DOI: http://dx.doi.org/10.18502/cjn.v20i2.6746

Current Journal of Neurology

Original Paper

Curr J Neurol 2021; 20(2): 102-10

Rapid screening for generalized anxiety disorder in patients with migraine

Received: 10 Dec. 2020
Accepted: 05 Feb. 2021

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Keywords
Patient Health Questionnaire; Generalized Anxiety Disorder; Migraine Disorders; Sensitivity and Specificity; Cut-Off Point

Abstract

Background: Generalized anxiety disorder (GAD) often remains undiagnosed in patients with migraine, while comorbidity of GAD with migraine is associated with increased dysfunction and risk of chronic migraine. Generalized Anxiety Disorder Scale 7-item (GAD-7) and Generalized Anxiety Disorder Scale 2-item (GAD-2) are the commonly employed screening measures for generalized anxiety symptoms in different patient groups. The present study aimed to evaluate psychometric properties of the Persian version of GAD-7 and GAD-2 in migraine.

Methods: In this cross-sectional study, patients were diagnosed with migraine headaches according to the International Classification of Headache Disorders, 3rd edition (ICHD-3); then they participated in the psychiatric diagnostic interview, and filled out GAD-7, GAD-2, Beck Anxiety Inventory (BAI), Headache Impact Test-6 (HIT-6), and Migraine-Specific Quality of Life Questionnaire version 2.1 (MSQv2.1). The psychometric properties of GAD-7 and GAD-2 were examined using SPSS and LISREL.

Results: Final samples were 186 patients with migraine that 83 patients received a diagnosis of GAD. Confirmatory factor analysis (CFA) indicated that the one-factor model of GAD-7 fit the data well. Internal consistency, test-retest, and Guttman split-half reliability of GAD-7 and GAD-2 were good. Significant correlation results, average variance extracted (AVE), and composite reliability (CR) supported the construct validity of the GAD-7. A score of ≥ 10 in GAD-7 and ≥ 3 in GAD-2 achieved satisfactory sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) (GAD-7: 92%, 90%, 88%, and 93%, respectively; GAD-2: 79%, 88%, 71%, and 91%, respectively).

Conclusion: Our findings supported GAD-7 and GAD-2 for assessing GAD in patients with migraine. It seems that GAD-7 and GAD-2 accurately diagnosed GAD in this group of patients.

How to cite this article: Veisy F, Farahani H, Togha M, Gharaee B, Janani L, Aghebati A. Rapid screening for generalized anxiety disorder in patients with migraine. Curr J Neurol 2021; 20(2): 102-10.

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Introduction

Headache is one of the frequent pain complaints with high level of dysfunction. International Headache Society divided headache into primary and secondary.[1] Migraine as a primary headache is a neurological disorder that causes excessive pain.[2] Besides, migraine is one of the most ten prevalent diseases and one of the five leading causes of Years Lived with Disability (YLD); it causes approximately 16.3% of worldwide disability-adjusted life-years (DALYs) across the neurological population.[3,4] Global Burden of Disease (GBD) 2016 study has considered migraine as an essential medical issue in all ages, especially at the age of 15 to 59 years. It has reported that the majority of migraine sufferers are women.[5,6] Migraine results in impairment in function and life quality.[7,8]

The severity of migraine headaches and comorbid conditions are linked together, so that patients with migraine with more headaches and higher levels of pain are more likely to have comorbid conditions such as psychiatric disorders.[9-13] On the other side, comorbid conditions contribute to the chronicity of the migraine.[14] The strong association between migraine headaches and anxiety disorders such as generalized anxiety disorder (GAD) has been observed.[15,16]

From the other side, GAD is one of the most common types of anxiety disorders in the general population, psychiatric clinics, and primary care.[17-27] GAD frequently co-occurs with psychiatric disorders or medical conditions,[28] but it may be misdiagnosed[29-31] and because of some of the physical symptoms such as irritability and agitation, it is difficult to be recognized.[32-34] Some symptoms of anxiety are observed in migraine, and migraine symptoms can also be seen in anxiety.[10]

GAD can mainly impact health-related quality of life (HRQOL) and cause impairment in many areas of functioning.[35-37] These effects are more significant than effects of major depression on quality of life (QOL).[37] But, the co-occurrence of migraine and psychiatric disorders such as anxiety disorders leads to marked reduced QOL, more health impairment, and challenges for disease management[12] that affect therapeutic plan and treatment pathway of migraine.[10]

Some guidelines suggest the utilization of standardized scales to screen anxiety disorders and to assess treatment.[38] Conducting structured interviews is more expensive in terms of time, money, and required training.[39,40] Generalized Anxiety Disorder Scale 7-item (GAD-7) was developed for screening, possible detection, and severity of GAD. The sensitivity and specificity of the GAD-7 were 0.89 and 0.82, respectively, in primary care settings (cut-off point: 10). Furthermore, GAD-7 is brief, time-saving, self-administrated according to Diagnostic and Statistical Manual of Mental Disorders (DSM) criteria,[41] and sensitive to clinical improvement;[42] therefore, it is well qualified for clinical and research purposes.[41]

A meta-analysis supported GAD-7 psychometric properties in the adult population.[43] In addition, the American Psychological Association (APA) suggested GAD-7 as one of the tools for assessing GAD intensity.[44] Studies proved the suitability of GAD-7 and GAD-2 for use in non-clinical populations[45-51] and several clinical populations.[52-65] Acceptable psychometric properties of GAD-7 and GAD-2 were reported in different languages[45,49,66-71] and versions.[72,73]

The Korean version of GAD-7 and GAD-2 has been studied in migraine, but the clinical sample was small (n = 32); factor structure, composite reliability (CR), and average variance extracted (AVE) have not been analyzed;[57] furthermore, cross-cultural bias of GAD-7 and possible subtypes of GAD[74] were discussed; thus, GAD-7 and GAD-2 should be studied in the context of culture and specific patient groups. The Persian version of GAD has been investigated in a small sample of patients with GAD (n = 24) who did not have a comorbid migraine, and the diagnostic validity of GAD-7 was not studied,[75] while it is influenced by clinical problems;[43] therefore, the present study aimed to investigate the psychometric properties of GAD-7 and GAD-2 as screening tools in a sample of patients with migraine.

Materials and Methods

Study participants: Based on Meyers et al.,[76] 150 participants were needed; with 20% drop, 188 participants were recruited from the headache clinic of university hospitals and headache specialty centers in Tehran, Iran, by convenience sampling method. They agreed to contribute in the research and gave written informed consent to participate in the study. Finally, 2 cases dropped and 186 participants were analyzed anonymously. Inclusion criteria were as follows: (a) age of at least 18 years, (b) the diagnosis of migraine based on the International Classification of Headache Disorders-3rd edition (ICHD-3), (c) ability to write and read in Persian, (d) not receiving any

anti-anxiety medications and psychotherapy. Participants who met these criteria were excluded: (a) inability to participate in the interview, (b) inability to perceive self-completion questionnaire due to medical condition, (c) mental defectiveness, (d) or receiving medical treatment that impairs comprehension of the questionnaire.

Procedure: Ethical committee permission was obtained, then sampling was done from August 2019 to February 2020. Relevant study information was provided to the participants. Psychiatric diagnostic interviews [Structured Clinical Interview for DSM-5 (SCID-5)] were conducted with those who received diagnosis of migraine by the professor of neurology according to ICHD-3 criteria, and were interested in participating in the study. Participants filled out the questionnaires privately in the interview room. Psychiatric diagnostic interview was administrated by a trained clinician (PhD candidate in clinical psychology) who answered the participants' questions too. The evaluation tools included GAD-7, Generalized Anxiety Disorder Scale 2-item (GAD-2), Beck Anxiety Inventory (BAI), Headache Impact Test-6 (HIT-6), and Migraine-Specific Quality of Life Questionnaire version 2.1 (MSQv2.1). Retesting of GAD-7 and GAD-2 was performed after 3 weeks. The ethical committee approval number is IR.IUMS.REC.1398.784.

Measurements

SCID-5: SCID-5 is a structured diagnostic interview that evaluates psychiatric disorders based on DSM-5 criteria. It contains different common categories of psychiatric disorders, separately. The Persian version of SCID-5 was validated.[77]

GAD-7: GAD-7 as a valid screening tool could be used for clinical practice and research goals. This measure consists of 7 items that examine GAD symptoms and their severity. Participants rated their level of agreement with the statements using a 4-point scale (0 = not at all, 1 = several days, 2 = more than half of the days, 3 = nearly every day). The score range is 0-27; the higher GAD-7 score, the greater symptom severity.[41] The reliability and validity of the Persian version of GAD-7 were supported in 199 students and 24 patients with GAD, but the cut-off point was not studied.[75]

GAD-2: This scale consists of 2 questions. This short form of GAD-7 is scored from 0 to 6. Area under curve (AUC) of GAD-2 has been reported from 0.80 to 0.91 for anxiety disorders.[30] The psychometric properties of the Persian version of GAD-2 have not been investigated.

BAI: BAI is a 21-item questionnaire that assesses anxiety symptoms (for example, fear of the worst happening and losing control, inability to relax, nervousness, …). Each statement is scored from 0 (not at all) to 3 (severely – it bothered me a lot). Final score ranges from 0 to 63. Higher scores reflect more severe anxiety.[78] Levels of anxiety are categorized into normal, mild, moderate, and severe. The validity and reliability of the Persian version of BAI were confirmed.[79]

HIT-6: HIT-6 consists of 6 Likert-type items. Items focus on impaired function in the job, school, home, and social situation due to headaches. HIT-6 includes various areas such as social, occupational, and intellectual functioning, day job, the severity of pain, and psychological problems. Patients answered to the sentences on a 5-point scale (6 = never, 8 = rarely, 10 = sometimes, 11 = very often, 13 = always). Total scores are 36 to 78 points with higher scores indicating significant influence. It has been shown that HIT-6 is reliable, valid, and sensitive to change.[80] The Persian version of the HIT-6 was validated in a sample of patients with migraine and tension-type headache.[81]

MSQv2.1: The MSQv2.1 examines the impact of migraine on sufferers' activities. This 14-item tool is composed of 3 subscales: role restrictive (RR, seven items), role preventive (RP, four items), and emotion function (EF, three items). The statements are scored from 1 (none of the time) to 6 (all of the time), then were reversed and standardized 0 to 100. Higher scores reflect better QOL. The validity and reliability of MSQv2.1 have been investigated and approved.[82] MSQv2.1 showed good reliability and validity in the Persian-speaking people.[83]

In this cross-sectional study, test-retest reliability of GAD-7 and GAD-2 was measured with an interval of 3 weeks by using correlation and interclass correlation coefficient (ICC), and Cronbach's alpha was used to assess internal consistency. To check the construct validity of GAD-7, confirmatory factor analysis (CFA) was performed. CR and AVE were computed using LISREL output. The correlation between GAD-7, GAD-2, and BAI as well-established tests was examined for concurrent validity. As criterion concurrent validity, the relation between MSQv2.1, HIT-6, GAD-7, and GAD-2 was computed to investigate whether higher scores in GAD-7 and GAD-2 were related to more significant function and migraine-specific QOL impairments or not. Independent samples t-test was administrated to compare GAD-7 and GAD-2 scores in patients

with migraine with and without GAD diagnosis based on SCID-5. Convergent, concurrent, concurrent criterion, and discriminant validity were checked as construct validity.[84] The accuracy and ability of GAD-7 and GAD-2 to differentiate GAD-positive and negative patients were analyzed using receiver operating characteristic (ROC) curve. Sensitivity, specificity, and predictive power were calculated as diagnostic accuracy estimates of these scales.

All statistical analyses except for the CFA were conducted using SPSS software (version 21, IBM Corporation, Armonk, NY, USA). CFA was performed using LISREL.

Results

The final samples were 186 patients with migraine: 55 men (30%) and 131 women (70%), 49 of whom were asked to complete GAD-7 and GAD-2 again after three weeks. The average age of the participants was 37 ± 9 years. Most patients were married (n = 130, 69%) and unemployed (n = 97, 52%). The level of education of the completers ranged from high school education (n = 67, 36%) to PhD (n = 11, 5.9%); the most common level of education was university graduate (n = 79, 42%). 44% (n = 83) of patients with migraine fulfilled the criteria of DSM-5 for GAD according to diagnostic interview (SCID-5). The participants with GAD and migraine compared to participants with migraine demonstrated higher anxiety level obtained with BAI [GAD-7: t(182) = -15.00, P < 0.001; GAD-2: t(182) = -15.27, P < 0.001], higher HIT-6 scores [GAD-7: t(180) = -5.00, P < 0.001; GAD-2: t(180) = -5.46, P < 0.001], and lower QOL when using the MSQv2.1 score [GAD-7: t(184) = 7.00, P < 0.001; GAD-2: t(184) = 8.63, P < 0.001].

Reliability: The results demonstrated that GAD-7 and GAD-2 possessed high internal consistency based on the approval threshold.[85] Additionally, Guttman split-half reliability and test-retest reliability after 3 weeks by using correlation and ICC have also been found to be satisfactory (Tables 1 and 2).

Construct validity: CFA was used to check the unidimensionality of GAD-7 (Table 3, Figure 1). The results showed that the model fit values were good [χ^2 (14) = 40.07, P = 0.0002, root mean square error of approximation (RMSEA) = 0.100, comparative fit index (CFI) = 0.97, goodness of fit index (GFI) = 0.94, adjusted GFI (AGFI) = 0.88]. This one-factor model had 7 items, with factor loadings ranging from 0.64 to 0.80.

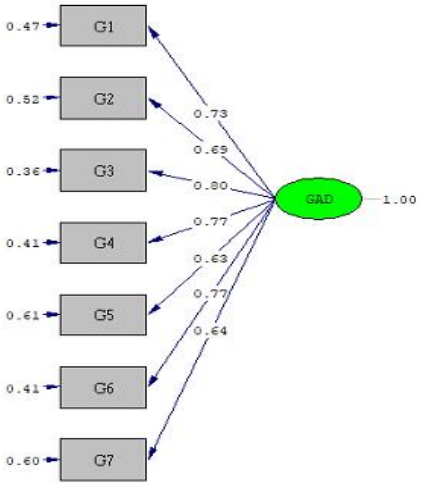

Figure 1. One-factor model of the Generalized Anxiety Disorder Scale 7-item (GAD-7)

AVE derived from CFA results was identified as one of the convergent validity indexes, that measures the construct's amount of variance in proportion to the variance of measurement error. In this study, AVE index was desirably accordant with the conventional threshold[84] (AVE = 0.51). CR was also called construct reliability;[84] values of 0.7 and above were introduced as a high degree of CR.[86] The results showed that CR was 0.88, indicating that all of the items represent a hidden structure.

The correlation between GAD-7, GAD-2, and BAI was significant (n = 186, P < 0.001). Increase in GAD-7 and GAD-2 scores was correlated with an increase in BAI scores, that shows strong concurrent validity. The relationship between GAD-7, GAD-2, MSQv2.1, and HIT-6 as the concurrent criterion validity was also significant.

Table 1. Reliability of Generalized Anxiety Disorder Scale 7-item (GAD-7) and Generalized Anxiety Disorder Scale 2-item (GAD-2) (n = 186)

	Internal consistency	Guttman reliability	Test-retest reliability	ICC
GAD-7	0.87	0.85	0.66*	0.79*
GAD-2	0.62	0.62	0.60*	0.65*

*P < 0.001

GAD-7: Generalized Anxiety Disorder Scale 7-item; GAD-2: Generalized Anxiety Disorder Scale 2-item; ICC: Interclass correlation coefficient

Table 2. Item-total statistics of Generalized Anxiety Disorder Scale 7-item (GAD-7) (n = 186)

Item	Scale mean if item deleted	Scale variance if item deleted	Corrected item-total correlation	Cronbach's alpha if item deleted
1	8.08	26.66	0.67	0.86
2	8.53	25.31	0.63	0.86
3	8.00	25.15	0.75	0.85
4	8.58	25.04	0.70	0.85
5	9.22	27.65	0.60	0.86
6	8.40	24.72	0.70	0.85
7	8.56	25.67	0.58	0.87

Table 3. Factor loadings of the Generalized Anxiety Disorder Scale 7-item (GAD-7) items in the one-dimensional model (n = 186)

Item	Unstandardized	Standardized	T-value
1	0.73	0.73	11.06*
2	0.69	0.69	10.28*
3	0.80	0.80	12.52*
4	0.77	0.77	11.84*
5	0.63	0.63	9.06*
6	0.77	0.77	11.84*
7	0.64	0.64	9.21*

*P < 0.001

GAD-7 and GAD-2 scores were significantly and negatively correlated with MSQv2.1, reflecting that the higher the GAD-7 and GAD-2 scores, the poorer the QOL (P < 0.001). Furthermore, higher GAD-7 and GAD-2 values were associated with more significant functional impairment and higher rates of psychological distress due to headache (P < 0.001) (Table 4).

To evaluate discriminant validity, an independent samples t-test was conducted to compare mean GAD-7 and GAD-2 scores in patients with migraine with and without GAD (Table 4). The significant difference was observed between patients with migraine with and without GAD conditions [GAD-7: t(184) = -18.55, P = 0.01; GAD-2: t(184) = -13.82, P = 0.001]. The results indicated that the co-occurrence of GAD and migraine could result in increase in GAD-7 and GAD-2 scores.

Sensitivity and specificity: To test the diagnostic accuracy of GAD-7 and GAD-2 for detecting patients with GAD, ROC curve analysis was done. Diagnosis of GAD based on SCID-5 was considered as the gold standard (state variable).

The area under the ROC curve indicates that the correct differentiation of the diseased group from non-diseased group was functional and highly accurate in GAD-7 and GAD-2 (0.96 and 0.90, respectively).[87] These values were exceedingly near 1, which means that GAD-7 and GAD-2 were highly accurate screening measures based on proposed values.[87,88] Besides, the nearer ROC curve to the top left corner is, the better the measure will be. Figures 2 and 3 met this design criterion.

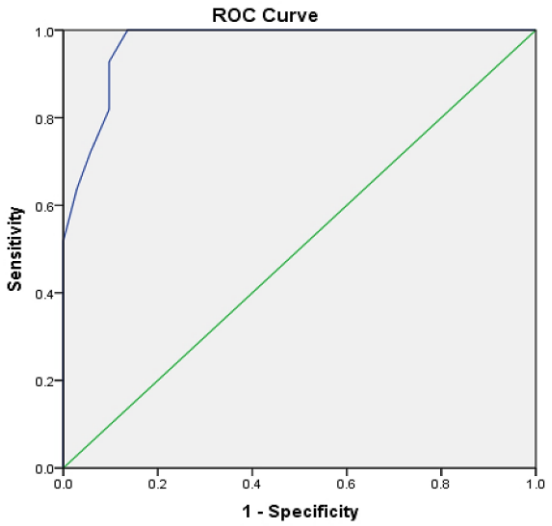

Figure 2. Receiver operating characteristic (ROC) curve of Generalized Anxiety Disorder Scale 7-item (GAD-7)

Table 4. Construct validity of Generalized Anxiety Disorder Scale 7-item (GAD-7) and Generalized Anxiety Disorder Scale 2-item (GAD-2) (n = 186)

	Convergent validity		Concurrent validity	Concurrent criterion validity		Discriminant validity
	CR	AVE	BAI	MSQv2.1	HIT-6	T-test
GAD-7	0.88	0.51	0.79**	-0.66**	0.40**	-18.55*
GAD-2	-	-	0.67**	-0.59**	0.39**	-13.82**

*P < 0.01; **P < 0.001

GAD-7: Generalized Anxiety Disorder Scale 7-item; GAD-2: Generalized Anxiety Disorder Scale 2-item; BAI: Beck Anxiety Inventory; MSQv2.1: Migraine-Specific Quality of Life version 2.1; HIT-6: Headache Impact Test-6; CR: Composite reliability; AVE: Average variance extracted

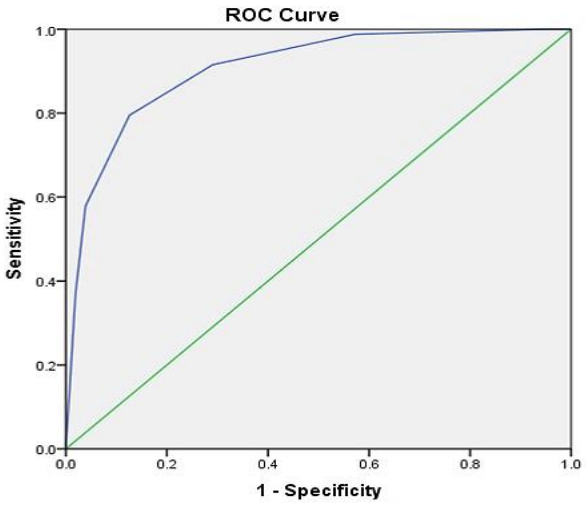

Figure 3. Receiver operating characteristic (ROC) curve of Generalized Anxiety Disorder Scale 2-item (GAD-2)

A series of sensitivity/specificity pairs in proportion to the entire range of cut-off points was produced by ROC curve; best cut-off points of GAD-7 and GAD-2 according to an optimal balance between sensitivity and specificity were 10 and 3, respectively. The sensitivity estimates the positive cases that are properly detected and the specificity estimates the negative cases that are properly detected. In other words, 92% and 79% of migraine patients with GAD would be recognized positive by GAD-7 and GAD-2, respectively, and 90% and 88% of migraine patients without GAD would be recognized as negative by GAD-7 and GAD-2, respectively. Positive predictive value (PPV) and negative predictive value (NPV) of GAD-7 and GAD-2 were good (Table 5). PPV indicates the likelihood that people will be positively diagnosed with a screening tool when they actually have the disease. NPV indicates the likelihood that people will be negatively diagnosed with a screening tool when they actually do not have the disease.

Discussion

Psychiatric comorbidity including GAD with migraine is associated with poor prognosis, greater disability, less satisfaction with drug treatment, and increased frequency of headache;[89,90] which is a risk factor for chronicity of migraine[14] and medication overuse headache;[91] therefore, psychiatric comorbidity in migraine must be considered. Thus, the scales should be studied in the context of culture and groups of patients, and the self-report questionnaires are cost-effective, so the present study supports the psychometric properties of Persian version of GAD-7 and GAD-2 in migraine.

Our finding showed that GAD-7 and GAD-2 were valid and reliable measures for detecting GAD in patients with migraine. Satisfactory consistency over three weeks, internal consistency, and split-half reliability of GAD-7 and GAD-2 were confirmed; Cronbach's alpha value of GAD-7 is similar to another study in patients with migraine,[57] patients with epilepsy,[52,53] psychiatric patients,[63,92] and patients with chronic obstructive pulmonary disease (COPD).[56] Internal consistency of GAD-2 was similar to other researches.[57,68]

One-dimensionality hypothesis of GAD-7 was evaluated by CFA or exploratory factor analysis (EFA) method in different studies. The CFA finding demonstrated that all seven items of GAD-7 had robust loadings to the general factor. Our finding is in line with the previous studies that showed that one-factor model of GAD-7 could fit the data well;[31,71] in some studies, the modified one-factor model was accepted.[63,74] Other studies claimed that the two-factor structure was better.[65,93]

Concurrent validity of GAD-7 in patients with migraine was supported by strong positive correlation with BAI (r = 0.79); this finding is comparable to another study in migraine population (r = 0.75),[57] original study (r = 0.72),[41] a study in heterogeneous psychiatric sample (r = 0.69),[63], and Korean version of study (r = 0.78).[68]

The present finding of correlation between GAD-2 and BAI (r = 0.67) was in line with the Korean version of GAD-2 in patients with migraine[57] and in nonclinical and psychiatric samples.[68]

In our sample, the t-test analysis indicated that the means of GAD-7 and GAD-2 were significantly different in patients with and without GAD; this statistical evidence proved discriminant validity. In some samples, GAD-7 discriminated between GAD and control groups too.[63,65,68,71,92]

Table 5. Operational characteristic of Generalized Anxiety Disorder Scale 7-item (GAD-7) and Generalized Anxiety Disorder Scale 2-item (GAD-2) (n = 186)

	Cut-off point	Sensitivity	Specificity	PPV	NPV
GAD-7	≥ 10	0.92	0.90	0.88	0.93
GAD-2	≥ 3	0.79	0.88	0.71	0.91

GAD-7: Generalized Anxiety Disorder Scale 7-item; GAD-2: Generalized Anxiety Disorder Scale 2-item; PPV: Positive predictive value; NPV: Negative predictive value

In line with the previous study,[57] GAD severity by GAD-7 and GAD-2 was negatively associated with QOL in patients with migraine and positively associated with headache intensity. As expected, the severity of general anxiety was related to impaired function and QOL in patients with migraine, that supports criterion concurrent validity.

CR and AVE which were calculated using factor loadings in CFA confirmed the internal consistency of the GAD-7 construct. Both values were above advocated thresholds[84] and acceptable. To our knowledge, compared to previous studies, these indexes present new evidence of construct validity.

Similar to the original study findings[41] and some studies in different patient groups,[64-66,70,71,92] the best possible sensitivity (0.92), specificity (0.90), and cut-off point ≥ 10 were suggested in GAD-7, but these findings are not in line with the Korean version in migraine.[57] Cut-off point ≥ 3 suggested in GAD-2 is in line with other samples in some studies,[21,54,68] but the cut point of Korean version in migraine was 7,[57] and this value is 4 in web-based version of GAD-2.[72]

Therefore, clinicians could use the GAD-7 and GAD-2 as cost-effective measures for rapid screening of GAD in patients with migraine. According to GAD-7, patients with migraine who received GAD diagnosis and truly had GAD (sensitivity), were recognized better than patients with migraine who did not receive GAD diagnosis and did not truly have GAD (specificity).

The less studied assessment of the construct validity of GAD-7 (CR and AVE) and administrating diagnostic interviews (SCID) by the trained clinician are the strengths of the present study. Besides, to our knowledge, the psychometric properties of the Persian version of GAD-2 and diagnostic validity of the Persian version of GAD-7 were studied for the first time.

The findings of this research should be given in view of the following limitation. The ability of GAD-7 and GAD-2 to precisely measure changes caused by the intervention in patients with migraine was not evaluated, while the responsiveness of the questionnaire is so helpful for clinical studies. The present findings may not apply to different kinds of headaches.

Conclusion

GAD-7 as a measure should be used primarily in the context of culture due to cultural bias and in specific groups, because its diagnostic accuracy is influenced by clinical problems, so our study focused on patients with migraine. Generally, our finding confirmed that this measure could detect GAD rapidly and relatively correct in patients with migraine, and the Persian version of GAD-7 and GAD-2 has yielded good results in this sample. For quick screening, GAD-7 and GAD-2 were supported in patients with migraine, but the diagnostic interview is suggested for important screening and intervention.

Conflict of Interests

The authors declare no conflict of interest in this study.

Acknowledgments

We thank all participants who involved in current research.

This work was supported by the Student Research Committee of Iran University of Medical Sciences, Tehran (grant number: 98-1-15-14919).

References

1. The international classification of headache disorders, 3rd edition (beta version). Cephalalgia 2013; 33(9): 629-808.
2. Hildreth CJ, Lynm C, Glass RM. JAMA patient page. Migraine headache. JAMA 2009; 301(24): 2608.
3. Global, regional, and national burden of neurological disorders, 1990-2016: A systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol 2019; 18(5): 459-80.
4. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990-2016: A systematic analysis for the Global Burden of Disease Study 2016. Lancet 2017; 390(10100): 1211-59.
5. Global, regional, and national burden of migraine and tension-type headache, 1990-2016: A systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol 2018; 17(11): 954-76.
6. Steiner TJ, Stovner LJ, Vos T, Jensen R, Katsarava Z. Migraine is first cause of disability in under 50s: Will health politicians now take notice? J Headache Pain 2018; 19(1): 17.
7. Bagley CL, Rendas-Baum R, Maglinte GA, Yang M, Varon SF, Lee J, et al. Validating migraine-specific quality of life questionnaire v2.1 in episodic and chronic migraine. Headache 2012; 52(3): 409-21.
8. Mosconi P. Health-related quality of life (HRQOL) and migraine. J Headache Pain 2001; 2(Suppl 1): s21-s24.
9. Buse DC, Reed ML, Fanning KM, Bostic R, Dodick DW, Schwedt TJ, et al. Comorbid and co-occurring conditions in migraine and associated risk of increasing headache pain intensity and headache frequency: Results of the migraine in America symptoms and treatment (MAST) study. J Headache Pain 2020; 21(1): 23.
10. Dresler T, Caratozzolo S, Guldolf K, Huhn JI, Loiacono C, Niiberg-Pikksoot T, et al. Understanding the nature of psychiatric comorbidity in migraine: A systematic review focused on interactions and treatment implications. J Headache Pain 2019; 20(1): 51.
11. Seng EK, Seng CD. Understanding migraine and psychiatric comorbidity. Curr Opin Neurol 2016; 29(3): 309-13.
12. Buse DC, Silberstein SD, Manack AN, Papapetropoulos S, Lipton RB. Psychiatric comorbidities of episodic and chronic migraine. J Neurol 2013; 260(8): 1960-9.
13. Minen MT, Begasse De Dhaem O, Kroon Van Diest DA, Powers S, Schwedt TJ, Lipton R, et al. Migraine and its psychiatric comorbidities. J Neurol

Neurosurg Psychiatry 2016; 87(7): 741-9.
14. Lipton RB, Fanning KM, Buse DC, Martin VT, Hohaia LB, Adams AM, et al. Migraine progression in subgroups of migraine based on comorbidities: Results of the CaMEO Study. Neurology 2019; 93(24): e2224-e2236.
15. Goulart AC, Santos IS, Brunoni AR, Nunes MA, Passos VM, Griep RH, et al. Migraine headaches and mood/anxiety disorders in the ELSA Brazil. Headache 2014; 54(8): 1310-9.
16. Jeyagurunathan A, Abdin E, Vaingankar JA, Chua BY, Shafie S, Chang SHS, et al. Prevalence and comorbidity of migraine headache: Results from the Singapore Mental Health Study 2016. Soc Psychiatry Psychiatr Epidemiol 2020; 55(1): 33-43.
17. Roy-Byrne PP, Wagner A. Primary care perspectives on generalized anxiety disorder. J Clin Psychiatry 2004; 65(Suppl 13): 20-6.
18. Wittchen HU, Zhao S, Kessler RC, Eaton WW. DSM-III-R generalized anxiety disorder in the National Comorbidity Survey. Arch Gen Psychiatry 1994; 51(5): 355-64.
19. Maier W, Gansicke M, Freyberger HJ, Linz M, Heun R, Lecrubier Y. Generalized anxiety disorder (ICD-10) in primary care from a cross-cultural perspective: A valid diagnostic entity? Acta Psychiatr Scand 2000; 101(1): 29-36.
20. Caballero L, Bobes J, Vilardaga I, Rejas J. Clinical prevalence and reason for visit of patients with generalized anxiety disorder seen in the psychiatry out-patient clinics in Spain. Results of the LIGANDO study. Actas Esp Psiquiatr 2009; 37(1): 17-20.
21. Kujanpaa T, Ylisaukko-Oja T, Jokelainen J, Hirsikangas S, Kanste O, Kyngas H, et al. Prevalence of anxiety disorders among Finnish primary care high utilizers and validation of Finnish translation of GAD-7 and GAD-2 screening tools. Scand J Prim Health Care 2014; 32(2): 78-83.
22. Kessler RC, Brandenburg N, Lane M, Roy-Byrne P, Stang PD, Stein DJ, et al. Rethinking the duration requirement for generalized anxiety disorder: evidence from the National Comorbidity Survey Replication. Psychol Med 2005; 35(7): 1073-82.
23. Kessler RC, Keller MB, Wittchen HU. The epidemiology of generalized anxiety disorder. Psychiatr Clin North Am 2001; 24(1): 19-39.
24. Wittchen HU. Generalized anxiety disorder: prevalence, burden, and cost to society. Depress Anxiety 2002; 16(4): 162-71.
25. Olfson M, Fireman B, Weissman MM, Leon AC, Sheehan DV, Kathol RG, et al. Mental disorders and disability among patients in a primary care group practice. Am J Psychiatry 1997; 154(12): 1734-40.
26. Leon AC, Olfson M, Broadhead WE, Barrett JE, Blacklow RS, Keller MB, et al. Prevalence of mental disorders in primary care. Implications for screening. Arch Fam Med 1995; 4(10): 857-61.
27. Lieb R, Becker E, Altamura C. The epidemiology of generalized anxiety disorder in Europe. Eur Neuropsychopharmacol 2005; 15(4): 445-52.
28. Judd LL, Kessler RC, Paulus MP, Zeller PV, Wittchen HU, Kunovac JL. Comorbidity as a fundamental feature of generalized anxiety disorders: Results from the National Comorbidity Study (NCS). Acta Psychiatr Scand Suppl 1998; 393: 6-11.
29. Parmentier H, Garcia-Campayo J, Prieto R. Comprehensive review of generalized anxiety disorder in primary care in Europe. Curr Med Res Opin 2013; 29(4): 355-67.
30. Kroenke K, Spitzer RL, Williams JB, Monahan PO, Lowe B. Anxiety disorders in primary care: prevalence, impairment, comorbidity, and detection. Ann Intern Med 2007; 146(5): 317-25.
31. Jordan P, Shedden-Mora MC, Lowe B. Psychometric analysis of the Generalized Anxiety Disorder scale (GAD-7) in primary care using modern item response theory. PLoS One 2017; 12(8): e0182162.
32. Ruscio AM, Chiu WT, Roy-Byrne P, Stang PE, Stein DJ, Wittchen HU, et al. Broadening the definition of generalized anxiety disorder: Effects on prevalence and associations with other disorders in the National Comorbidity Survey Replication. J Anxiety Disord 2007; 21(5): 662-76.
33. Wittchen HU, Hoyer J. Generalized anxiety disorder: Nature and course. J Clin Psychiatry 2001; 62(Suppl 11): 15-9.
34. Wittchen HU, Kessler RC, Beesdo K, Krause P, Hofler M, Hoyer J. Generalized anxiety and depression in primary care: Prevalence, recognition, and management. J Clin Psychiatry 2002; 63(Suppl 8): 24-34.
35. Rapaport MH, Clary C, Fayyad R, Endicott J. Quality-of-life impairment in depressive and anxiety disorders. Am J Psychiatry 2005; 162(6): 1171-8.
36. Ruiz MA, Zamorano E, Garcia-Campayo J, Pardo A, Freire O, Rejas J. Validity of the GAD-7 scale as an outcome measure of disability in patients with generalized anxiety disorders in primary care. J Affect Disord 2011; 128(3): 277-86.
37. Stein DJ. Comorbidity in generalized anxiety disorder: impact and implications. J Clin Psychiatry 2001; 62(Suppl 11): 29-34.
38. The National Institute for Health and Care Excellence (NICE). Generalised anxiety disorder and panic disorder in adults: management [Online]. [cited 2011]; Available from: URL: https://www.nice.org.uk/guidance/cg113/resources/generalised-anxiety-disorder-and-panic-disorder-in-adults-management-35109387756997
39. First MB. Structured clinical interview for DSM-IV (SCID-I/SCID-II). In: Kreutzer J, Caplan DB, Editors. Encyclopedia of clinical neuropsychology. Hoboken, NJ: John Wiley & Sons, Inc; 2011.
40. World Health Organization (WHO). Composite International Diagnostic Interview (CIDI core) Version 2.1 [Online]. [cited 1998]; Available from: URL: https://pubs.niaaa.nih.gov/publications/assessingalcohol/InstrumentPDFs/20_CIDI.pdf
41. Spitzer RL, Kroenke K, Williams JB, Lowe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med 2006; 166(10): 1092-7.
42. Toussaint A, Husing P, Gumz A, Wingenfeld K, Harter M, Schramm E, et al. Sensitivity to change and minimal clinically important difference of the 7-item Generalized Anxiety Disorder Questionnaire (GAD-7). J Affect Disord 2020; 265: 395-401.
43. Plummer F, Manea L, Trepel D, McMillan D. Screening for anxiety disorders with the GAD-7 and GAD-2: A systematic review and diagnostic metaanalysis. Gen Hosp Psychiatry 2016; 39: 24-31.
44. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders (DSM-5®). Washington, DC: American Psychiatric Publishing; 2013.
45. Tiirikainen K, Haravuori H, Ranta K, Kaltiala-Heino R, Marttunen M. Psychometric properties of the 7-item Generalized Anxiety Disorder Scale (GAD-7) in a large representative sample of Finnish adolescents. Psychiatry Res 2019; 272: 30-5.
46. Wild B, Eckl A, Herzog W, Niehoff D, Lechner S, Maatouk I, et al. Assessing generalized anxiety disorder in elderly people using the GAD-7 and GAD-2 scales: Results of a validation study. Am J Geriatr Psychiatry 2014; 22(10): 1029-38.
47. Garabiles MR, Lao CK, Yip P, Chan EWW, Mordeno I, Hall BJ. Psychometric validation of PHQ-9 and GAD-7 in Filipino migrant domestic workers in Macao (SAR), China. J Pers Assess 2020; 102(6): 833-44.
48. Bartolo A, Monteiro S, Pereira A. Factor structure and construct validity of the Generalized Anxiety Disorder 7-item (GAD-7) among Portuguese college students. Cad Saude Publica 2017; 33(9): e00212716.
49. Hinz A, Klein AM, Brahler E, Glaesmer H, Luck T, Riedel-Heller SG, et al. Psychometric evaluation of the Generalized Anxiety Disorder Screener GAD-7, based on a large German general population sample. J Affect Disord 2017; 210: 338-44.
50. Lowe B, Decker O, Muller S, Brahler E, Schellberg D, Herzog W, et al. Validation and standardization of the Generalized Anxiety Disorder Screener (GAD-7) in the general population. Med Care 2008; 46(3): 266-74.
51. Omani-Samani R, Maroufizadeh S, Ghaheri A, Navid B. Generalized Anxiety Disorder-7 (GAD-7) in people with infertility: A reliability and validity study. Middle East Fertil Soc J 2018; 23(4): 446-9.
52. Micoulaud-Franchi JA, Lagarde S, Barkate G, Dufournet B, Besancon C, Trebuchon-Da FA, et al. Rapid detection of generalized anxiety disorder and major depression in epilepsy: Validation of the GAD-7 as a complementary tool to the NDDI-E in a French sample. Epilepsy Behav 2016; 57(Pt A): 211-6.
53. Budikayanti A, Larasari A, Malik K, Syeban Z, Indrawati LA, Octaviana F. Screening of generalized anxiety disorder in patients with epilepsy: Using a valid and reliable indonesian version of generalized anxiety disorder-7 (GAD-7). Neurol Res Int 2019; 2019: 5902610.
54. Delgadillo J, Payne S, Gilbody S, Godfrey

C, Gore S, Jessop D, et al. Brief case finding tools for anxiety disorders: Validation of GAD-7 and GAD-2 in addictions treatment. Drug Alcohol Depend 2012; 125(1-2): 37-42.
55. Esser P, Hartung TJ, Friedrich M, Johansen C, Wittchen HU, Faller H, et al. The Generalized Anxiety Disorder Screener (GAD-7) and the anxiety module of the Hospital and Depression Scale (HADS-A) as screening tools for generalized anxiety disorder among cancer patients. Psychooncology 2018; 27(6): 1509-16.
56. Baker AM, Holbrook JT, Yohannes AM, Eakin MN, Sugar EA, Henderson RJ, et al. Test Performance Characteristics of the AIR, GAD-7, and HADS-Anxiety Screening Questionnaires for Anxiety in Chronic Obstructive Pulmonary Disease. Ann Am Thorac Soc 2018; 15(8): 926-34.
57. Seo JG, Park SP. Validation of the generalized anxiety disorder-7 (GAD-7) and GAD-2 in patients with migraine. J Headache Pain 2015; 16: 97.
58. Simpson W, Glazer M, Michalski N, Steiner M, Frey BN. Comparative efficacy of the generalized anxiety disorder 7-item scale and the Edinburgh Postnatal Depression Scale as screening tools for generalized anxiety disorder in pregnancy and the postpartum period. Can J Psychiatry 2014; 59(8): 434-40.
59. Zhong QY, Gelaye B, Zaslavsky AM, Fann JR, Rondon MB, Sanchez SE, et al. Diagnostic Validity of the Generalized Anxiety Disorder - 7 (GAD-7) among Pregnant Women. PLoS One 2015; 10(4): e0125096.
60. Quon BS, Bentham WD, Unutzer J, Chan YF, Goss CH, Aitken ML. Prevalence of symptoms of depression and anxiety in adults with cystic fibrosis based on the PHQ-9 and GAD-7 screening questionnaires. Psychosomatics 2015; 56(4): 345-53.
61. Teymoori A, Real R, Gorbunova A, Haghish EF, Andelic N, Wilson L, et al. Measurement invariance of assessments of depression (PHQ-9) and anxiety (GAD-7) across sex, strata and linguistic backgrounds in a European-wide sample of patients after Traumatic Brain Injury. J Affect Disord 2020; 262: 278-85.
62. Doi S, Ito M, Takebayashi Y, Muramatsu K, Horikoshi M. Factorial Validity and Invariance of the 7-Item Generalized Anxiety Disorder Scale (GAD-7) Among Populations with and Without Self-Reported Psychiatric Diagnostic Status. Front Psychol 2018; 9: 1741.
63. Johnson SU, Ulvenes PG, Oktedalen T, Hoffart A. Psychometric Properties of the General Anxiety Disorder 7-Item (GAD-7) Scale in a Heterogeneous Psychiatric Sample. Front Psychol 2019; 10: 1713.
64. Rutter LA, Brown TA. Psychometric properties of the generalized anxiety disorder scale-7 (GAD-7) in outpatients with anxiety and mood disorders. J Psychopathol Behav Assess 2017; 39(1): 140-6.
65. Kertz S, Bigda-Peyton J, Bjorgvinsson T. Validity of the generalized anxiety disorder-7 scale in an acute psychiatric sample. Clin Psychol Psychother 2013; 20(5): 456-64.
66. Munoz-Navarro R, Cano-Vindel A, Moriana JA, Medrano LA, Ruiz-Rodriguez P, Aguero-Gento L, et al. Screening for generalized anxiety disorder in Spanish primary care centers with the GAD-7. Psychiatry Res 2017; 256: 312-7.
67. Ahmad S, Hussain S, Shah FS, Akhtar F. Urdu translation and validation of GAD-7: A screening and rating tool for anxiety symptoms in primary health care. J Pak Med Assoc 2017; 67(10): 1536-40.
68. Ahn JK, Kim Y, Choi KH. The psychometric properties and clinical utility of the Korean version of GAD-7 and GAD-2. Front Psychiatry 2019; 10: 127.
69. Sousa TV, Viveiros V, Chai MV, Vicente FL, Jesus G, Carnot MJ, et al. Reliability and validity of the Portuguese version of the Generalized Anxiety Disorder (GAD-7) scale. Health Qual Life Outcomes 2015; 13: 50.
70. Sawaya H, Atoui M, Hamadeh A, Zeinoun P, Nahas Z. Adaptation and initial validation of the Patient Health Questionnaire - 9 (PHQ-9) and the Generalized Anxiety Disorder - 7 Questionnaire (GAD-7) in an Arabic speaking Lebanese psychiatric outpatient sample. Psychiatry Res 2016; 239: 245-52.
71. Garcia-Campayo J, Zamorano E, Ruiz MA, Pardo A, Perez-Paramo M, Lopez-Gomez V, et al. Cultural adaptation into Spanish of the generalized anxiety disorder-7 (GAD-7) scale as a screening tool. Health Qual Life Outcomes 2010; 8: 8.
72. Donker T, van Straten A, Marks I, Cuijpers P. Quick and easy self-rating of Generalized Anxiety Disorder: Validity of the Dutch web-based GAD-7, GAD-2 and GAD-SI. Psychiatry Res 2011; 188(1): 58-64.
73. Belk RA, Pilling M, Rogers KD, Lovell K, Young A. The theoretical and practical determination of clinical cut-offs for the British Sign Language versions of PHQ-9 and GAD-7. BMC Psychiatry 2016; 16(1): 372.
74. Parkerson HA, Thibodeau MA, Brandt CP, Zvolensky MJ, Asmundson GJ. Cultural-based biases of the GAD-7. J Anxiety Disord 2015; 31: 38-42.
75. Naeinian MR, Shairi MR, Sharifi M, Hadian M. To study reliability and validity for a brief measure for assessing Generalized Anxiety Disorder (GAD-7). Clinical Psychology & Personality 2011; 3(4): 41-50. [In Persian].
76. Meyers LS, Gamst G, Guarino AJ. Applied multivariate research design and interpretation. Thousand Oaks, CA: SAGE Publications; 2016.
77. Masoumian S, Shabani A, Zamirinejad S, Yaghmaeizade H. Psychometric properties of the Structured Clinical Interview for DSM-5, clinician version(SCID-5-CV). Proceedings of the 36th Annual Congress of Iranian Psychiatric Association; 2019 Oct. 15-18; Tehran, Iran. [In Persian].
78. Beck AT, Epstein N, Brown G, Steer RA. An inventory for measuring clinical anxiety: Psychometric properties. J Consult Clin Psychol 1988; 56(6): 893-7.
79. Hossein Kaviani H, Mousavi AS. Psychometric properties of the Persian version of Beck Anxiety Inventory (BAI). Tehran Univ Med J 2008; 66(2): 136-40. [In Persian].
80. Kosinski M, Bayliss MS, Bjorner JB, Ware JE Jr, Garber WH, Batenhorst A, et al. A six-item short-form survey for measuring headache impact: the HIT-6. Qual Life Res 2003; 12(8): 963-74.
81. Zandifar A, Banihashemi M, Haghdoost F, Masjedi SS, Manouchehri N, Asgari F, et al. Reliability and Validity of the Persian HIT-6 Questionnaire in Migraine and Tension-type Headache. Pain Pract 2014; 14(7): 625-31.
82. Martin BC, Pathak DS, Sharfman MI, Adelman JU, Taylor F, Kwong WJ, et al. Validity and reliability of the migraine-specific quality of life questionnaire (MSQ Version 2.1). Headache 2000; 40(3): 204-15.
83. Zandifar A, Masjedi SS, Haghdoost F, Asgari F, Manouchehri N, Banihashemi M, et al. The psychometric properties of the Persian migraine-specific quality of life questionnaire version 2.1 in episodic and chronic migraines. ScientificWorldJournal 2013; 2013: 950245.
84. Netemeyer RG, Bearden WO, Sharma S. Scaling procedures: Issues and applications. Thousand Oaks, CA: SAGE Publications; 2003.
85. Nunnally JC. Psychometric theory. New York, NY: McGraw-Hill; 1978.
86. Di Martino S., Di N, I, Esposito C, Prilleltensky I, Arcidiacono C. Measuring subjective well-being from a multidimensional and temporal perspective: Italian adaptation of the I COPPE scale. Health Qual Life Outcomes 2018; 16(1): 88.
87. Swets JA. Measuring the accuracy of diagnostic systems. Science 1988; 240(4857): 1285-93.
88. Greiner M, Pfeiffer D, Smith RD. Principles and practical application of the receiver-operating characteristic analysis for diagnostic tests. Prev Vet Med 2000; 45(1-2): 23-41.
89. Baskin SM, Lipchik GL, Smitherman TA. Mood and anxiety disorders in chronic headache. Headache 2006; 46(Suppl 3): S76-S87.
90. Lanteri-Minet M, Radat F, Chautard MH, Lucas C. Anxiety and depression associated with migraine: Influence on migraine subjects' disability and quality of life, and acute migraine management. Pain 2005; 118(3): 319-26.
91. Radat F, Creac'h C, Swendsen JD, Lafittau M, Irachabal S, Dousset V, et al. Psychiatric comorbidity in the evolution from migraine to medication overuse headache. Cephalalgia 2005; 25(7): 519-22.
92. Beard C, Bjorgvinsson T. Beyond generalized anxiety disorder: Psychometric properties of the GAD-7 in a heterogeneous psychiatric sample. J Anxiety Disord 2014; 28(6): 547-52.
93. Moreno E, Munoz-Navarro R, Medrano LA, Gonzalez-Blanch C, Ruiz-Rodriguez P, Limonero JT, et al. Factorial invariance of a computerized version of the GAD-7 across various demographic groups and over time in primary care patients. J Affect Disord 2019; 252: 114-21.