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The Influence of Current Mood States on Screening Accuracy of the Mood Disorder Questionnaire

Hee Ryung Wang[1], Won-Myong Bahk[2], Bo-Hyun Yoon[3], Moon-Doo Kim[4], Young-Eun Jung[4], Kyung Joon Min[5], Jeongwan Hong[6], Young Sup Woo[2]

[1]Seoul Health Foundation, [2]Department of Psychiatry, College of Medicine, The Catholic University of Korea, Seoul, [3]Department of Psychiatry, Naju National Hospital, Naju, [4]Department of Psychiatry, Jeju National University Hospital, Jeju, [5]Department of Psychiatry, Chung-Ang University, Seoul, [6]Department of Psychiatry, Iksan Hospital, Iksan, Korea

Objective: In this study we investigated whether current mood states of patients with bipolar disorder have an influence on the screening accuracy of the Mood Disorder Questionnaire (MDQ).
Methods: A total of 452 patients with mood disorder (including 192 with major depressive disorder and 260 with bipolar disorder completed the Korean version of the MDQ. Patients with bipolar disorder were subdivided into three groups (bipolar depressed only, bipolar euthymic only, bipolar manic/hypomanic only) according to current mood states. The screening accuracy of the MDQ including sensitivity, specificity and area under the curve (AUC) of receiver operating characteristic (ROC) curves were evaluated according to current mood states.
Results: The optimal cutoff of MDQ was 5 in this study sample. Sensitivity and specificity were not significantly different according to current mood states. Significant differences in AUCs of four independent ROC curves were not found (ROC 1st curve included all bipolar patients; ROC 2nd curve included only bipolar depressed patients; ROC 3rd curve included only bipolar manic/hypomanic patients; ROC 4th curve included only bipolar euthymic patients).
Conclusion: The study results showed that current mood states (either euthymic state, depressed or manic/hypomanic) did not significantly influence the screening accuracy of the MDQ suggesting that the MDQ could be a useful screening instrument for detecting bipolar disorder in clinical practice regardless of the current mood symptoms of subjects.

KEY WORDS: Mood Disorder Questionnaire; Current mood states; Sensitivity; Specificity; Area under the curve.

INTRODUCTION

Bipolar disorder is a chronic psychiatric disorder associated with significant morbidity and mortality. Patients with bipolar disorder tend to spend much more time in the depressed phase than in the manic or hypomanic phase, thus, accurately detecting bipolar disorder when patients present with depressive symptoms is difficult [1]. Misdiagnosis or delayed diagnosis of bipolar disorder is associated with detrimental prognosis such as increased suicidality, poor treatment response, mood destabilization and severe impairment in socio-occupational functions [2]. Thus, many efforts have been made to develop useful screening instruments for detecting bipolar disorder and various instruments are used in clinical practice [3].

The Mood disorder questionnaire (MDQ) developed by Hirschfeld *et al.* [4] in 2000, is a commonly used screening instrument for screening bipolar disorder. The MDQ is composed of 3 parts; the first part is composed of 13 statements to identify whether hypomanic or manic symptoms were present; the second part is composed of one question determining whether the symptoms in the first part occurred simultaneously; the third part is composed of one question regarding the consequences of the symptoms mentioned above. Hirschfeld *et al.* [4] suggested a standard cutoff of 7 (i.e., 7 or more symptoms detected in the first part, and those symptoms occurred simulata-

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Address for correspondence: Won-Myong Bahk
Department of Psychiatry, Yeouido St. Mary's Hospital, College of Medicine, The Catholic University of Korea, 10 63-ro, Yeongdeungpo-gu, Seoul 07345, Korea
E-mail: wmbahk@catholic.ac.kr
ORCID: https://orcid.org/0000-0002-0156-2510

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neously in the second part, and the consequences of those symptoms caused moderate or serious impairment in the third part) as the optimal cutoff value. The screening accuracy of the MDQ among clinical samples has been confirmed in many previous validation studies and meta-analyses [3,5-15]. In our previous meta-analysis [5], several clinical correlates were shown to impact the screening accuracy of the MDQ. Due to its property of a self-rating instrument, various patient-related factors can affect the subjects' response to the questions in the MDQ. Memory disturbances, poor insight for their symptoms, consequences of their problem or cognitive dysfunction can affect the screening accuracy of the MDQ. Mood states are associated with changes in memory function, impaired insight and altered cognitive function [16-20]. Thus, different current mood states can possibly impact the screening accuracy of the MDQ for bipolar disorder. Despite this concern, to date, limited information exists regarding whether different mood states influence the screening accuracy of the MDQ [21]. The information regarding whether current mood states change the screening accuracy of the MDQ is very important because clinicians could choose the best time for administering the MDQ to their patients in their clinical practice. Thus, we compared the screening accuracy including sensitivity and specificity and area under the curve (AUC) of receiver operating characteristic (ROC) curves of the MDQ by subdividing bipolar patients according to current mood states.

METHODS

Subjects and Assessments

This study was performed in 10 university hospitals or psychiatric hospitals in Korea from September 1, 2013 to March 31, 2015. Patients with major depressive disorder (MDD) or bipolar disorder were recruited regardless of whether they were inpatients or outpatients. The diagnosis of mood disorder (either MDD or bipolar disorder) was based on the Structural Clinical Interview of the Diagnostic and Statistical Manual of Mental Disorders 4th edition (SCID) conducted by participating psychiatrists. The patients who provided independent written informed consent were included and those who had mood disorders secondary to general medical conditions, unstable medical conditions or received electroconvulsive therapy (ECT) within 4 weeks of the study entry were excluded. This study was approved by the Institutional Review Boards of the 10 participating hospitals. After study enrollment, clinical information including various sociodemographic and disease-related variables were obtained by participating psychiatrists in this study. At the study entry, subjects were required to complete the Korean version of the MDQ and other clinical rating scales such as the Young Mania Rating Scale (YMRS) [22] and Montgomery-Asberg Depression Rating Scale (MADRS) [23].

Statistical Analysis

Patients with bipolar disorder were divided into three groups according to their current mood states (manic/hypomanic, depressed or euthymic). We compared clinical characteristics between the four groups (group 1, MDD patients; group 2, patients with bipolar disorder currently in the manic/hypomanic state; group 3, patients with bipolar disorder currently in the euthymic state; group 4, patients with bipolar disorder currently in a depressed state). ANOVA was conducted for continuous variables and Pearson's chi-square test was conducted for categorical variables.

To compare the screening accuracy of the MDQ according to current mood states, we calculated the sensitivity, specificity and AUC of each ROC curve in four occasions (the first occasion was when the MDQ was applied among patients with MDD and all patients with bipolar disorder; the second occasion was when the MDQ was applied among patients with MDD and patients with bipolar disorder currently in the manic/hypomanic state, the third occasion was when the MDQ was applied among patients with MDD and patients with bipolar disorder currently in the euthymic state, the fourth occasion was when the MDQ was applied among patients with MDD and patients with bipolar disorder currently in a depressed state). To investigate whether screening accuracy of MDQ significantly differs according to current mood states of bipolar patients, we compared the AUCs of the four independent ROC curves of the four occasions mentioned above.

For ANOVA, Pearson's chi-square test and ROC curve analyses, we used the PASW Statistics, version 18 (IBM Corp., Armonk, NY, USA). For comparison of independent ROC curves, we used MedCalc version 16.8. A p value of 0.05 was considered to indicate statistical sig-

nificance for ANOVA, Pearson's chi-square test and ROC curve analyses. However, for comparison of independent ROC curves, due to multiple comparisons, a p value of 0.0083 (0.05/6) was considered to indicate statistical significance.

RESULTS

A total of 452 patients were included in the analysis. Of those, 192 were diagnosed with MDD and 260 with bipolar disorder. Among the 260 bipolar patients, 66 were currently manic/hypomanic (bipolar manic/hypomanic group), 88 were currently depressed (bipolar depressed group) and 106 were in the euthymic state (bipolar euthymic group). The sociodemographic and disease-related variables that differed significantly between the four groups (MDD group, bipolar manic/hypomanic group, bipolar euthymic group and bipolar depressed group) were age (p = 0.011), educational years (p = 0.007), marital status ($p <$ 0.001), number of previous depressive episodes ($p <$ 0.001), age at onset of illness ($p <$ 0.001), family history of bipolar disorder (p = 0.002), history of recurrent depressive episode (more than 3 episodes; $p <$ 0.001) and history of suicidal ideation ($p <$ 0.001). The total mean YMRS scores differed across the 4 groups (MDD group, 3.8 ± 3.6; bipolar manic/hypomanic group, 27.7 ± 12.5; bipolar euthymic group, 3.4 ± 4.1; bipolar depressed group, 4.9 ± 4.3; $p <$ 0.001). The total mean MADRS scores also differed across the 4 groups (MDD group, 19.3 ± 10.2; bipolar manic/hypomanic group, 11.7 ± 8.2; bipolar euthymic group, 4.3 ± 5.8; bipolar depressed group, 23.5 ± 8.6; $p <$ 0.001). The total scores of the first part of the MDQ also differed (MDD group, 5.3 ± 3.8; bipolar manic/hypomanic group, 8.3 ± 3.6; bipolar euthymic group, 9.2 ± 3.1; bipolar depressed group, 8.9 ± 3.2; p = 0.019). The characteristics of study subjects are shown in Table 1.

To assess the screening accuracy of the MDQ, we calculated sensitivity, specificity and AUCs by applying the standard cutoff of 7 suggested by the original authors [4]. At the standard cutoff of 7, when including all bipolar patients (bipolar manic/hypomanic group, bipolar euthymic group, and bipolar depressed group), the sensitivity was 33.8%, specificity was 90.6%, and AUC was 0.622. When including only the bipolar manic/hypomanic group, the sensitivity, specificity, and AUC were 33.3%, 90.6%, and 0.620, respectively. When including only the bipolar depressed group, the sensitivity, specificity, and AUC were 29.5%, 90.6%, and 0.601, respectively. When including only the bipolar euthymic group, the sensitivity, specificity, and AUC were 37.7%, 90.6%, and 0.642, respectively (Table 2).

The optimal cutoff of MDQ in this study was 5 in the first part of the MDQ without considering the other 2 parts of the MDQ (the second and third parts). At the optimal cutoff of 5, when including all bipolar patients, the sensi-

Table 1. Characteristics of study subjects

Characteristic	Bipolar manic	Bipolar depressed	Bipolar euthymic	MDD	p value
Age (yr)	37.9 ± 13.8	39.7 ± 12.3	38.9 ± 11.1	43.0 ± 14.0	0.011
Education (yr)	13.4 ± 3.1	12.7 ± 3.1	13.4 ± 2.5	12.4 ± 2.8	0.007
Depressive episodes (n)	1.5 ± 2.2	4.1 ± 3.3	3.7 ± 5.9	2.4 ± 2.0	< 0.001
Age at onset (yr)	25.7 ± 11.1	28.2 ± 10.8	26.1 ± 9.2	37.0 ± 13.1	< 0.001
MDQ total	8.3 ± 3.6	8.9 ± 3.2	9.2 ± 3.1	5.3 ± 3.8	0.019
YMRS total	27.7 ± 12.5	4.9 ± 4.3	3.4 ± 4.1	3.8 ± 3.6	< 0.001
MADRS total	11.7 ± 8.2	23.5 ± 8.6	4.3 ± 5.8	19.3 ± 10.2	< 0.001
Marital status (%)					< 0.001
Unmarried	54.5	50.0	47.2	31.3	
Married	42.4	31.8	37.7	54.2	
Separated, divorced, bereaved	3.0	18.2	15.1	14.6	
Family history of bipolar disorder (%)	3.0	15.9	11.3	4.2	0.002
History of more than 3 depressive episodes (%)	18.2	45.5	49.1	28.1	< 0.001
Age at onset < 25 yr (%)	27.3	36.4	39.6	26	0.06
Presence of suicidal ideation (%)	6.1	34.1	1.9	12.5	< 0.001

Values are presented as mean ± standard deviation or percent only.
MDD, major depressive disorder; MDQ, Mood Disorder Questionnaire; YMRS, Young Mania Rating Scale; MADRS, Montgomery-Asberg Depression Rating Scale.

Table 2. Screening accuracy and ROC curve analysis at the standard cutoff of 7

Variable	Sensitivity (%)	Specificity (%)	AUC	95% CI	*p* value
Bipolar total vs. MDD	33.8	90.6	0.622	0.571−0.673	< 0.001
Bipolar manic/hypomanic vs. MDD	33.3	90.6	0.620	0.536−0.704	0.004
Bipolar depressed vs. MDD	29.5	90.6	0.601	0.526−0.676	0.007
Bipolar euthymic vs. MDD	37.7	90.6	0.642	0.573−0.711	< 0.001

ROC, receiver operating characteristic; AUC, area under the curve; CI, confidence interval; MDD, major depressive disorder.

Table 3. Screening accuracy and ROC curve analysis at the optimal cutoff of 5

Variable	Sensitivity (%)	Specificity (%)	AUC	95% CI	*p* value
Bipolar total vs. MDD	84.6	47.9	0.76	0.715−0.805	< 0.001
Bipolar manic/hypomanic vs. MDD	78.8	47.9	0.717	0.645−0.789	< 0.001
Bipolar depressed vs. MDD	88.6	47.9	0.766	0.709−0.824	< 0.001
Bipolar euthymic vs. MDD	84.9	47.9	0.782	0.73−0.834	< 0.001

ROC, receiver operating characteristic; AUC, area under the curve; CI, confidence interval; MDD, major depressive disorder.

Table 4. Comparison of AUC of Independent ROC curves according to mood states

	AUC	SE	*p* value			
			Bipolar total	Bipolar manic/hypomanic	Bipolar depressed	Bipolar euthymic
Bipolar total	0.76	0.023		0.324	0.871	0.535
Bipolar manic/hypomanic	0.717	0.037	0.324		0.297	0.156
Bipolar depressed	0.766	0.029	0.871	0.297		0.686
Bipolar euthymic	0.782	0.027	0.535	0.156	0.686	

AUC, area under the curve; ROC, receiver operating characteristic; SE, standard error.

tivity was 84.6% and the specificity was 47.9%. The AUC of the ROC curve was 0.760 (95% confidence interval [CI], 0.715−0.805). When only the bipolar manic/hypomanic group is included, the sensitivity was 78.8%, specificity was 47.9%, and AUC of the ROC curve was 0.717 (95% CI, 0.645−0.789). When only the bipolar depressed group is included, the sensitivity, specificity, and AUC of the ROC were 88.6%, 47.9%, and 0.766 (95% CI, 0.709−0.824), respectively. When only the bipolar euthymic group is included, the sensitivity, specificity, and AUC of the ROC were 84.9%, 47.9%, and 0.782 (95% CI, 0.730−0.834), respectively (Table 3).

When AUCs of the 4 independent ROC curves (all bipolar patients; only the bipolar manic/hypomanic group; only the bipolar euthymic group; and only the bipolar depressed group) were compared with each other, significant differences were not observed (p = 0.324 for all bipolar patients vs. only the bipolar manic/hypomanic group, p = 0.871 for all bipolar patients vs. only the bipolar depressed group, p = 0.535 for all bipolar patients vs. only the bipolar euthymic group, p = 0.297 for only the bipolar manic/hypomanic group vs. only the bipolar depressed group, p = 0.156 for only the bipolar manic/hypomanic group vs. only the bipolar euthymic group, p = 0.686 for only the bipolar depressed group vs. only the bipolar euthymic group) (Table 4).

DISCUSSION

To the best of our knowledge, this was the first study that compared the screening accuracy of the MDQ according to the current mood states by comparing AUCs of independent ROC curves of the MDQ. Previous bipolar studies suggested that degree of impairment of insight could differ according to current mood states of bipolar disorder patients [16-18]. The impairment of insight for their symptoms or consequences of their behaviors could make patients respond to the MDQ items differently depending on the mood states present at the time of assessment indicating that current mood states of patients could

alter the screening ability of the MDQ. Although a previous study suggested that insight was not significantly associated with false negativity of MDQ screening [24], the association between insight level and false negativity was calculated from only 16 patients and due to the small sample size (n = 16), was too weak to confirm that level of insight is not associated with false negativity of the MDQ. In addition to insight, memory or recall bias according to mood states could influence the screening ability of the MDQ. Previous reports suggested that depressive symptoms are associated with memory biases [19,20]. These findings also suggest the possibility that patients with mood disorders respond to the MDQ differently due to memory problems according to whether they are in a depressed state or euthymic state. Accordingly, various factors changing with current mood states could contribute to the differences in the MDQ's performance; however, to date, limited information exists on whether differences in current mood states impact the ability of the MDQ to differentiate bipolar disorder from MDD [21]. Gervasoni *et al.* [21] investigated whether symptom severity of depression or hypomania at the time of assessment influences the MDQ's performance among a total of 146 patients with mood disorder (MDD = 102, bipolar disorder = 44). They concluded that the MDQ's performance was independent of depressive symptom severity among their subjects; however, the influence of manic symptoms required further evaluation. Collectively, our study results showed that current mood states (whether being hypomanic/manic or depressed or euthymic) did not alter the screening accuracy of the MDQ among a large number of patients with mood disorders indicating that the MDQ could be used adequately as a screening instrument for bipolar disorder in clinical practice regardless of the subjects' current mood states.

In this study, the optimal cutoff of MDQ was 5 and resulted in a sensitivity of 84.6% and specificity of 47.9%. When applying the original standard cutoff of 7 recommended by Hirschfeld *et al.* [4], the sensitivity for bipolar disorder was lowered to 33.8%. This finding is consistent with previous studies [6,8,9,11-13,25], where low sensitivity was shown when applying the standard cutoff of 7; thus, a lower cutoff value for adequate sensitivity for screening bipolar disorder was suggested. In our current meta-analysis based on 21 studies [5], the summary sensitivity was 0.78 and summary specificity was 0.76 when applying the optimal cutoff values. Compared with this summary sensitivity and specificity, our study sample showed similar sensitivity (84.6%) but lower specificity (47.9%). We do not exactly know why our study sample showed significantly lower specificity, however, our research included all patients with bipolar disorder who were hypomanic/manic, depressed or euthymic. The majority of previous studies included in our meta-analysis [5] calculated sensitivity and specificity among patients who were currently in a depressed state [7,10,13,25-27]. This difference in population characteristics in our study sample could contribute to lower specificity of MDQ compared with previous studies included in our meta-analysis [5]. Previous studies suggested that MDQ combined with other screening instruments screened bipolar disorder more effectively [13,28]. Considering the lower specificity of the MDQ shown in this study, further studies that investigate whether a combination of two or more screening instruments improve the ability to differentiate bipolar disorder from other mood disorders is needed.

In accordance with previous findings, our study showed that patients with bipolar disorder were younger, had a younger age at onset, greater family history of bipolar disorder, greater history of recurrent depressive episodes (defined by more than 3 episodes) and greater history of suicidal ideation compared with patients with MDD [29,30]. These findings confirmed more disease-related burden of patients with bipolar disorder. Consistent with previous findings, our study showed that patients with bipolar disorder had higher MDQ total scores compared with patients with MDD [7,31,32]. Interestingly, the bipolar manic/hypomanic group showed similar total MDQ scores compared with bipolar depressed or euthymic groups. In a previous report, bipolar disorder patients currently in the manic state showed significantly poorer insight than those currently in a depressed state [33]. Nonetheless, because the bipolar manic/hypomanic group showed similar MDQ scores compared with the bipolar depressed or euthymic groups, this result indicates although subjects are currently in hypomanic or manic states, they could adequately respond to the MDQ.

This study had several limitations. First, this study had a "between-subjects design". For more accurate detection of the possible differences in screening accuracy of the MDQ, a "within-subjects design" would be ideal and

would enable clinicians to show whether each patient responds differently to the MDQ according to their mood states. However, we were only able to perform the between-subjects design. Second, other clinical correlates known to impact the screening ability of the MDQ exist, such as the presence of other Axis I disorders [26]. However, we could not concurrently evaluate their impact on the screening accuracy of MDQ except for current mood states. Thus, further comprehensive studies investigating MDQ's screening ability while considering various clinical correlates are warranted. Third, the mean total YMRS score among the bipolar manic/hypomanic group was 27.7 and the MADRS score among the bipolar depressed group was 23.5. Thus, this result cannot be generalized to bipolar disorder patients with more severe manic or depressed symptoms.

In conclusion, our study indicated the optimal cutoff value of MDQ is 5 and the screening accuracy of MDQ is not influenced by the current mood states of subjects. The results from this study are meaningful because they indicate that MDQ could be administered to patients with mood disorders regardless of their current mood states. Further studies on the usefulness of the MDQ combined with other screening instruments, or studies investigating differences in screening accuracy with within-subjects design and long-term follow up of patients with mood disorders are needed.

■ Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

■ Author Contributions

All authors were involved in the design of the study, interpretation of the data, writing of the manuscript, and the decision to submit the manuscript for publication. All authors read and approved the final manuscript.

■ ORCID

Hee Ryung Wang https://orcid.org/0000-0003-2589-8024
Won-Myong Bahk https://orcid.org/0000-0002-0156-2510
Bo-Hyun Yoon https://orcid.org/0000-0002-3882-7930
Moon-Doo Kim https://orcid.org/0000-0002-6441-630X
Young-Eun Jung https://orcid.org/0000-0001-7608-0009
Kyung Joon Min https://orcid.org/0000-0001-7037-8904
Jeongwan Hong https://orcid.org/0000-0003-0458-6750
Young Sup Woo https://orcid.org/0000-0002-0961-838X

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