Suicide Attempts in Patients With Panic Disorder

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• **In a clinical sample of 100 outpatients with panic disorder, 42% had a history of suicide attempt. Female sex and being single, divorced, or widowed were associated with an increased risk of suicide attempt. Thirty-one (73.8%) of the suicide attempts occurred after the first panic attack and 27 (64.3%) after the onset of panic disorder. Eighty-eight of these patients met *DSM-III-R* criteria for at least one other diagnosis in addition to panic disorder. Moreover, 52% had a history of major depressive episode and 31% had a lifetime diagnosis of alcohol and/or other substance abuse. Compared with those who did not attempt suicide, those who attempted suicide were significantly more likely to have suffered from major depressive episode and alcohol or other substance abuse in their lifetime. Among the 35 patients with no comorbidity with either major depression or addictive behaviors, 17.1% had a history of suicide attempt. All had suffered from depressive symptoms and/or a personality disorder. The same association was found in four of 19 patients suffering from panic disorder only with or without agoraphobia.**

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The hierarchical rules of *DSM-III*,[1] which exclude a diagnosis of panic disorder when major depressive episode is present, limit the study of joint diagnoses. These exclusionary rules have been dropped in *DSM-III-R*,[2] largely as a result of findings showing that panic disorder and major depressive episode may share a common vulnerability. The advent of *DSM-III-R* and the use of standardized diagnostic interviews to assess the form and frequency of mental illness, either current or lifetime, induced a growing interest in clinical research for the study of the phenomenon of comorbidity. The Epidemiological Catchment Area (ECA) study showed that 7% to 9% of the adult population have recurrent attacks without meeting the frequency criterion and that 1.0% to 1.5% had at least one attack in the previous 6 months.[3] However, the clinical status of panic disorder remains an unresolved issue.

One major conceptual problem is the nosologic borders of panic disorder. Support for the distinction between panic disorder and generalized anxiety disorder comes from a number of sources: different responses to pharmacologic treatments,[4] higher frequency of autonomic symptoms in patients with panic disorder than in patients with generalized anxiety disorder,[5] different patterns of childhood and family characteristics,[6] different courses,[7] and induction of panic by lactate infusion in patients with panic disorder but generally not in those who have no history of panic attacks.[8] Panic disorder is often associated with other anxiety disorders and with depression. There are reports that 35% to 91% of patients with panic disorder also suffer from major depressive episode in their lifetime.[7,9-21] In many cases, both disorders occur at the same time[22] or panic disorder occurs before the onset of depressive disorder as well as before the onset of substance abuse.[23] The frequent co-occurrence of panic disorder, depression, and/or substance abuse has been described by many authors,[15,17,24-27] although the nature and the meaning of this relationship remains an unresolved issue.

The overlap of anxiety and depressive symptoms, the temporal relationship of the symptoms, and their longitudinal course remain unclear.[28] Breier et al[12] found that patients with panic disorder and/or agoraphobia who had a current or past major depressive episode had more severe symptoms of both anxiety and depression than those who had never been depressed. In a naturalistic study, Van Valkenburg et al[14] reported that patients with secondary depression had an earlier age at onset of their panic disorder but did not differ from nondepressed patients with panic disorder in their treatment response or psychosocial outcome. If patients with panic disorder are at greater risk of developing depression than are healthy individuals, they may share a common psychological and/or neurobiologic vulnerability. Finally, another risk factor in panic disorder is the development of alcohol abuse, which some view as "self-medication."[15] Unquestionably, intake of alcohol initially decreases anticipatory anxiety in patients with panic disorder, but alcoholism later becomes a complication.[25]

Because depression and alcoholism are risk factors for suicide attempt,[29-32] patients with panic disorder may be at higher risk for suicidal behavior. In a follow-up study of hospitalized patients with panic disorder, Coryell et al[33] found unexpectedly high death rates from both suicide and cardiovascular diseases. Recently, in a general population study, Weissman et al[34] found a very high rate of suicide attempt and suicidal ideation in subjects suffering from panic disorder even when controlling for lifetime major depressive episode and alcoholism.

The principal aim of our study was to evaluate, in a clinical population, the lifetime prevalence and severity of suicide attempt in patients with panic disorder. Then, comparing panickers who had attempted suicide and those who had not, we wanted to assess the clinical and temporal relationships between suicidal behavior and course and severity of panic disorder and lifetime comorbidity mostly with depression and alcohol and/or other substance abuse. Lastly, as regards the controversial issue of the status of uncomplicated panic disorder and suicide

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attempt, we wanted to describe the clinical profile of such, if any, subgroups of patients.

PATIENTS AND METHODS

We studied a consecutive series of 100 referrals for treatment of panic disorder in our anxiety clinic. All subjects were outpatients either self-referred or referred by general practitioners or other departments of our hospital because of anxiety problems. Our process of patient selection was as follows: First, screening for probable panic disorder was performed either by the physicians who referred the patients or by a trained nurse in the cases of self-referred patients. Second, the diagnosis of current panic disorder according to *DSM-III-R* as the principal complaint at the time of referral was made by a psychiatrist after a clinical evaluation, excluding all subjects with organic, psychotic, and primary affective disorders. We excluded from this study patients suffering from alcoholism or other substance abuse when these disorders were the main reason for referral. Third, the diagnosis of panic disorder was confirmed after an interview by another clinician, either a psychiatrist or a clinical psychologist, trained in using the Schedule for Affective Disorders and Schizophrenia–Lifetime Version modified for the study of anxiety disorders (SADS-LA).[35]

This standardized and semistructured diagnostic instrument, the SADS-LA, allows making different diagnoses according to Research Diagnostic Criteria and *DSM-III* criteria. According to the authors, reliability is high for most of anxiety disorders, namely, panic disorder, agoraphobia, obsessive-compulsive disorder, and, to a lesser extent, social phobia, GAD, and simple phobia.[36] Using the French version of this instrument, we found quite good interrater reliability, with κ values ranging from 0.61 to 1.00, with the lowest value for simple phobia (M. Leboyer, MD, PhD, and J.P.L., unpublished data, 1990). We use a modified version of the SADS-LA by adding new questions allowing the use of *DSM-III-R* criteria.

Ratings and diagnoses for the SADS-LA were based on all possible sources of information, including interviews with patients and clinical records. All information was reviewed in weekly meetings before a consensus assessment was reached. The severity of the worst episode of panic disorder was assessed according to the specific items of the SADS-LA, rating the frequency of panic during this period according the following scale: 1, one panic attack in 3 weeks; 2, two panic attacks in 3 weeks; 3, panic attacks once a week; 4, panic attacks more than once a week but not daily; and 5, one or more panic attacks per day.

Any suicide attempt was screened for each patient during his or her lifetime, and its severity was retrospectively estimated according to type of gesture and pathways to medical care, including any hospitalization and its length.

Demographic variables included age, sex, and marital status (single, divorced or widowed, married) at the time of the study. For comorbidity results, only the following diagnoses were considered: major depressive episode, agoraphobia, social phobia, obsessive-compulsive disorder, and alcohol and/or other substance abuse. Generalized anxiety disorder and simple phobia were excluded in the analysis, as previous results from our group have shown poor agreement for these disorders in consensus statements (M. Leboyer, MD, PhD, and J.P.L., unpublished data, 1990). Mean values are presented with the SD as the index of dispersion. Statistical comparisons for categorical variables were made by using χ^2 and Yate's-corrected χ^2 when necessary. Continuous variables were compared by using the unpaired t test or the Mann-Whitney U test when necessary.

RESULTS

Clinical Characteristics

Among 100 patients with panic disorder, 37 (37%) were male and 63 (63%) were female. The mean age of the total patient sample was 38.1 years (SD, 11.6 years; range, 17 to 69 years), with no significant difference between male and female patients (t=.18; P=.86). Demographic data are presented in Table 1. We found no difference in marital status between the two genders.

Table 1.—Demographic and Clinical Characteristics of the 100 Patients With Panic Disorder (PD)*

	Men (n=37)	Women (n=63)	Total (N=100)
Age, y	38.4 (11.7)	38.0 (11.7)	38.1 (11.6)
Age at time of first PA, y	26.4 (10.1)	25.5 (11.0)	25.8 (10.6)
Age at onset of PD	31.0 (11.6)	29.2 (10.3)	29.9 (10.8)
Duration of PD	7.4 (7.0)	8.7 (7.9)	8.2 (7.6)
Current marital status, No. (%)			
Married	22 (59.5)	34 (54)	56 (56)
Single	13 (35.1)	18 (28.6)	31 (31)
Divorced	2 (5.4)	8 (12.6)	10 (10)
Widowed	0 (0)	3 (4.8)	3 (3)
MDE	14 (37.8)	38 (60.3)	52 (52)†
Alcohol and/or other substance abuse	14 (37.8)	17 (27.0)	31 (31)
Agoraphobia	13 (35.1)	26 (41.3)	39 (39)
OCD	13 (35.1)	13 (20.6)	26 (26)
Social phobia	15 (40.5)	21 (33.3)	36 (36)

*Values are mean (SD). PA indicates panic attack; MDE, major depressive episode; and OCD, obsessive-compulsive disorder.
† $P<.05$.

Twelve patients (five male [13.5%] and seven female [11.1%]) suffered from panic disorder alone and seven patients suffered from panic disorder with agoraphobia without any lifetime comorbid diagnosis. Moreover, we found a 19% rate of uncomplicated panic disorder when using the definition described by Johnson et al.[37]

As shown in Table 1, we found a high level of comorbidity. Agoraphobia was present in 39% of patients with panic disorder, obsessive-compulsive disorder in 26%, social phobia in 36%, major depression in 52%, and alcohol and/or other substance abuse in 23%. There was no statistically significant difference between male and female patients for the prevalence of all the anxiety and addictive disorders, but female sex was associated with a higher lifetime prevalence of major depressive episode (60.3% vs 37.8%, χ^2=4.72, $P<.05$). Thirty-two patients (nine male [24.3%] and 23 female [36.5%]) met *DSM-III-R* criteria for panic disorder and one other psychiatric diagnosis. Fifty-six percent of our clinical sample (23 male [62.2%] and 33 female [52.4%] patients) had two or more other lifetime psychiatric disorders in addition to panic disorder. The proportion of patients who met *DSM-III-R* criteria for one, two, or more lifetime psychiatric disorders was similar in both genders. The presence of another lifetime anxiety disorder in addition to panic disorder did not influence either the rate of history of major depressive episode (48.4% vs 57.8%, χ^2=.85) or alcohol and/or other substance abuse (30.6% vs 31.6%, χ^2=.01). The mean (SD) age at the time of the first panic attack was 25.8 (10.6) years, and the mean age at onset of panic disorder was 29.9 (10.8) years, with no statistically significant difference between male and female patients.

In this population, 42 patients (42%) had attempted suicide at least once in their lives. Eleven (29.7%) of the 37 male patients and 31 (49.2%) of the 63 female patients attempted suicide during their lifetime (χ^2=3.63, P=.06). All suicide attempts were by drug overdose. Eighteen patients (42.9%) required medical care and/or hospitalizations of less than 24 hours. Eighteen (42.9%) of the 42 suicide attempters required hospitalizations of longer than 24 hours, and six (14.3%) of these 42 patients required hospitalization in an intensive care unit.

Comparisons of demographic and clinical characteristics between suicide attempters and nonattempters are presented in Table 2.

The marital status of suicide attempters and nonattempters was statistically different: 26 (61.9%) of the suicide attempters were single, divorced, or widowed vs 18 (31%) in nonattempters (χ^2=9.42, $P<.01$). A similar result was found for female sex (64.5% vs 28.1%, χ^2=8.39, $P<.01$).

Table 2.—Demographic and Clinical Characteristics of Suicide Attempters and Nonattempters With Panic Disorder (PD)*

	Men (n=37)		Women (n=63)		Total (N=100)	
	Attempt (n=11)	No Attempt (n=26)	Attempt (n=31)	No Attempt (n=32)	Attempt (n=42)	No Attempt (n=58)
Age at referral, y	40.6 (10.8)	37.5 (12.1)	38.2 (9.8)	37.7 (13.5)	38.8 (10.0)	37.6 (12.8)
Age at time of first PA, y	26.7 (11.5)	26.2 (9.7)	24.3 (10.5)	26.7 (11.4)	24.9 (10.7)	26.5 (10.6)
Age at onset of PD, y	30.7 (10.2)	31.1 (12.3)	27.7 (9.5)	30.7 (11.0)	28.5 (9.7)	30.9 (11.5)
Duration of PD, y	9.9 (7.3)	6.4 (6.7)	10.5 (7.0)	7 (8.5)	10.3 (7.0)	6.7 (7.7)†
Current marital status, No. (%)						
Married	5 (45.5)	17 (65.4)	11 (35.5)	23 (71.9)‡	16 (38.1)	40 (69.0)‡
Single	5 (45.5)	8 (3.8)	10 (32.3)	8 (25)	15 (35.7)	16 (27.6)
Divorced	1 (9.1)	1 (3.8)	8 (25.8)	0 (0)	9 (21.4)	1 (1.7)
Widowed	0 (0)	0 (0)	2 (6.4)	1 (3.1)	2 (4.8)	1 (1.7)
MDE	6 (54.6)	8 (30.8)	24 (77.4)	14 (43.8)‡	30 (71.4)	22 (37.9)§
Alcohol and/or other substance abuse	7 (63.6)	7 (26.9)	12 (38.7)	5 (15.6)†	19 (45.2)	12 (20.7)‡
Agoraphobia	4 (36.4)	9 (34.6)	11 (35.4)	15 (46.9)	15 (35.7)	24 (41.4)
OCD	3 (27.3)	10 (38.5)	7 (22.6)	6 (18.7)	10 (23.8)	16 (27.6)
Social phobia	5 (45.4)	10 (38.5)	9 (29.0)	12 (37.5)	14 (33.3)	22 (37.9)

*Values are mean (SD). PA indicates panic attack; MDE, major depressive episode; and OCD, obsessive-compulsive disorder.
†$P<.05$.
‡$P<.01$.
§$P<.001$.

The difference in age at the time of referral between suicide attempters and nonattempters was not statistically significant (38.8±10.0 years vs 37.6±12.8 years, $t=.512$, $P=.60$). There was also no difference in age at the time of the first panic attack (24.9±10.7 years vs 26.5±10.6 years, $U=1092.5$, $P=.47$) or onset of panic disorder (28.5±9.7 years vs 30.9±11.5 years, $U=1088$, $P=.27$). The severity of the worst episode of panic disorder did not differ between suicide attempters and nonattempters among the male or the female population (4±1.3 vs 4±1.3, $U=615.5$, $P=.94$).

Influence of Comorbidity

Among suicide attempters, four patients (9.5%) suffered from panic disorder alone, 12 (28.6%) from panic disorder and one other psychiatric disorder, and 26 (61.9%) from panic disorder and two or more other disorders. Among those who did not attempt suicide, eight (13.8%) met *DSM-III-R* criteria for panic disorder alone, 21 (36.2%) for panic disorder and one other diagnosis, and, in 29 (50%) of these 58 patients, panic disorder was associated with two or more lifetime psychiatric disorders. The proportion of patients who met *DSM-III-R* criteria for one, two, or more lifetime psychiatric disorders was similar in suicide attempters and nonattempters. Among the 19 patients with panic disorder with or without agoraphobia but without any other defined lifetime comorbid diagnosis (ie, uncomplicated panic disorder), the rate of history of suicide attempt was 21.1%, and this prevalence was higher (46.9%) in comorbid panic disorder although not statistically different (21.1% vs 46.9%, $\chi^2=3.23$, $P=.09$).

Significantly more suicide attempters than nonattempters met lifetime *DSM-III-R* criteria for major depressive episode (71.4% vs 37.9%, $\chi^2=10.95$, $P<.10^{-4}$) and for alcohol and/or other substance abuse (45.2% vs 20.7%, $\chi^2=6.87$, $P<.01$). Similar results were found in female suicide attempters for major depressive episode (77.4% vs 43.8%, $\chi^2=7.47$, $P<.01$) and for alcohol and/or other substance abuse (38.7% vs 15.6%, $\chi^2=4.26$, $P<.05$). In the 11 male suicide attempters, there was no significantly higher prevalence for lifetime major depressive episode than in nonattempters (54.5% vs 30.8%, χ^2 with continuity correction=.98, $P=.32$). Although not statistically significant, comorbidity with alcohol and/or other substance abuse was higher in suicide attempters (63.6% vs 26.9%, χ^2 with continuity correction=3.01, $P=.08$). Age at the time of the first suicide attempt was not different in male and female patients (30.5±8.7 years vs 33.1±9.8 years, $U=138$, $P=.45$).

In the 48 nondepressed patients (23 male and 25 female), 12 (25%) attempted suicide. In this subgroup, there was no difference between suicide attempters and nonattempters for demographic data and prevalence of anxiety disorders. However, we found a significantly higher prevalence for alcohol and/or other substance abuse in suicide attempters than in nonattempters (50% vs 19.4%, $\chi^2=4.26$, $P<.05$). Among these 12 nondepressed patients who attempted suicide, three (25%) were agoraphobics, two (16.7%) suffered from obsessive-compulsive disorder, and three (25%) suffered from social phobia. Six (50%) of these patients (three male and three female) were alcohol and/or other substance abusers.

Rates of suicide attempts according to the presence of lifetime major depressive episode and/or alcohol and/or other substance abuse are shown in Table 3. In patients who suffered from major depressive episode and addictive disorders, 72.2% attempted suicide. We found a lower, although not statistically significant, frequency of suicide attempters in patients who met lifetime criteria for major depressive episode without alcoholism (50.0%) and in those who suffered from alcohol and/or other substance abuse without major depressive episode (46.2%). In patients who never suffered from major depressive episode or alcohol and/or other substance abuse, the prevalence of suicide attempt was 17.1%.

Assessing the severity of suicide attempt according to three grades (simple medical care and/or hospitalization less than 24 hours, hospitalization longer than 24 hours, and hospitalization in an intensive care unit), we found a major influential role of comorbidity; in fact, the rates of major depressive episode were 61.1%, 72.2%, and 100%, respectively. For alcohol and/or other substance abuse, the corresponding rates were 33.5%, 50%, and 66.7%.

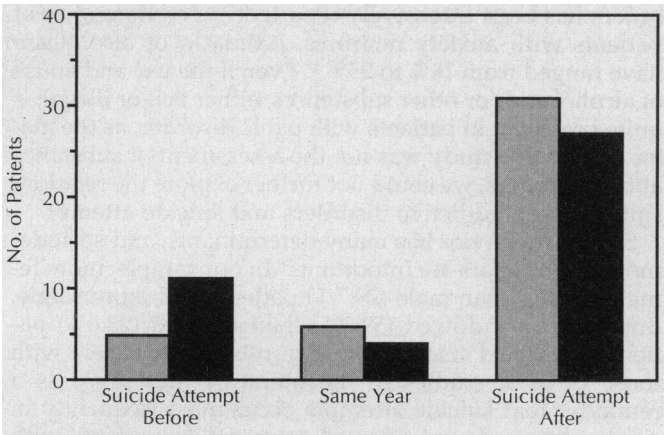
Time Sequencing of Disorders

Five (11.9%) of 42 patients attempted suicide before their first panic attack, six (14.3%) in the same year, and 31 (73.8%) after the occurrence of their first panic attack. Eleven (26.2%) of these 42 patients, attempted suicide before the onset of panic disorder, four (9.5%) in the same year, and 27 (64.3%) after the onset of panic disorder. There was no difference between male and female pa-

Table 3.—Rates of Suicide Attempts in Patients With Panic Disorder According to the Presence of Lifetime Diagnoses of Major Depressive Episode (MDE), Alcoholism, and Other Substance Abuse*

	Men (n=37)	Women (n=63)	Total (N=100)
MDE with alcoholism and/or other substance abuse	4/7 (57.1)	9/11 (81.8)	**13/18** (72.2)
MDE without alcoholism or other substance abuse	2/7 (28.6)	15/27 (55.6)	**17/34** (50.0)
Alcoholism and/or other substance abuse without MDE	3/7 (42.9)	3/6 (50.0)	**6/13** (46.2)
No alcoholism, other substance abuse, or MDE	2/16 (12.5)	4/19 (21.1)	**6/35** (17.1)

*Values are number attempting suicide/total number with feature (percent).



Time sequencing of suicide attempt, first panic attack (shaded bars), and onset of panic disorder (solid bars). Among the 42 suicide attempters, five patients (11.9%) attempted suicide before their first panic attack, six (14.3%) in the same year, and 31 (73.8%) after their first panic attack. Regarding the onset of panic disorder, 11 (26.2%) of these 42 patients attempted suicide before the onset of panic disorder, four (9.5%) attempted suicide in the same year as the onset of panic disorder, and 27 (64.3%) suffered from panic disorder before they attempted suicide.

tients. The time sequence of suicide attempt, first panic attack, and onset of panic disorder is presented in the Figure.

As regards comorbidity between panic disorder and major depressive episode, depression occurred before panic disorder in 22 patients (42.3%), in the same year in 11 patients (21.2%), and after in 19 patients (36.5%). Among these 52 patients, 30 had a history of suicide attempt. In 15 patients, depression occurred before panic disorder: in the same year in four patients, and after in 11 patients. This time sequencing pattern was not statistically different than that found in panic patients with lifetime comorbid depression who did not attempt suicide (χ^2=3.04, *df*=2, *P*=.22). Comparing patients with depression before the onset of panic disorder and those with the reverse pattern, we found a same rate of history of suicide attempt (68.2% vs 57.9%, χ^2=.50). Analysis of the temporal ordering of panic disorder, major depressive episode, and suicide attempt revealed a complex pattern. In 14 patients, the suicide attempt occurred after the onset of both depression and panic disorder. Six patients attempted suicide in the same year that panic disorder (two patients) or major depressive episode (four patients) occurred. In the 10 remaining patients, eight attempted suicide before the onset of panic disorder and two in the same year.

Nondepressed, Nonaddicted Panic Disorder

In these 100 outpatients with panic disorder, 35 never suffered from major depressive episode or alcohol and/or other substance abuse in their lifetime. Among them, six patients (17.1%; two male and four female) attempted suicide in their lifetime. There was no difference between the six suicide attempters and the 29 nonattempters for sociodemographic characteristics or for lifetime evaluated diagnoses. Age at onset and severity of the worst episode of panic disorder were similar in suicide attempters and nonattempters. In these six suicide attempters, the mean age at the time of the first suicide attempt was 23.3 years (SD, 8.0 years; range, 17 to 39 years). Among them, one patient attempted suicide before the occurrence of his first panic attack, three after, and two in the same year that they experienced their first attack. Three of these six patients attempted suicide before and three after the onset of panic disorder.

Four of these patients were single and two were married. As regards comorbidity, four among these six suicide attempters manifested uncomplicated panic disorder and five met *DSM-III-R* criteria for major depressive episode, except for duration criterion.

COMMENT

In our study, we found that 42% of outpatients with panic disorder had attempted suicide at some time during their lives. Some limitations of our study must be underlined. Our results were generally obtained from retrospective data, and we used the SADS-LA. The validity of lifetime diagnoses has been questioned because of the problems of accurate recall,[38] and we did not study the accuracy of recall of suicide attempts. In fact, 42.9% of suicide attempts were suicidal gestures that required minimal medical care or hospitalization shorter than 24 hours. Only 14.3% of these suicide attempters required hospitalization in an intensive care unit.

We found a very high comorbidity rate. Even if we observed a low rate of agoraphobia, 56% of our clinical sample met *DSM-III-R* criteria for two or more diagnoses in addition to panic disorder, and 32% of them suffered from panic disorder associated with only one other lifetime diagnosis. This high comorbidity rate could be explained by our process of referrals at the time of the study and by the fact that in the clinical setting, patients presenting for psychiatric treatment tend to have high comorbidity. These patients were self-referred or referred by general practitioners or other departments of our hospital because of anxiety problems, not only for panic disorder. However, there were no significant differences between suicide attempters and nonattempters with respect to the presence of one other or two or more lifetime diagnoses in addition to panic disorder. We found that 52% of the patients with panic disorder experienced at least one episode of major depression at some time during their course of illness to date.

Major depressive episode appears to occur in 35% to 91% of patients with panic disorder; most studies report rates of approximately 50%.[7,9-21,39] Differences in methods, particularly in the choice of diagnostic criteria, may account for some of this large variance.[9,11] Our rate would appear to be consistent with that of most studies in the literature and confirms that depressive illness may occur in a large group of patients with panic disorder. In our sample, 23% of the patients with panic disorder met diagnostic criteria for alcohol and/or other substance abuse. These results are consistent with those of most studies in the literature.[27] Comorbidity between alcohol problems and anxiety dis-

orders has been extensively reported.[15,17,24-27] In studies of patients with anxiety neuroses, estimates of alcoholism have ranged from 16% to 25%.[17] Even if the use and abuse of alcohol and/or other substances, either licit or illegal, is quite prevalent in patients with panic disorder, as the major goal of this study was not the assessment of substance abuse disorders, we could not further explore the relationship between addictive disorders and suicide attempt.

Suicidal behavior has many determinants, and sociodemographic factors are important.[30] In our sample, more female (49.2%) than male (29.7%) patients and more single, divorced, or widowed (59.1%) than married (28.6%) patients attempted suicide. These results are consistent with those of most studies in the literature and serve as a reminder that suicide attempts occur most frequently in single, divorced, or widowed women.[30] In patients with panic disorder, we found demographic determinants for suicide attempt to be similar to those of other clinical populations, such as depressed patients.

Suicide attempters were more likely to have history of major depression and alcohol and/or other substance abuse. In our clinical sample, 71.4% of the suicide attempters met *DSM-III-R* criteria for major depressive episode at least once in their lives, alcohol abuse was present in 33.3% of patients, and alcohol and/or other substance abuse was present in 45.2% of the 42 suicide attempters. It is well established that depression is the most common diagnosis in patients who commit suicide.[30] In fact, in suicide attempters, the lifetime prevalence of major depressive episode is reported in the literature in a range of 30% to 66%.[30] Alcohol and/or other substance abuse is the other psychiatric disorder most often associated with an increased risk of suicidal behavior.[29,40] The prevalence of suicide attempt in patients with lifetime major depressive episode and addictive disorders is higher (72.2%) than in those suffering either from major depressive episode (50.0%) or alcohol and/or other substance abuse (46.2%) and is also higher than in those suffering from neither major depression nor addictive disorder (17.1%).

Even if major depressive episode is the most common diagnosis associated with self-harm,[31] suicide attempt has been shown to be related to other affective disorders.[30] Moreover, Weissman[40] reported that only 35% to 80% of patients who harm themselves have diagnosed depression at the time of self-injury. Disagreement exists concerning the prevalence, type, and severity of this depression. This confusion persists due to the use of different diagnostic classification systems to establish a diagnosis of depression. The diagnosis of *DSM-III-R* major depressive episode is mostly obtained for severely ill, unipolar and bipolar patients with a typical phasic course.[14] It has been shown that patients suffering from other depressive disorders, such as atypical depression, hysteroid dysphoria,[41] or brief recurrent depression[42] are at high risk for suicide.

In our study, among the never-depressed and never-addicted patients, six attempted suicide. For analyzing comorbidity with depression, we focused on *DSM-III-R* major depressive episode criteria. Nonetheless, five of these patients suffered from depressive symptoms during their lifetime but never had a 2-week period of major depressive episode. Further investigations on the relationship among panic disorder, affective disorders, and suicide attempt require another study design.

We found a high rate of suicide attempts in patients with panic disorder. In fact, in a general population study involving 1927 French subjects (1046 females and 631 males), we found a lifetime prevalence of 5.9% of suicide attempts (J.P.L. and J. Lellouch, PhD, unpublished data, 1991). So, in a clinical population, our results echo those of Weissman et al,[34] who, in a large sample of subjects with panic disorder in the community, namely, the ECA study, reported a high risk for suicide attempts. This was not explained on the basis of comorbidity with depression, but the risk was increased by the presence of drug abuse. In the same sample, Johnson et al[37] reported that 7% of patients with uncomplicated panic disorder and 26.3% of patients with comorbid panic had attempted suicide. It should be mentioned that, in the ECA study, the diagnostic assessment was performed by using the Diagnostic Interview Schedule, which does not generate *DSM-III* Axis II diagnoses, except for Antisocial Personality. Moreover, this diagnostic instrument does not consider other depressive disorders (eg, Recurrent Brief Depression) than those that are described in *DSM-III*. In a clinical population, using the SADS-LA, we found a 21.1% lifetime prevalence of suicide attempt in patients with uncomplicated panic disorder and a 46.9% rate in those with comorbid panic disorder, that is, a twofold and threefold increase when compared with ECA results.

Personality disorders are another risk factor for suicide attempt.[30] Personality features of suicide attempters have been the subject of several studies.[30,31] Unfortunately, all of the assessments were made shortly after the attempt, when the patients were psychiatrically ill and it was shown that even a slight level of depression greatly affects personality assessment.[30] In general, suicide attempters have been characterized to have more personality disorders compared with controls.[31] Moreover, suicide attempt is often associated with personality disorders, even in the absence of an Axis I diagnosis.[30] Despite the fact that we did not use formal personality assessment, we did evaluate patients according to the Axis II criteria. The only patient without any history of depressive symptoms met diagnostic criteria for narcissistic personality disorder.

In the ECA, Weissman et al[34] found that the risk of suicide attempt in patients with panic disorder was increased by earlier age at the onset of panic disorder. In our sample, the age at the occurrence of panic attacks and the age at onset of panic disorder did not differ between suicide attempters and nonattempters. However, we found a significantly longer duration of panic disorder at the time at referral in suicide attempters. Otherwise, severity of the worst episode of panic disorder did not differ between suicide attempters and nonattempters.

The age at the time of the first suicide attempt seems to be high. However, in another ongoing study involving adult patients hospitalized in a French general hospital because of a suicide attempt, a similar age at the time of first suicide attempt was found (male, 29.5±12.5 years; female, 30.7±14.8 years).[43] Considering the time sequence of first panic attack, onset of panic disorder, and first suicide attempt, suicide attempts occurred after the first panic attack in 73.8% of these patients and after the onset of panic disorder in 64.4%. Otherwise, when comparing patients with an earlier onset of depression than panic disorder and those with the reverse pattern, we found a similar rate of history of suicide attempt.

The role of lifetime comorbidity with depression and alcohol and/or other substance abuse remains uncertain. In most of the cases, suicide attempt occurred after the onset

of both panic disorder and depression and seemed to be a complication of the illness in patients with panic disorder. The question remains whether panic disorder and other Axis I diagnoses are separate, cumulative, or interactive risk factors for suicide attempts.

Our study might be connected with studies underlying an increased risk of premature death by suicide in patients with panic disorder. In fact, Coryell[44] stressed that panic disorder "may imply as much risk for suicide as primary affective disorder." More recently, Allgulander and Lavori,[45] in a Swedish cohort of inpatients with "pure" anxiety neurosis, observed an excess of premature deaths mostly due to suicide in both male and female subjects.

In summary, we found that suicide attempt in patients with panic disorder is common and often associated with a lifetime diagnosis of major depressive episode and alcohol and/or other substance abuse. In addition, suicide attempters without a history of major depression and/or addictive disorder suffered from short depressive episode and/or from personality disorder. In fact, no patients in our study with panic disorder without a history of depressive symptoms or addictive disorder and/or Axis II comorbidity attempted suicide.

A comprehensive assessment of suicide risk in patients with panic disorder should include such clinical predictors of suicide as the presence of an affective disorder, a history of alcohol and/or other substance abuse, and presence of personality disorders. Further studies, including prospective ones, should be conducted to determine relevant clinical, environmental, and personality factors as risk factors for suicide attempts in patients with panic disorder.

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