

Assessment of Risk Factors Related to Suicide Attempts in Patients With Bipolar Disorder

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Abstract: We compared the characteristics of patients with bipolar disorder with and without a history of suicide attempts to identify the risk factors of suicide in this disorder. Among 212 patients with bipolar disorder, 44 (21.2%) patients had histories of suicide attempts. Suicide attempters were younger and more likely to be diagnosed with bipolar II. The variables that differentiated those who did from those who did not attempt suicide included age at first contact, lifetime history of antidepressant use, major depressive episode, mixed episode, auditory hallucinations, rapid cycling, the number of previous mood episodes, age of first depressive episode, and age of first psychotic symptoms. Strong predictors of suicide attempts were younger age at onset, lifetime history of auditory hallucinations, and history of antidepressant use. Antecedent depressive episodes and psychotic symptoms predicted the first suicide attempt in patients with bipolar disorder. This study could help clinicians to understand the major risk factors of suicidal behavior in bipolar disorder.

Key Words: Bipolar disorder, suicide, risk factor, DIGS.

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Suicide is one of the most common causes of death and one of the largest contributors to the burdens related to disease in the world. Although a significant amount of research has attempted to understand suicidal behavior and the increased number of people who attempt suicide in treatment, the overall rate of suicidal behaviors has not changed (Kessler et al., 2005; Nock et al., 2008b). Suicide attempts carry substantial importance not only because these cause significant distress in their own right but also because these are among the most consistent predictors of subsequent deaths from suicide (Fawcett et al., 1990; Harris and Barraclough, 1997; Shaffer et al., 1996). Using the data of 84,850 samples from the 17 countries that participated in the World Health Organization (WHO) World

Mental Health (WMH) survey, the cross-national lifetime prevalence of suicide attempts was 2.7% (SE, 0.1) in the general population (Nock et al., 2008a).

The causes of suicidal behavior are multiple and complex. Many studies have attempted to identify the risk factors of suicidal behaviors. A recent literature review revealed cross-national variability in several risk factors of suicidal behavior but consistency in some key risk factors. Suicide was more prevalent among men, whereas nonfatal suicidal behaviors were more prevalent among women, younger individuals, those who are unmarried, and those with a psychiatric disorder (Nock et al., 2008b). Numerous studies have shown that the presence of mental disorders constitutes one of the strongest risk factors of attempted and completed suicide (Harris and Barraclough, 1997; Phillips et al., 2002; Pokorny, 1983). Psychological autopsy studies have suggested that more than 90% of people who die by suicide had a diagnosable mental disorder (Cavanagh et al., 2003), and similar figures have been reported for clinical samples of suicide attempters (Beautrais et al., 1996). The lifetime presence of each mental disorder was significantly predictive of subsequent first suicide attempts (odds ratios [ORs], 2.9–8.9) according to the data obtained from 108,664 respondents from 21 countries that participated in the WHO WMH surveys (Nock et al., 2009).

Bipolar disorder is one of the mental disorders most strongly associated with attempted and completed suicides (Bostwick and Pankratz, 2000). According to the Epidemiological Catchment Area study, 29% of bipolar patients in the general population have attempted suicide at least once during their lives (Chen and Dilsaver, 1996). In clinical samples, 25% to 56% of patients with bipolar disorder report at least one suicide attempt during their lives, and 10% to 19% die by suicide (Goodwin and Jamison, 1990; Harris and Barraclough, 1997; Valtonen, 2007). This figure is 20 times the comparable figure in the general population (Tondo et al., 2003). Several of the largest studies have reported that the ORs for suicide attempts were highest in those with bipolar disorder as compared with any other disorder (Chen and Dilsaver, 1996; Kessler et al., 1999). Bipolar disorder was significantly predictive of subsequent suicide attempts not only in bivariate (OR, 6.7; 95% confidence interval [CI], 4.6–9.7) but also in multivariate (OR, 2.3; 95% CI, 1.5–3.5) analyses according to the National Comorbidity Survey Replication study (Nock et al., 2010).

Many studies have attempted to identify the particular demographic, psychological, biological, and clinical risk factors associated with suicide and suicide attempts in patients with bipolar disorder (Brown et al., 2000; Hawton et al., 2005; Mann et al., 1999; Maser et al., 2002; Oquendo et al., 2006, 2004). However, the predictors of suicide or suicide attempts identified by these studies have been generally inconsistent (Valtonen, 2007). Because suicide and suicidal behaviors are the result of a combination of individual risk factors, precipitating stressors, and current disease features, the prediction of a suicide attempt for a given patient on the basis of risk factors statistically associated with suicide or suicide attempts in populations of patients with bipolar disorder is difficult. A recent meta-analysis reported that the main risk factors of nonfatal suicidal behavior

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included family history of suicide, early onset of bipolar disorder, extent of depressive symptoms, increasing severity of affective episodes, presence of mixed affective states, rapid cycling, comorbid axis I disorders, and abuse of alcohol or drugs (Hawton et al., 2005). Nonetheless, whether suicide attempts are predictable on the basis of the risk factors identified by previous studies remains unclear (Mann et al., 2006; Oquendo et al., 2006). Clinicians need information about warning characteristics that may help to identify subgroups of high-risk patients during different stages of their illness (Slama et al., 2004).

In 1994, the NIMH Genetics Initiative developed the Diagnostic Interview for Genetic Studies (DIGS), a semistructured clinical interview designed to collect a comprehensive database of psychiatric symptoms, signs, and histories for the purpose of genetic studies (Nurnberger et al., 1994). The DIGS, which has become one of the most widely used interview tools in psychiatric genetic studies, has unique features. First, it has a polydiagnostic capacity, which makes it possible to identify multiple diagnoses according to different diagnostic systems. Second, it is designed to facilitate the collection and storage of a comprehensive database of information that allows for detailed assessments of the course of illnesses, the chronology of psychotic and mood syndromes, and the presence of comorbid disorders. All data are collected using both qualitative and quantitative methodologies. The DIGS was developed not only to identify *DSM-IV* diagnoses but also to collect comprehensive information about psychopathology and lifetime psychiatric histories. Researchers are thereby able to collect detailed and comprehensive histories for current and past episodes of psychiatric illnesses and psychopathology.

The current study was designed to a) compare the main characteristics of patients with bipolar disorder who have attempted suicide and those who have not attempted suicide and b) determine the risk factors associated with suicide attempts in this sample.

METHODS

Subjects

The patients with bipolar disorder were recruited from Seoul National University Hospital in Korea. All participants satisfied the *DSM-IV* diagnostic criteria for bipolar disorder. The participants were individually interviewed by trained nurses using the Korean version of the DIGS. Consensual final diagnoses were reached during regular meetings among three or more psychiatrists. The subjects with a history of any kind of organic brain abnormality, substance dependence, drug abuse, or other physical conditions possibly manifesting as psychiatric symptoms were excluded from this study. The final analyses were thus based on 212 patients with bipolar disorder (107 men and 115 women; mean [SD] age, 32.2 [11.0]). Of these, 157 met the *DSM-IV* diagnostic criteria for bipolar I disorder, and 55 met the criteria for bipolar II disorder.

All subjects participating in this study provided written informed consent. The study protocol was approved by the Ethics Committee of Seoul National University Hospital.

Clinical Measures

The patients were classified as *attempters* if they answered “yes” to the question “Have you ever tried to kill yourself?” which is included in the suicidal behaviors section of the DIGS and as *nonattempters* if they answered “no” to this question. The sociodemographic characteristics (e.g., sex and age) of the attempters and the nonattempters were compared. The items from the section addressing an overview of psychiatric disturbances were also included. Although questions about family history of suicide were not included in the DIGS, we collected data on this issue during the interview, and these data were also analyzed.

We compared both the number of mood episodes and the mood episode indices (number of mood episodes/duration of illness [DUI]) of the two groups. It has been reported that the most valid method for comparing the general clinical features of bipolar disorder involves comparisons among the most severe episodes (Parker and Eysers, 2008). Thus, this study analyzed the most severe depressive episodes. Mood-incongruent psychotic symptoms have been reported to increase the risk for suicide among those with bipolar disorder (Toni et al., 2001). Therefore, we gathered data on whether psychotic symptoms were mood congruent. Antidepressant-induced mania has been reported as a possible risk factor of suicide among those with bipolar disorder; for this reason, we also compared rates of antidepressant-induced mania (Slama et al., 2004).

Statistical Analyses

We used chi-square or Fisher's exact test for comparisons involving categorical variables between the groups. We used independent *t*-tests for comparisons involving continuous variables between the groups.

A stepwise logistic regression model was then used to identify the factors associated with lifetime suicide attempts. Those variables significantly associated with suicide attempts according to the univariate analyses ($p \leq 0.05$) were entered into the model as independent variables. ORs with 95% CIs were used for observed associations.

RESULTS

Comparative Analyses of Attempters and Nonattempters

One hundred sixty-eight (78.8%) patients were classified as attempters, and the remaining 44 (21.2%) were classified as nonattempters. The sociodemographic characteristics of the attempters and the nonattempters are summarized in Table 1. The mean ages of the groups differed significantly: the mean (SD) age of the nonattempters was 32.9 (11.0) and the mean (SD) age of the attempters was 29.1 (10.6; $p = 0.039$). We found no significant difference between the groups in the proportions of men and women: the women comprised 51.2% ($n = 86$) of the nonattempter group and 65.9% ($n = 29$) of the attempter group. The groups also did not differ with respect to other sociodemographic characteristics such as education or marital status. However, the attempters were significantly more likely to carry diagnoses of bipolar II than were the nonattempters ($p = 0.0011$).

The suicide attempters had a significantly younger age at first contact (AFC) with the mental health system than did the nonattempters (mean [SD], 21.7 [6.1] years vs. 26.6 [9.2] years; $p < 0.001$). The suicide attempters were more likely to have histories of taking antidepressants than were the nonattempters (54.5% vs. 31.5%, $p = 0.004$), whereas the two groups did not differ with respect to the proportions of patients with histories of taking antipsychotics or mood stabilizers. Although the two groups did not differ in the number of psychiatric hospitalizations, the attempters had a significantly younger age at onset of psychiatric hospitalization than did the nonattempters (mean [SD], 22.2 [5.4] years vs. 26.9 [9.1]; $p < 0.001$). There was no statistically significant difference in DUI, present Global Assessment Scale scores, lack of insight, poor rapport, and family history of suicide between the two groups (Table 2).

Comparisons of the depressive symptoms are presented in Table 3. The suicide attempters were more likely to have histories of depressed mood or loss of interest lasting at least 1 week ($p = 0.003$ and $p = 0.002$, respectively). The attempters had more patients with previous major depressive episode than did the nonattempters (90.9% vs. 71.4%, $p = 0.004$). When we compared the psychotic symptoms

TABLE 1. Demographic Variables of Patients With Bipolar Disorder With and Without a History of Suicide Attempts

	Nonattempters	Attempters	Total	<i>p</i>
<i>n</i> (%)	168 (78.8)	44 (21.2)	212 (100)	
Sex (female), <i>n</i> (%)	86 (51.2)	29 (65.9)	115 (54.2)	0.057
Age, mean (SD), yrs	32.9 (11.0)	29.1 (10.6)	32.2 (11.0)	0.039*
Marital status, <i>n</i> (%)				0.082 ^a
Married	62 (37.1)	9 (20.5)	71 (33.6)	
Never married	99 (59.3)	34 (77.3)	133 (63.0)	
Divorced, widowed, separated	6 (3.6)	1 (2.3)	7 (3.3)	
Occupation, <i>n</i> (%)				0.312
Employed	45 (30.8)	8 (19.5)	53 (28.3)	
Full-time student	38 (26.0)	14 (34.1)	52 (27.8)	
Unemployed	63 (43.2)	19 (46.3)	82 (43.9)	
Education, mean (SD), yrs	14.32 (2.5)	13.72 (2.6)	14.19 (2.5)	0.167
Bipolar subtype, <i>n</i> (%)				0.011*
Bipolar I disorder	131 (78.0)	26 (59.1)	157 (74.1)	
Bipolar II disorder	37 (22.0)	18 (40.9)	55 (25.9)	

^aValues were obtained using Fisher's exact test.**p* < 0.05.

during the most severe depressive episode, the attempters were more likely to experience auditory hallucination than were the nonattempters (23.1% vs. 6.5%, *p* = 0.006). We found no significant difference in the presence of delusion or mood-incongruent psychotic feature during the most severe depressive episode between the two groups. The attempters had a younger age at onset of the depressive episode than did the nonattempters (mean [SD], 18.0 [4.3] years vs. 23.2 [9.5] years; *p* < 0.001). The number of previous depressive episodes and the frequency of psychiatric hospitalizations caused by depressive episodes did not differ between the two groups. There was no significant association of antidepressant-induced hypomania or mania and suicide attempts.

We found no difference in the history of elated or irritable moods and manic episodes between the attempters and the nonattempters. The two groups also did not differ significantly in age at onset of the manic episode, the number of manic episodes, and the psychiatric hospitalizations caused by manic episodes. The attempters were more likely to have mixed episodes and hypomanic episodes than were the nonattempters (*p* = 0.047 and *p* = 0.031,

respectively). The attempters were more likely to be rapid cyclers than were the nonattempters (38.6% vs. 19.0%, *p* = 0.007). The attempters had more manic or hypomanic episodes and more mood episodes than did the nonattempters (*p* = 0.038 and *p* = 0.030, respectively). Comparisons of the mood episode indices, that is, the number of mood episodes divided by the DUI, showed that the attempters had a significantly higher mood episode index (mean [SD], 12.6 [5.4] vs. 2.3 [1.3]; *p* = 0.044; Table 4).

The suicide attempters were more likely to have previous auditory hallucination than were the nonattempters (44.2% vs. 27.7%, *p* = 0.031), whereas the two groups did not differ in visual hallucination and delusion. The attempters also had a younger age at onset of psychotic symptom than did the nonattempters (mean [SD], 19.9 [5.2] years vs. 27.2 [9.6] years, *p* < 0.001; Table 5).

Predictors of Suicide Attempts

The predictors of suicide attempts in bipolar disorder were analyzed by logistic regression among the main variables that showed

TABLE 2. Overview of Psychiatric Disturbance of Patients With Bipolar Disorder With and Without a History of Suicide Attempts

	Nonattempters		Attempters		Total		<i>p</i>
	<i>n</i>		<i>n</i>		<i>n</i>		
AFC, mean (SD), yrs	26.6 (9.2)	154	21.7 (6.1)	42	25.6 (8.8)	196	<0.001*
History of AP, <i>n</i> (%)	132 (78.6)	168	32 (72.7)	44	164 (77.4)	212	0.422
History of AD, <i>n</i> (%)	53 (31.5)	168	24 (54.5)	44	77 (36.3)	212	0.004*
History of MS, <i>n</i> (%)	142 (84.5)	168	40 (90.9)	44	182 (85.8)	212	0.204
History of PH, <i>n</i> (%)	124 (78.5)	158	33 (76.7)	43	157 (78.1)	201	0.836
No. PHs, mean (SD)	2.8 (2.9)	123	2.6 (2.1)	33	2.8 (2.8)	156	0.640
AAO of PH, mean (SD), yrs	26.9 (9.1)	121	22.2 (5.4)	32	26.0 (8.6)	153	<0.001*
DUI, mean (SD), yrs	11.2 (9.3)	145	11.6 (9.5)	41	11.3 (9.3)	186	0.793
GAS, present, mean (SD)	45.6 (10.9)	77	41.4 (14.8)	25	44.6 (12.1)	102	0.200
Lack of insight, <i>n</i> (%)	81 (66.4)	122	14 (50.0)	28	95 (63.3)	150	0.104
Poor rapport, <i>n</i> (%)	6 (9.4)	64	1 (7.1)	14	7 (9.0)	78	1.000
Family history of suicide, <i>n</i> (%)	8 (4.8)	168	4 (9.1)	44	12 (5.7)	212	0.221

**p* < 0.05.

AFC indicates age at first contact; AP, antipsychotics; AD, antidepressants; MS, mood stabilizers; PH, psychiatric hospitalization; AAO, age at onset; DUI, duration of illness; GAS, Global Assessment Scale.

TABLE 3. Characteristics of Depressive Episode of Patients With Bipolar Disorder With and Without a History of Suicide Attempts

	Nonattempters		Attempters		Total		<i>p</i>
		<i>n</i>		<i>n</i>		<i>n</i>	
History of depressed mood, ^a <i>n</i> (%)	137 (81.5)	168	43 (97.7)	44	180 (84.9)	212	0.003*
History of loss of interest, ^a <i>n</i> (%)	127 (84.1)	151	43 (100)	43	170 (87.6)	194	0.002*
Depressed mood, last month, ^a <i>n</i> (%)	96 (41.8)	134	26 (60.5)	43	82 (46.3)	177	0.025*
History of major DE, <i>n</i> (%)	120 (71.4)	168	40 (90.9)	44	160 (75.5)	212	0.004*
Current major DE, <i>n</i> (%)	13 (7.7)	168	6 (13.6)	44	19 (9.0)	212	0.176
History of delusion, ^b <i>n</i> (%)	28 (23.1)	121	11 (26.2)	42	39 (23.9)	163	0.418
History of hallucination, ^b <i>n</i> (%)	8 (6.5)	124	9 (23.1)	39	17 (10.4)	163	0.006*
Mood-incongruent feature, ^b <i>n</i> (%)	3 (10.3)	29	2 (25.0)	8	5 (13.5)	37	0.292
AAO of DE, mean (SD)	23.2 (9.5)	123	18.0 (4.3)	38	22.0 (8.8)	161	<0.001*
No. DEs, mean (SD)	6.1 (11.0)	115	15.0 (30.0)	37	8.3 (17.9)	152	0.086
DE index (per year), mean (SD)	0.67 (0.8)	115	2.30 (5.5)	37	1.1 (2.9)	152	0.078
No. hospitalizations for DE, mean (SD)	0.46 (1.1)	124	0.79 (1.0)	39	0.5 (1.1)	163	0.097
AD-induced (hypo)mania, <i>n</i> (%)	16 (13.4)	119	6 (15.8)	38	22 (14.0)	157	0.449

^aLasting for a period of at least 1 week.^bDuring the most severe depressive episode.**p* < 0.05.

DE indicates depressive episode; AAO, age at onset; AD, antidepressant.

significant differences between the suicide attempters and the non-attempters from the comparative analyses: age, bipolar subtype, age at first contact, history of antidepressant use, auditory hallucination, mixed episode, rapid cycling, and mood episode index. The significant predictors of suicide attempts in bipolar disorder are displayed in Table 6. A history of major depressive episode and auditory hallucination increased the odds of suicide attempts (OR, 9.784; 95% CI, 1.224–78.179, and OR, 2.361; 95% CI, 1.062–5.249, respectively). A higher mood episode index also increased the odds of suicide attempts in bipolar disorder (OR, 1.079; 95% CI, 1.001–1.163), whereas an older AFC decreased the odds (OR, 0.927; 95% CI, 0.872–0.986).

To identify the predictors of the first suicide attempt, age, depressive episodes, manic episodes, hypomanic episodes, and psychotic symptoms were analyzed by discrete-time survival analysis (Table 7). Whereas the precedent depressive episode predicted the

initial suicide attempt, the preceding manic episode was associated with a decreased risk for the first suicide attempt (OR, 25.60; 95% CI, 8.45–77.60; *p* < 0.001, and OR, 0.26; 95% CI, 0.11–0.60; *p* = 0.001, respectively). The preceding psychotic symptoms also predicted suicide attempts (OR, 4.09; 95% CI, 1.79–9.34; *p* = 0.001).

DISCUSSION

This study analyzed the data from the DIGS interviews to compare the differences between the patients with bipolar disorder who have attempted suicide and those who have not attempted suicide in sociodemographic variables, illness course, and mood and psychotic symptoms. Compared with the nonattempters, the attempters were younger at their first contact with the mental health system, were more likely to report histories of auditory hallucinations and major

TABLE 4. Characteristics of Manic or Hypomanic Episode of Patients With Bipolar Disorder With and Without a History of Suicide Attempts

	Nonattempters		Attempters		Total		<i>p</i>
		<i>n</i>		<i>n</i>		<i>n</i>	
History of elevated/irritable mood, <i>n</i> (%)	147 (92.5)	159	35 (94.6)	37	182 (92.9)	196	0.486
History of ME, <i>n</i> (%)	125 (74.4)	168	29 (65.9)	44	154 (72.6)	212	0.342
Current ME, <i>n</i> (%)	10 (6.0)	168	2 (4.5)	44	12 (5.7)	212	1.000
AAO of ME, mean (SD)	24.3 (8.7)	122	21.7 (7.8)	29	23.8 (8.6)	151	0.135
No. MEs, mean (SD)	6.5 (15.4)	124	21.0 (37.1)	28	9.2 (21.7)	152	0.052
ME index (per year), mean (SD)	0.8 (1.6)	121	2.9 (6.2)	28	1.17 (3.1)	149	0.087
No. hospitalization for ME, mean (SD)	1.9 (2.9)	117	1.7 (2.2)	27	1.85 (2.8)	144	0.710
History of mixed episode, <i>n</i> (%)	28 (16.7)	168	13 (29.5)	44	41 (19.3)	212	0.047*
With rapid cycling, <i>n</i> (%)	32 (19.0)	168	17 (38.6)	44	49 (23.1)	212	0.007*
History of hypomanic episode, <i>n</i> (%)	7 (4.2)	168	6 (13.6)	44	13 (6.1)	212	0.031*
No. (hypo)manic episode	6.1 (20.1)	168	18.1 (35.7)	44	8.57 (24.6)	212	0.038*
(Hypo)manic episode index (per year), mean (SD)	0.6 (1.7)	168	3.1 (8.8)	44	1.14 (4.4)	212	0.075
No. mood episode, <i>n</i> (%)	10.3 (28.0)	168	30.7 (58.9)	44	14.5 (37.3)	212	0.030*
Mood episode index (per year), mean (SD)	1.3 (2.3)	145	5.4 (12.6)	41	2.17 (6.4)	186	0.044*

**p* < 0.05.

ME indicates manic episode; AAO, age at onset.

TABLE 5. Psychotic Symptom Characteristics in Patients With Bipolar Disorder With and Without a History of Suicide Attempts

	Nonattempters		Attempters		Total		<i>p</i>
		<i>n</i>		<i>n</i>		<i>n</i>	
History of AH, <i>n</i> (%)	46 (27.7)	166	19 (44.2)	43	65 (31.1)	209	0.031*
History of VH, <i>n</i> (%)	26 (15.6)	167	9 (20.5)	44	35 (16.6)	211	0.285
History of delusion, <i>n</i> (%)	81 (48.5)	167	15 (34.9)	43	96 (45.7)	210	0.124
Currently psychotic, <i>n</i> (%)	20 (11.9)	168	7 (15.9)	44	27 (12.7)	212	0.314
AAO of psychotic symptoms, mean (SD), yrs	27.2 (9.6)	85	19.9 (5.2)	20	25.8 (9.4)	105	<0.001*

**p* < 0.05.

AH indicates auditory hallucination; VH, visual hallucination; AAO, age at onset.

depressive episodes, were more likely to experience rapid cycling and mixed episodes, and tended to report a higher number of previous mood episodes. Among the aforementioned variables, age at first contact, histories of auditory hallucinations and major depressive episodes, and mood episode index were independent predictors of suicide attempts in patients with bipolar disorder. Whereas previous depressive episodes and psychotic symptoms predicted the first suicide attempts, previous manic episodes were associated with a decreased risk for suicide attempts.

In this sample of 212 patients with bipolar disorder, 21.2% had attempted suicide at least once in their lifetimes. This figure is consistent with the 25% to 50% rate of attempted suicide in patients with bipolar disorder reported in both retrospective and cross-sectional studies (Valtonen, 2007). The attempters were more likely than were the nonattempters to have bipolar disorder type II in this study. A review of six independent studies reported that the lifetime prevalence of suicide attempts was 17% (range, 10%–18%) for those with bipolar disorder type I and 24% (range, 18%–56%) for those with bipolar type II (Abreu et al., 2009).

AFC has been reported to be a more reliable predictor of age of onset than is age at first episode (Ouali et al., 2005). The attempters with younger AFC tended to be younger at the age of onset according to the present study. Although a few studies have found no significant association between age at onset and suicide attempts (Marangell et al., 2006; Oquendo et al., 2000), most studies have found positive associations between early age at onset of bipolar disorder and suicide attempts (Abreu et al., 2009; Galfalvy et al., 2006; Grunebaum et al., 2006; Hawton et al., 2005; Leverich et al., 2003; Lopez et al., 2001; Perlis et al., 2004; Tondo et al., 2007). Whether age at onset is an independent predictor of suicidal behavior or whether it increases this risk via associations with other factors such as the severity of bipolar disorder, comorbidity with a greater number of axis I and axis II disorders, and more rapid cycling remains unclear. In addition to AFC, age at first psychiatric hospitalization and at onset of depressive episodes and psychotic symptoms were also lower in the attempters.

Among the sociodemographic variables, only age differentiated between the attempters and the nonattempters. Being female,

less educated, and of a particular marital status, the variables that have been reported to be associated with suicide attempts in the general population, did not differentiate between the two groups in this study. Although the attempters were significantly younger than were the nonattempters, the two groups did not significantly differ in DUI. Many studies have reported a preponderance of women among suicide attempters in the general population. However, conflicting results with regard to the presumed association between sex and suicide attempts in patients with bipolar disorder have been reported. Consistent with the aforementioned statistics on the general population, although some studies have reported that women with bipolar disorder attempt suicide more frequently than do men with bipolar disorder (Azorin et al., 2009; Oquendo et al., 2007; Tondo et al., 2003), many studies have found no differences between men and women in the prevalence of suicide attempts (Hawton et al., 2005; Leverich et al., 2003; Lopez et al., 2001).

Many depressive symptoms were associated with suicide attempts. The attempters were more likely than were the nonattempters to have histories of depressive moods or of experiencing loss of interest for at least 1 week. The attempters were also significantly more likely to report histories of major depressive episodes and auditory hallucinations during their most severe depressive episodes. However, the groups did not differ with respect to histories of elevated moods or manic episodes. The observation that patients with histories of hypomanic episodes were more prevalent in the attempter group seems consistent with the preponderance of those with subtype II of bipolar disorder in this group. The higher incidence of mixed episodes and rapid cycling in the suicide attempters was in accordance with many previous studies (Valtonen, 2007). Although the numbers of depressive or manic episodes did not differ between the two groups, the numbers of (hypo)manic episodes and mood episodes were higher in the attempters. The mood episode index, which is the number of episodes divided by the duration of the illness, was also higher in the attempters. The patients with a higher mood episode index may represent not only rapid cyclers but also a more severe subtype of bipolar disorder.

Evidence regarding the association between psychotic symptoms in bipolar disorder and suicide attempts has been inconsistent. A few studies have argued that fewer patients with bipolar disorder with psychotic symptoms attempt suicide. Several authors have suggested that psychotic symptoms may impair the ability to plan

TABLE 6. Predictors for the Suicide Attempt in Patients With Bipolar Disorder: Stepwise Logistic Regression

	<i>p</i>	Odds Ratio	95% Confidence Interval
AFC	0.015	0.927	0.872–0.986
History of major depressive episode	0.031	9.784	1.224–78.179
History of AH	0.035	2.361	1.062–5.249
Mood episode index	0.046	1.079	1.001–1.163

AH indicates auditory hallucination; AFC, age at first contact; AD, antidepressants.

TABLE 7. Predictors for the First Onset of Suicide Attempt in Patients With Bipolar Disorder: Discrete-Time Survival Analysis

	<i>p</i>	Odds Ratio	95% Confidence Interval
Depressive episode	<0.001	25.60	8.45–77.60
Manic episode	0.001	0.26	0.11–0.60
Psychotic symptom	0.001	4.09	1.79–9.34

and execute suicide attempts (Oquendo et al., 2000). One study has reported similar incidences of psychotic symptoms in attempters and nonattempters with bipolar I disorder (Johnson et al., 2005). An association between the presence of psychotic symptoms and a higher prevalence of suicidal ideation and planning was also reported in pediatric patients with bipolar disorder (Caetano et al., 2006; Goldstein et al., 2005; Papolos et al., 2005). The attempters were more likely to report histories of auditory hallucinations in the present study. The patients with auditory hallucinations were reported to experience more anxiety-related and depression-related cognitive intrusions than did the controls. They were also more distressed by intrusions and interpreted intrusive thoughts as more uncontrollable and unacceptable than did the controls (Morrison and Baker, 2000). Our findings are consistent with these results.

Younger AFC, more previous mood episodes, and histories of major depressive episodes and auditory hallucinations were identified as predictors of suicide attempts in this study. Assessment of the symptoms that contributed to the first suicide attempts in patients with bipolar disorder underscored that depressive episodes and psychotic symptoms elevate the risk for subsequent suicidal attempts. However, manic episodes were associated with a decreased risk for the onset of the first suicide attempts. These results may suggest how to identify patients with bipolar disorder at high risk for suicidal attempts.

Age at onset has been proposed as a clinical marker of etiology and genetic heterogeneity in bipolar disorder. Age at onset was reported to be a significant predictor of prognosis in bipolar disorder. In the present study, early onset of bipolar disorder was associated with increased risk for morbidity in relatives, suggesting that the early-onset subtype may have a higher familial liability to bipolar disorder than does the later-onset subtype. The early-onset subtype of bipolar disorder was suggested to be a more homogeneous and severe form of bipolar disorder (Bellivier et al., 2001; Lin et al., 2006). Our findings add further support to the hypothesis that age at onset acts as a clinical marker of bipolar disorder.

The results of the current study must be considered in the context of several limitations. The factors reported in previous studies, such as temperament or history of child abuse, were not evaluated. The patients with substance dependence were excluded from this study. Therefore, the results of the current study cannot be generalized to all individuals with bipolar disorder. In addition, most of our data were retrospectively collected and are therefore subject to recall bias. Correction for multiple testing was also not performed.

Despite these limitations, this study could help clinicians to understand the major risk factors of suicidal behavior in bipolar disorder. The findings of this study may suggest an approach to the assessment of suicide risk in patients with bipolar disorder. The DIGS, usually used as diagnostic tool in genetic studies, was able to assess the detailed clinical features of patients and to predict factors related to prognosis. Further prospective studies are also needed.

DISCLOSURES

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