure of anxiety, and that analyses will yield a sensitive and specific GAD-2 cutoff score for detecting clinically significant anxiety symptoms in MS. Importantly, results of this study will help directly inform clinical rehabilitation and neurological care of individuals with MS by offering a brief, useful, and accurate tool that (1) can readily be integrated into clinical practice; (2) does not require significant provider time or resources; and (3) can facilitate decision making for directing appropriate referrals to rehabilitation-focused mental health services.

List of abbreviations:

AUC	area under the curve
GAD-2	Generalized Anxiety Disorder Scale-2 (GAD-2)
GAD-7	Generalized Anxiety Disorder Scale-7
HADS	Hospital Anxiety and Depression Scale
MS	multiple sclerosis
PHQ	Patient Health Questionnaire
SCID-I	Structured Clinical Interview for DSM-IV-TR Axis I Disorders

Method

Participants and Procedures

All procedures were approved by the Institutional Review Board. Community-dwelling individuals with MS were recruited from a university-affiliated MS center to participate in a study of cognitive function in MS. The present study featured a secondary analysis of data collected from that primary study. To be eligible for the study, patients were required to be 18 years or older and have a physician-confirmed MS diagnosis. Exclusion criteria included a neurologic disorder other than MS, symptomatic involvement of the upper extremities severe enough to interfere with writing or pressing keys on a computer tablet, and cognitive impairment severe enough to interfere with comprehension of study instructions. Participants were recruited during the course of their routine clinic visits. Participants completed a series of self-report questionnaires, which assessed demographics, MS characteristics, depressive symptoms, and anxiety symptoms. A total of 100 participants were enrolled in the primary study. One participant did not complete the self-report measures; thus, 99 participants were included in the final sample for the present study.

Measures

GAD-7 and GAD-2

The GAD-7 is a 7-item self-report screening tool assessing the severity of an individual's anxiety symptoms.[19] The items on the scale correspond to criteria for diagnosing generalized anxiety disorder based on the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision. Each item is rated on a 4-point Likert scale based