Regional update

Clinical characteristics of patients with diagnostic uncertainty of major depressive disorder

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ABSTRACT

Background: Physicians do not always confidently diagnose psychiatric disorders. The present study was conducted to identify the clinical characteristics of patients in whom a definitive diagnosis of major depressive disorder (MDD) could not be established.
Methods: The participants were 199 consecutive outpatients with MDD, who were comprehensively diagnosed using the Mini International Neuropsychiatric Interview (MINI). The physician in charge of each patient quantified his/her sense of self-confidence in diagnosing the patient with MDD using the self-rating questionnaire in which the score ranged from 1 (not at all confident) to 5 (definitely MDD). Using multiple logistic regression, the demographic and clinical factors of the patients in the low diagnostic confidence group (score less than or equal to 3, n = 79) were compared with those in the high diagnostic confidence group (more than 3, n = 120).
Results: Comorbidity of anxiety disorders (odds ratio (OR), 4.7), absence of remission (OR, 3.6), and non-melancholic features (OR, 3.5) were identified as the most discriminative variables associated with the low diagnostic confidence of MDD.
Conclusion: The results show that physicians were unable to confidently diagnose MDD in 40% of the cases, and that comorbidity of anxiety disorders, absence of remission, and non-melancholic features independently predicted the diagnostic uncertainty of MDD.

1. Introduction

Daily psychiatric practice shows how physicians must deal with uncertainty and ambiguity. In order to reduce uncertainties such as diagnostic inconsistency, the operational diagnostic criteria have been widely used even in psychiatry.

Until approximately 30 years ago, physicians had been diagnosing psychiatric disorders using the procedure for typological diagnosis, which relied mainly on descriptions of typical cases. A diagnosis was made based on maximal similarity to a typical case, the so-called prototype (Dilling, 2001). The physicians thus had considerable freedom in determining which cases were sufficiently comparable to their own prototype case to merit the corresponding diagnosis. However, Feighner et al. (1972) pointed out that typological diagnosis possessed low validity because the typical prototype referred to was substantially different among physicians, and proposed to develop the operational diagnostic criteria in psychiatry. Subsequently, the DSM-III appeared

and physicians had to change their diagnostic procedures from traditional typology to criteria-oriented diagnosis (Arolt and Dilling, 1994).

Operational diagnosis is based on the phenomenological characterization of psychiatric disorders. Typical diagnostic features of each disorder are listed, including the severity and duration of the symptoms. Operational diagnosis is not concerned with the etiology of disorders and thus does not obey the classical principle of nosology, according to which an etiology and a constellation of symptoms together constitute a disease entity (Dilling, 2001). However, even operational diagnosis has prototypes; these are the ideal cases that fulfill all the diagnostic criteria for a particular disorder. The number of criteria that are fulfilled in a particular case can be considered as a measure of similarity of that case to the prototype (Maier et al., 1988).

The reliability of operational diagnosis is estimated by the agreement between two physicians regarding the same diagnosis in the same patient. This agreement is typically indexed with the kappa coefficient. In the field trials for the DSM-III and DSM-III-R, the kappa coefficient of

major depressive disorder (MDD) diagnosis was greater than 0.6, indicating that the agreement between diagnoses was fairly good (Spitzer et al., 1979; Williams et al., 1992). However, the kappa coefficient in the DSM-IV slipped toward 0.4 (Keller et al., 1995). In the DSM-5 field trials, the kappa coefficient was 0.28, which was the lowest reliability ever reported for the diagnosis of MDD (Regier et al., 2013). Speculations regarding the cause of declining kappa coefficients from the DSM-III to DSM-5 were not completely reliable since the diagnostic criteria of MDD were changed minimally, however, some researchers pointed out that the marked heterogeneity of patients, the comorbidity with other disorders, and change of attitude among clinicians might be associated with lower reliability of MDD diagnosis in DSM-5 (Regier et al., 2013; Uher et al., 2014).

Even the latest operational diagnostic criteria do not provide highly reliable diagnosis of MDD, suggesting that physicians do not always diagnose MDD confidently. To our knowledge, however, no previous study has evaluated the sense of self-confidence of physicians while diagnosing patients with MDD and explored the clinical characteristics of patients associated with this diagnostic uncertainty. The present study was conducted with an aim to investigate these issues.

2. Methods

2.1. Participants

This study was approved by the Ethics Committee of the National Defense Medical College. The participants comprised of 210 consecutive outpatients who visited our clinic from December 2010 to May 2012. These patients were clinically diagnosed as suffering from depression and had been visiting the clinic regularly for six months or more. Out of the 210 patients, we excluded 11 patients who did not meet the DSM-IV criteria of current or lifetime MDD. Finally, we analyzed 199 patients (115 females and 84 males; age, 53.1 ± 14.3). All the patients were provided a detailed description of the study, and signed a written informed consent form.

The physician in charge of each patient quantified his/her sense of self-confidence in diagnosing the patient with MDD, using the self-rating questionnaire named as the Diagnostic Confidence Scale (DCS) in which the score ranged from 1 (not at all confident) to 5 (definitely MDD). The participating physicians consisted of 13 psychiatrists; 7 in their thirties, 3 in their forties, and 3 in their fifties. The patients were classified into two respective groups using the DCS score: a low diagnostic confidence (DC) group (DCS score less than or equal to 3) and a high DC group (more than 3) (Fig. 1).

2.2. Assessments

The patients were comprehensively diagnosed using the Mini International Neuropsychiatric Interview (MINI) (Sheehan et al., 1998), which is a structured interview to diagnose 15 psychiatric disorders. The Japanese version of the MINI has already been standardized (Otsubo et al., 2005). The MINI has been confirmed to have high diagnostic concordance rates with ICD-10, DSM-III-R, and DSM-IV (Lecrubier et al., 1997; Sheehan et al., 1998, 1997). Melancholic features of MDD and suicidal risk were also evaluated. The criteria for melancholic features of MINI include anhedonia in nearly all activities and/or lack of reactivity in addition to three or more of the following signs: distinct quality of depressed mood, extent of depression being regularly worse in the morning, early morning awakening, remarkable psychomotor retardation or agitation, significant anorexia or weight loss, and excessive or inappropriate guilt. The MINI defined suicidal risk by the existence of at least one of the following: recent suicidal thoughts, self-harm ideation, suicidal ideation, suicide planning, suicide attempt, and previous suicide attempt. Each patient was also evaluated with respect to his/her familial history of MDD, educational status, somatic comorbidity, and past history of relapse. The 17-item
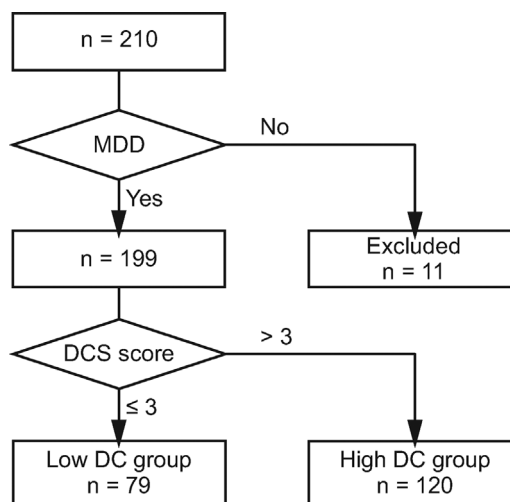

Fig. 1. Consort diagram.
MDD, major depressive disorder; DCS, the Diagnostic Confidence Scale; DC, diagnostic confidence.

Hamilton Depression Rating Scale (HAM-D-17) (Hamilton, 1960) and Neuroticism scale scores were also obtained from each patient. Neuroticism was measured using a 12-item scale from the short-form Eysenck Personality Questionnaire-Revised (EPQ-R) (Eysenck and Barrett, 1985; Hosokawa and Ohyama, 1993).

The number of adequate and inadequate trials of antidepressants was also evaluated. An adequate trial was defined as an antidepressant treatment lasting for at least 6 weeks, with the dosage being at least as high as the lowest dose defined as effective in the product datasheet (if the lowest dose was not mentioned, the maximal dose was used as the benchmark). A trial not fulfilling the definition of adequate trial was defined as inadequate. Remission was defined as a HAM-D-17 score of 7 or less.

2.3. Statistical analysis

The data were analyzed using JMP 11 (SAS Institute Inc., Cary, NC, USA). In order to identify the clinical features of the patients associated with the diagnostic uncertainty of MDD, the demographic and clinical differences between the low and high DC groups were first compared using a univariate analysis. All the variables that were significantly different between the groups were then used to perform a second-step backward-elimination logistic regression for multivariate analysis, with the p value for acceptance into the model set at .05. The multivariate analysis was used in order to test for factors independently associated with the diagnostic uncertainty, and allowed the selection of the most discriminative predictive factors by testing, at each step, the association between all the variables and by eliminating the less significant ones.

3. Results

Fig. 2 shows the score distribution of DCS. The mean DCS score for all the patients was 3.6 ± 1.3. The number of patients with DCS score of 1, 2, 3, 4, and 5 was 21, 25, 33, 52, and 68, respectively; the higher the DCS score, the greater the number of patients. A DCS score of less than or equal to 3 was considered as low self-confidence in the diagnosis, and the physicians were unable to confidently diagnose MDD in 40.0% (79/199) of the patients.

Table 1 shows a comparison of the demographic and clinical characteristics between the low and high DC groups. Concerning the comorbid psychiatric diagnoses, we compared only the comorbidity ratios of dysthymia, anxiety disorders, and alcohol dependence/abuse between the groups since the numbers of patients with other psychiatric