Comparison of the 32-item Hypomania Checklist (HCL-32), the 33-item Hypomania Checklist (HCL-33) and the Mood Disorders Questionnaire (MDQ) for bipolar disorder

Running Head: Screening tools for bipolar disorder

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ABSTRACT

Aim: Bipolar disorder (BD) is frequently misdiagnosed as major depression and hence reliable and culturally appropriate screening tools are needed. This study compared the 32-item Hypomania Checklist (HCL-32), the 33-item Hypomania Checklist (HCL-33), and the Mood Disorders Questionnaire (MDQ) for BD.

Methods: Altogether, 350 depressed patients were included. The HCL-32, the HCL-33 and the MDQ were completed by patients to identify manic and/or hypomanic symptoms. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and area under the curve between the HCL-32, the HCL-33 and the MDQ for BD and major depression were calculated and compared, using cutoffs suggested by respective validation studies.

Results: Of the three scales, the MDQ had the highest sensitivity and NPV (sensitivity = 0.90, 0.81, and 0.90 for BD vs MDD, BD-I vs MDD and BD-II vs MDD, respectively; NPV = 0.78, 0.86, and 0.86 for BD vs MDD, BD-I vs MDD and BD-II vs MDD, respectively), while the HCL-33 has the highest specificity and PPV (specificity = 0.74, 0.69, and 0.66 for BD vs MDD, BD-I vs MDD and BD-II vs MDD, respectively; PPV = 0.74, 0.55, and 0.56 for BD vs MDD, BD-I vs MDD and BD-II vs MDD, respectively).

Conclusions: Compared to both HCL scales, the MDQ had higher sensitivity and lower specificity in screening for BD. These results contradict previous findings in Western populations. As a screening instrument, the MDQ for BD in Chinese clinical settings appears appropriate.

Key words: Bipolar disorder, screening, self-report, sensitivity, specificity

INTRODUCTION

Bipolar disorder (BD) is a recurrent illness characterized by depressive and manic or hypomanic episodes [1]. Depressive symptoms usually appear first at the onset of BD, and depressive episodes are more often compared to manic or hypomanic episodes [2]. Therefore, BD is often misdiagnosed as other psychiatric disorders, particularly major depression [1, 3], which can lead to poor clinical outcome, such as increased risk for suicide [4]. Compared with unipolar depressed patients, bipolar patients are at higher suicide risk [5-7]. Clinical recommendations for improving the identification of BD include comprehensive clinical evaluation and the administration of screening tools [8, 9].

Standardized diagnostic instruments, such as the Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders (DSM) (SCID), are widely used in clinical studies, but the interview is time-consuming and requires trained raters [10]. Instead, in order to improve the detection of BD, several brief self-reported screening questionnaires have been developed, such as the Mood Disorders Questionnaire (MDQ), the 32-item Hypomania Checklist (HCL-32) and the 33-item Hypomania Checklist (HCL-33) that is a recently modified version of the HCL-32 including some additional items [11-13]. All the instruments have been validated in psychiatric settings with satisfactory psychometric properties [14-16].

Several Western studies compared the psychometric properties of the MDQ and the HCL-32 and commonly found that the HCL-32 had a relatively high sensitivity, and the MDQ had a high specificity in detecting BD [17, 18].

There is compelling evidence that Western psychiatric diagnostic systems could not cover the full range of mood symptoms experienced by Chinese patients [19, 20], therefore the findings in the West need to be examined in Chinese patients separately. A transcultural study of depressed patients [21], however, found that total scores on the HCL-32 varied across cultures, being lowest in the Far East. Therefore, it is necessary to examine the usefulness of these instruments in Chinese patients with mood disorders.

The HCL-33 is a newly developed tool by Angst and colleagues; its psychometric properties have been only tested in Chinese clinical settings [12]. To date there has been no existing study directly comparing the HCL-32, the HCL-33 and the MDQ in the same sample, let alone in a Chinese sample. We aim to compare the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and area under the curve (AUC) between the HCL-32, the HCL-33 and the MDQ for BD and major depression.

METHOD

Study sample and sites

This study was conducted between January 1 and December 28, 2014 in Beijing Anding Hospital. Inpatients were included if they (1) were adults (18 - 65 years), (2) were diagnosed as BD depressive episode or MDD by a review of medical record and confirmed in a clinical interview by two psychiatrists according to the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10) (ascertained by a review of medical records) [22], (3) had

the ability to understand the contents of the interview. Participants were excluded if they had a depressive disorder secondary to major medical conditions affecting the cardiovascular, respiratory, digestive, hematological, endocrine, urinary, connective tissue, and nervous systems. The study protocol was approved by the Ethics Committee at Beijing Anding Hospital. Written informed consent was obtained from each patient.

Instruments and evaluation

Hospitalized depressed patients treated in this hospital were consecutively screened for eligibility. Their basic demographic and clinical characteristics were collected by a data collection form.

The HCL-32 is a self-reported scale for identifying hypomanic symptoms in depressed patients [11]. There are 32 hypomanic symptoms with yes/no answers. The total score of the HCL-32 is calculated by adding up positive answers. The HCL-33 is a self-reported scale with yes/no questions for identifying hypomanic symptoms in depressed patients. The total score is obtained by adding up positive answers. The HCL-32 and the HCL-33, Chinese versions, have been validated in China [12, 23]. The MDQ is a self-reported scale with 13 yes/no questions used to screen hypomania or mania [13]. The final question measures the level of impairment due to the symptoms using a 4-point scale. The Chinese version of the MDQ has been validated in China [15].

The Chinese version of the Hamilton Depression Rating Scale (HAMD) 17-item [24, 25] was used to assess depressive symptoms. The Chinese version of

the Mini-International Neuropsychiatric Interview (MINI), Version 5.0 was used to establish the DSM-IV diagnoses of MDD and BD [26, 27].

Eligible patients completed the HCL-33, followed by the clinical assessment, the MDQ and the HCL-32. Patients' clinical diagnoses were established with the MINI by four psychiatrists who were blind to the MDQ, the HCL-33 and the HCL-32 results. All four raters were trained using the MINI in patients with bipolar depression and their judgments were compared with the best estimate clinical diagnoses with kappa values > 0.85.

Statistical analyses

All analyses were conducted using the SPSS, 20.0. Patients' socio-demographic and clinical characteristics were characterized by descriptive statistics. Criterion validity of the HCL-33, the HCL-32 and the MDQ were estimated with sensitivity, specificity, PPV and NPV. In order to examine the threshold to discriminate between bipolar and non-bipolar patients, Receiver Operating Characteristic (ROC) curves were calculated for the HCL-32, the HCL-33 and the MDQ. The level of significance was set at 0.05 (two-sided).

RESULTS

Of the 375 patients screened for the study, 350 (161 with MDD, 90 with BD-I and 99 with BD-II based on the MINI assessment) fulfilled the study criteria and were included in the analysis. Table 1 presents demographic and clinical characteristics of patients with MDD and BD.

Table 2 compared the sensitivity, specificity, PPV, NPV and AUC between the HCL-33, the HCL-32 and the MDQ for BD and major depression using the cutoffs suggested by respective validation studies. Of the three instruments, the MDQ had the highest sensitivity and NPV, while the HCL-33 had the highest specificity and PPV (Figures 1.1-1.3).

Cohen's Kappa value was calculated to examine the interrater agreement between MINI and the three questionnaires (the HCL-33, HCL-32 and MDQ) for the diagnosis of BD and MDD. There was poor agreement between the MINI and HCL-33 (k= 0.35, 95% CI=0.25-0.44, p<0.001), between the MINI and HCL-32 (k=0.33, 95%CI=0.23-0.43, p<0.001) and between the MINI and MDQ (k=0.30, 95%CI= 0.21-0.39, p<0.001) [28].

DISCUSSION

This is the first study comparing the HCL-33, the HCL-32 and the MDQ in screening BD and major depression in the same sample. All three instruments had acceptable psychometric properties in terms of sensitivity, specificity, PPV, NPV, and AUC in BD screening.

Several Western studies found that the HCL-32 had higher sensitivity while the MDQ showed higher specificity [17, 29, 30]. However, this study of Chinese patient cohort found opposite result; i.e., the MDQ has the highest sensitivity and NPV, while the HCL-33 has the highest specificity and PPV, suggesting that the MDQ is the most appropriate instrument in identifying patients with BD, while the HCL-33 is the most appropriate instrument in identifying patients without BD. We

assumed that the discrepancy between Chinese and Western studies could be due to cultural influence on the expression of psychiatric symptoms in mood disorders [31]. For example, Chinese patients with depressive episodes are more likely to somatize depressive symptoms than their Western counterparts [20, 32]. Therefore, it is likely that the cultural nuances in Chinese patients can result in different expression of hypomanic symptoms compared with patients from Western cultures, which may explain the differences in instrument sensitivities and specificities in BD. A previous study also found that the loadings and clinical burden of the HCL items varied across different cultures and settings [21]. For example, the Arabic and Italian versions of the HCL-32 showed different factor loadings [33, 34]. The HCL-33 is a modified version of the HCL-32 including some additional questions [12]. We found that compared to the HCL-32, the HCL-33 has better or similar psychometric properties in terms of specificity, PPV and AUC indicating the HCL-33 is a reliable screening tool for BD. In addition, compared to the HCL-32 and the HCL-33, the MDQ has relatively less items on hypomania, which could perhaps partly contribute to its fair specificity for BD-I, but lower specificity for BD-II.

In terms of study limitations, first, only inpatients in a major psychiatric hospital were included. Second, psychiatric co-morbidities were not recorded, which could have influenced the sensitivity and specificity of the three instruments. Third, the diagnoses were ascertained using the MINI, rather than more sophisticated diagnostic instruments, such as the SCID. Fourth, these instruments are clinically useful to screen for BD, but they could not provide

clinical diagnosis as standard diagnostic instruments, such as the SCID or MINI, which could partly account for the poor agreements between the MINI and these instruments. Finally, this study was cross-sectional and both MDD and BD patients were recruited in depressive phase.

In conclusion, the results showed that the sensitivity, specificity, PPV and NPV of the HCL scales and the MDQ in Chinese patients are different compared to findings in Western studies. Due to the high sensitivity, as screening instrument, the routine use of the MDQ for BD in Chinese clinical settings appears appropriate.

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DISCLOSURE STATEMENT

There is no conflict of interest concerning the authors in conducting this study and preparing the manuscript.

AUTHOR CONTRIBUTIONS

Conception and design of the study: YF, YTX. Acquisition and analysis of data: YF, WH, YYW, YTX. Drafting the manuscript or figures: YYW, YTX, GW, GSU, CHN, ZY.

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Figure legends

Figure 1.1. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and Area Under the Curve (AUC) for the HCL-33, the HCL-32 and the MDQ for bipolar disorder vs. major depressive disorder

Figure 1.2. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and Area Under the Curve (AUC) for the HCL-33, the HCL-32 and the MDQ for type I bipolar disorder vs. major depressive disorder

Figure 1.3. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and Area Under the Curve (AUC) for the HCL-33, the HCL-32 and the MDQ for type II bipolar disorder vs. major depressive disorder

Table 1. Basic demographic and clinical characteristics of patients diagnosed with major depressive disorder and bipolar disorder

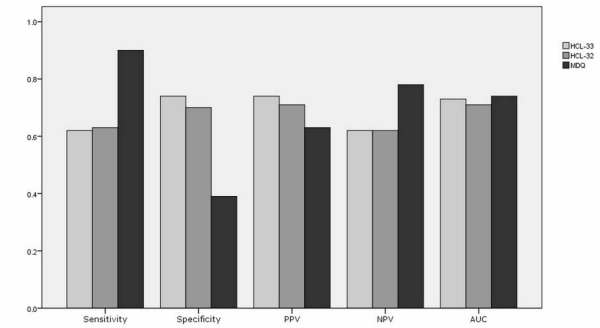
	The whole sample (n=350)		MDD (n=161)		BD				MDD vs. BD		MDD vs. BD-I		MDD vs. BD-II	
					BD-1 (n=90)		BD-2 (n=99)							
	N	%	N	%	N	%	N	%	X^2	P	X^2	P	X^2	P
Male	109	31.1	58	36.0	28	31.1	23	23.2	3.3	0.09	0.6	0.41	4.6	0.01
Married	223	63.7	116	72.0	59	65.6	48	48.5	8.6	**0.03**	1.1	0.23	14.6	**0.001**
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	T	P	T	P	T	P
Age (years)	37.7	13.0	40.6	13.2	34.6	12.2	35.7	12.5	4.0	**0.001**	3.7	**0.001**	3.0	**0.003**
Education (years)	12.3	5.2	12.0	6.9	12.5	3.0	12.4	3.1	-0.7	0.46	-0.6	0.59	-0.5	0.63
Age of onset (years)	29.6	12.6	33.1	13.1	26.3	10.5	26.9	12.1	1.3	0.19	4.4	**0.001**	3.9	**0.001**
Number of episodes	3.5	3.8	2.8	3.3	3.9	3.3	4.3	4.8	-3.2	**0.001**	0.2	**0.02**	2.7	**0.007**
HAMD total	20	7.1	20.7	6.8	20.2	6.7	18.7	7.9	1.6	0.10	0.5	0.53	2.0	**0.07**

Bolded value: P<0.05; BD=bipolar disorder; MDD=major depressive disorder; HAMD=Hamilton Depression Rating Scale

Table 2. Sensitivity, specificity, PPV, NPV, and Area Under the Curve (AUC) for the HCL-33, the HCL-32 and the MDQ for BD and MDD

	Scales	Cut-off value	Setting	Sensitivity	Specificity	PPV	NPV	AUC	95% CI
BD vs. MDD	HCL-33	15 [12]	Inpatients	0.62	0.74	0.74	0.62	0.73	0.68-0.79
	HCL-32	14 [16]	Inpatients and outpatients	0.63	0.70	0.71	0.62	0.71	0.65-0.76
	MDQ	3 [15]	Inpatients and outpatients	0.90	0.39	0.63	0.78	0.74	0.68-0.79
BD-I vs. MDD	HCL-33	14 [12]	Inpatients	0.67	0.69	0.55	0.79	0.74	0.68-0.80
	HCL-32	13 [23]	Inpatients and outpatients	0.69	0.67	0.54	0.79	0.72	0.66-0.79
	MDQ	5 [15]	Inpatients and outpatients	0.81	0.63	0.55	0.86	0.77	0.71-0.83
BD-II vs. MDD	HCL-33	13 [12]	Inpatients	0.72	0.66	0.56	0.79	0.73	0.66-0.79
	HCL-32	12 [16]	Inpatients and outpatients	0.71	0.64	0.55	0.78	0.69	0.63-0.76
	MDQ	3 [15]	Inpatients and outpatients	0.90	0.39	0.47	0.86	0.71	0.64-0.77

PPV = Positive Predictive Value, NPV = Negative Predictive Value, AUC = Area under the curve (ROC), CI = 95 % confidence interval for AUC, MDQ = Mood Disorder Questionnaire, and HCL-33 = Hypomania Checklist-33.



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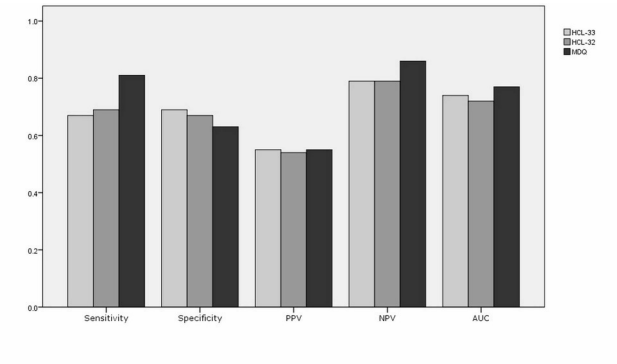

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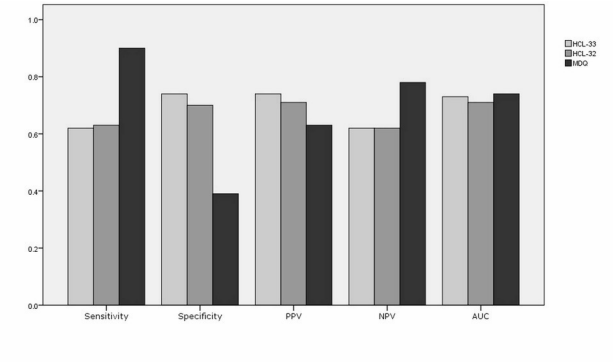

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