Health-Related Quality of Life in Euthymic Bipolar Disorder Patients: Differences Between Bipolar I and II Subtypes

Giuseppe Maina, M.D.; Umberto Albert, M.D., Ph.D.; Laura Bellodi, M.D.; Cristina Colombo, M.D.; Carlo Faravelli, M.D.; Palmiero Monteleone, M.D.; Filippo Bogetto, M.D.; Giovanni B. Cassano, M.D., F.R.C.Psych.; and Mario Maj, M.D., Ph.D.

Objective: The aim of the present study was to compare health-related quality of life (HRQoL) measures in euthymic patients with bipolar I and II disorder. We included as comparison samples a group of subjects with recurrent major depression (RMD) and a group of non–psychiatrically ill individuals.

Method: HRQoL was assessed using the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36) in 253 subjects recruited in 5 Italian centers: 90 patients with bipolar I disorder, 52 patients with bipolar II disorder, 61 subjects with RMD, and 50 healthy comparison individuals. All subjects were evaluated with the Structured Clinical Interview for DSM-IV; psychiatric patients had to be in a euthymic state for at least 2 months prior to the inclusion in the study, as confirmed by a Hamilton Rating Scale for Depression total score < 8 and a Young Mania Rating Scale total score < 6. Data were drawn from a study that was performed from May 2003 to December 2004.

Results: When we compared the bipolar and RMD groups with the control group of non–psychiatrically ill individuals and controlled for differences in mean actual age, both bipolar subgroups and subjects with RMD had lower SF-36 mean scores on several subscales; differences in mean SF-36 scores were also detected between bipolar subtypes: bipolar II patients showed HRQoL that was poorer than that of bipolar I patients, even after controlling for age, age at onset, and length of illness, and equal to that of RMD subjects.

Conclusion: Our study provides evidence that bipolar type II is associated with poorer HRQoL compared to type I even during sustained periods of euthymia and excluding residual symptoms. Interventions targeting rehabilitation and/or functional enhancement may be helpful to improve HRQoL, especially among patients with bipolar II disorder.

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Received June 29, 2006; accepted Aug. 18, 2006. *From the Department of Neurosciences, Mood and Anxiety Disorders Unit, University of Turin, Turin (Drs. Maina, Albert, and Bogetto); the Department of Neuropsychiatric Sciences, Scientific Institute and University Vita-Salute San Raffaele, Milan (Drs. Bellodi and Colombo); the Department of Neurology and Psychiatry, University of Florence, Florence (Dr. Faravelli); the Department of Psychiatry, University of Naples SUN, Naples (Drs. Monteleone and Maj); and the Department of Psychiatry, Neurobiology, Pharmacology, and Biotechnology, University of Pisa, Pisa (Dr. Cassano), Italy.*

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Corresponding author and reprints: Giuseppe Maina, M.D., Department of Neurosciences, Mood and Anxiety Disorders Unit, University of Turin, Via Cherasco 11–10126 Torino, Italy (e-mail: giuseppemaina@hotmail.com).

Bipolar disorder negatively impacts the individual, reducing health-related quality of life (HRQoL) in all phases of the disorder compared to that in the general population; bipolar patients, moreover, have HRQoL scores equal to or even lower than those of individuals with major depressive disorder.[1–3]

HRQoL comparisons between different bipolar subgroups have focused on demographic and clinical characteristics such as gender, age, age at onset, number of previous episodes, predominance of manic versus depressive episodes, psychotic features, and rapid cycling. There is a lack of data, however, on HRQoL according to bipolar I or II subtype: only 2 studies, performed in the same sample of 55 bipolar disorder type I and 13 type II euthymic patients, are available, and both suggest poorer HRQoL in bipolar II disorder. In the first study,[4] bipolar II subjects reported significantly lower scores on the Medical Outcomes Study 20-Item Short-Form Health Survey

TAKE-HOME POINTS

- Patients with bipolar disorder had poorer health-related quality of life (HRQoL) than controls without psychiatric illness, even during sustained periods of euthymia.
- Bipolar disorder type II was associated with poorer HRQoL compared with type I.
- Clinicians should include HRQoL measures in the assessment of patients with bipolar disorder after symptomatic recovery from the index episode.

social functioning and mental health subscales. The same group[5] evaluated the level of intrusiveness due to bipolar subtype using the Illness Intrusiveness Rating Scale: bipolar II patients reported higher overall levels of intrusiveness. However, the group with bipolar II disorder at the time of rating was experiencing more severe depression as indicated by higher Hamilton Rating Scale for Depression (HAM-D) scores; when the HAM-D score was treated as a covariate in the statistical analysis, it was found to be the most significant indicator of intrusiveness, suggesting that differences between the 2 groups could be accounted for by residual depressive symptoms. Depressive symptoms, in fact, have been found to be the primary determinant of HRQoL in bipolar disorder.[6–10]

No studies are available, to our knowledge, comparing HRQoL measures between bipolar I and II disorder in larger samples of euthymic patients without residual depressive or hypomanic symptoms.

The aim of the present study was to compare HRQoL measures in euthymic patients with bipolar I and bipolar II disorder. We included as comparison samples a group of subjects with recurrent major depression (RMD) and a group of non–psychiatrically ill individuals.

METHOD

Data were drawn from a multicenter Italian study that was performed in euthymic patients at the Universities of Florence, Milan, Naples, Pisa, and Turin from May 2003 to December 2004. The primary objective of the study was to assess clinical, biological, and psychosocial aspects of bipolar II disorder in a large sample of patients and to compare them with those of patients with bipolar I disorder, euthymic subjects with RMD, and healthy (non–psychiatrically ill) individuals.

To be enrolled, patients had to fulfill the following criteria: (1) DSM-IV diagnosis of bipolar I disorder, bipolar II disorder, or RMD, confirmed by the Structured Clinical Interview for DSM-IV-Patient Edition (SCID-I)[11]; (2) euthymic state for at least 2 months, confirmed by a HAM-D[12] total score < 8 and a Young Mania Rating Scale (YMRS)[13] total score < 6; (3) age between 18 and 60 years; (4) written informed consent to undergo the experimental procedures; and (5) absence of brain and/or severe physical diseases.

The healthy volunteer group included subjects without current or past mental disorders as ascertained by the Structured Clinical Interview for DSM-IV-Nonpatient Edition.[14] It was a convenience sample and thus not representative of the Italian general population; we tried to enroll subjects in the age ranges of the bipolar patients, and we maintained the male-to-female ratio of approximately 1:1 (as for bipolar patients).

The protocol was reviewed and approved by the local ethical committees of the 5 Italian centers.

Health-related quality of life was assessed using the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36). The SF-36 contains 8 scales for assessing physical functioning, role limitations due to physical health, bodily pain, general health, vitality, social functioning, role limitations due to emotional problems, and mental health.[15–17] Scores are given on a range from 0 (worst possible health) to 100 (best health) for each scale. Summary scales include a physical composite and a mental composite that are expressed as t scores (mean = 50, SD = 10). The SF-36 has been validated for its use in Italian, and Italian norms are available for it.[18]

In the early phase of the study, interrater reliability of the diagnosis of Axis I disorders with the SCID-I and of the HAM-D and YMRS scores was ascertained. The interrater reliability was found to be good: Cohen kappa coefficient was 0.89 for the presence of any current or lifetime Axis I disorder, 0.80 for HAM-D scores, and 0.85 for YMRS scores.

Between-group comparisons of categorical variables were made with the Pearson χ^2 test, except when the expected cell size fell below 5, in which case the Fisher exact test (2-tailed) was used. Continuous variables were compared using analysis of variance. A p value less than .05 (2-tailed) was considered statistically significant. A pairwise deletion of missing data was used for statistical analyses.

RESULTS

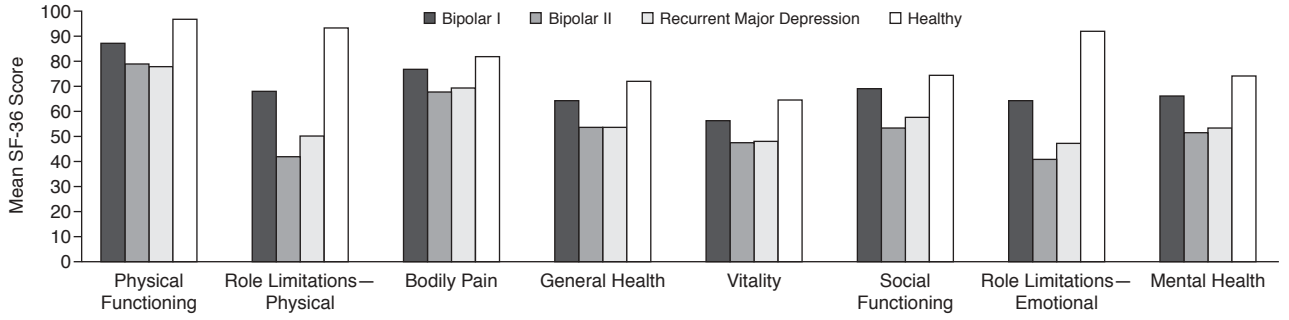
We included 253 subjects: 90 patients with bipolar I disorder, 52 patients with bipolar II disorder, 61 subjects with RMD, and 50 healthy comparison individuals. Demographic and clinical variables of the 4 groups are reported in Table 1. A lifetime comorbid Axis I disorder was

Table 1. SF-36 Scores and Demographic and Illness Characteristics for Bipolar Disorder Type I, Bipolar Disorder Type II, and Recurrent Major Depression (RMD) Patients and Healthy Comparison Subjects

Variable	Bipolar I Disorder	Bipolar II Disorder	RMD	Healthy Controls	Test Result[a]	p	Post Hoc Analysis
Actual age, mean (SD), y	41.04 (11.80)	47.92 (10.76)	51.07 (10.44)	38.36 (10.33)	F = 17.094	< .001	Bipolar I = healthy < RMD = bipolar II
Gender, males, N (%)	43 (47.8)	21 (40.4)	18 (29.5)	23 (46.0)	χ^2 = 5.518	.138	…
Age at onset, mean (SD), y	27.05 (8.49)	30.43 (9.83)	35.07 (11.52)	…	F = 11.652	< .001	Bipolar I = bipolar II < RMD
Length of illness, mean (SD), y	13.47 (9.54)	18.02 (9.28)	16.42 (12.32)	…	F = 3.315	.038	Bipolar I < bipolar II
SF-36 subscale, mean (SE)[b]							
Physical functioning	85.76 (2.05)	80.05 (2.69)	79.91 (2.59)	94.66 (2.79)	F = 5.898	.001	RMD = bipolar II = bipolar I < healthy
	85.69 (2.37)	80.13 (3.00)	78.32 (2.88)	…	F = 2.001	.138	…
Role limitations due to physical health	66.17 (4.14)	43.21 (5.39)	51.50 (5.19)	91.14 (5.61)	F = 13.536	< .001	RMD = bipolar II < bipolar I < healthy
	67.67 (4.78)	42.07 (6.03)	47.76 (5.76)	…	F = 6.120	.003	RMD = bipolar II < bipolar I
Bodily pain	76.02 (3.40)	68.37 (4.45)	72.55 (4.24)	80.06 (4.62)	F = 1.155	.327	…
	75.09 (3.89)	68.45 (4.93)	70.61 (4.67)	…	F = 0.578	.562	…
General health	63.50 (2.19)	55.03 (2.85)	56.19 (2.72)	69.89 (2.95)	F = 5.333	.001	RMD = bipolar II < bipolar I = healthy
	64.45 (2.46)	55.06 (3.10)	53.84 (2.94)	…	F = 4.312	.015	RMD = bipolar II < bipolar I
Vitality	56.17 (2.39)	47.20 (3.13)	48.58 (3.01)	64.31 (3.25)	F = 5.668	.001	All < healthy; bipolar II < bipolar I
	56.75 (2.71)	47.87 (3.44)	46.88 (3.29)	…	F = 3.096	.048	RMD = bipolar II < bipolar I
Social functioning	68.90 (2.76)	53.17 (3.61)	58.33 (3.45)	74.02 (3.75)	F = 6.585	< .001	RMD = bipolar II < bipolar I = healthy
	70.55 (3.07)	53.22 (3.89)	55.93 (3.69)	…	F = 7.124	.001	RMD = bipolar II < bipolar I
Role limitations due to emotional problems	63.02 (4.04)	42.12 (5.23)	49.80 (5.12)	90.17 (5.44)	F = 14.441	< .001	RMD = bipolar II < bipolar I < healthy
	64.04 (4.68)	42.56 (5.86)	47.70 (45.86)	…	F = 5.71	.010	RMD = bipolar II < bipolar I
Mental health	67.08 (2.26)	50.54 (2.96)	52.16 (2.84)	75.34 (3.07)	F = 15.069	< .001	RMD = bipolar II < bipolar I < healthy
	67.50 (2.55)	51.58 (3.23)	51.36 (3.09)	…	F = 10.210	< .001	RMD = bipolar II < bipolar I
Physical summary score	49.90 (0.85)	47.16 (1.10)	47.12 (1.07)	52.66 (1.14)	F = 5.136	.002	RMD = bipolar II < bipolar I = healthy
	49.89 (0.96)	46.84 (1.20)	46.30 (1.16)	…	F = 3.162	.045	RMD < bipolar I
Mental summary score	43.43 (1.26)	35.31 (1.64)	37.05 (1.60)	49.11 (1.70)	F = 13.275	< .001	RMD = bipolar II < bipolar I < healthy
	43.95 (1.43)	35.75 (1.79)	36.24 (1.74)	…	F = 8.046	< .001	RMD = bipolar II < bipolar I

[a]Value for gender results from χ^2 analysis, and values for SF-36 result from analysis of covariance. All other values result from analysis of variance, with Bonferroni correction used in post hoc analysis.
[b]For results given on the first line, actual age (years) was the covariate; for results given on the second line, actual age (years), age at onset (years), and length of illness (years) were the covariates.
Abbreviation: SF-36 = Medical Outcomes Study 36-Item Short-Form Health Survey.

Figure 1. SF-36 Score Profiles for Bipolar Disorder Type I, Bipolar Disorder Type II, and Recurrent Major Depression Patients and Healthy Comparison Subjects



Abbreviation: SF-36 = Medical Outcomes Study 36-Item Short-Form Health Survey.

found in 23.6% of the whole sample, without significant differences between groups (bipolar I: 23.3%, bipolar II: 30.8%, RMD: 18.0%; $\chi^2 = 2.531$, df = 2, p = .282).

Figure 1 shows the HRQoL profiles according to the principal diagnosis. Table 1 shows the mean (± SE) SF-36 scores for bipolar I and II patients, RMD subjects, and healthy comparison subjects; 2 separate analyses were performed for each subscale: (1) an analysis of covariance (ANCOVA) with actual age as the covariate and (2) an ANCOVA with actual age, age at onset, and length of illness as covariates (excluding healthy subjects). Gender and comorbid Axis I disorders were not included as covariates, as they did not differ between groups, although subjects with a lifetime comorbid disorder had significantly lower scores on the subscales for role limitations due to physical health (44.15 ± 46.10 vs. 58.66 ± 42.10; F = 4.088, df = 1, p = .045), bodily pain (63.85 ± 32.46 vs. 75.30 ± 34.03; F = 4.238, df = 1, p = .041), vitality (45.00 ± 27.33 vs. 53.57 ± 23.03; F = 4.626, df = 1, p = .033), and social functioning (52.85 ± 29.77 vs. 64.27 ± 26.89; F = 6.278, df = 1, p = .013) and on the mental summary score (36.05 ± 13.89 vs. 40.59 ± 12.51; F = 4.471, df = 1, p = .036).

Healthy comparison subjects scored significantly higher (better HRQoL; ANCOVA with actual age as the covariate) than the 3 psychiatric groups on several SF-36 subscales: physical functioning, role limitations due to physical health, vitality, role limitations due to emotional problems, and mental health and on the mental summary score. Concerning the 3 psychiatric groups, analysis of covariance with actual age, age at onset, and length of illness as covariates showed a significant difference between bipolar I subjects, on one hand, and RMD subjects and bipolar II patients, on the other, who had lower scores (poorer HRQoL) for role limitations due to physical health, general health, vitality, social functioning, role limitations due to emotional problems, mental health, and mental summary score.

DISCUSSION

When we compared the bipolar and RMD groups with a control group of non–psychiatrically ill individuals and controlled for differences in mean actual age, we found lower SF-36 mean scores on several subscales in both bipolar subgroups and in subjects with RMD; this confirms data in the literature indicating a poorer perceived QoL even in euthymic periods.[1–3] Our sample of healthy volunteers, however, was a convenience sample and thus not representative of the Italian general population; our results are in agreement with those of previous research, then, but the interpretation of our data cannot be extended to say that euthymic bipolar patients show a poorer HRQoL than that of the Italian general population.

Differences in mean SF-36 scores were detected between bipolar subtypes: bipolar II patients showed HRQoL that was poorer than that of bipolar I patients, even after controlling for age, age at onset, and length of illness, and equal to that of RMD subjects. This is in agreement with results of the only 2 studies published to date.[4,5]

It is possible that differences found in perceived QoL are due to a longer time spent depressed in patients with bipolar II disorder. It has already been shown that the course of the disorder is different according to the subtype of bipolar disorder: in a prospective investigation of the natural history of the disorder, the ratio of depression to mania (mean percentage of weeks spent with depressive symptoms to mean percentage of weeks spent with manic/hypomanic symptoms) was 37:1 in bipolar II subjects as compared to 3:1 in bipolar I subjects.[19] Although bipolar I has generally been viewed as the more severe variant of bipolar disorder, then, bipolar II, with its persistent depressive features, appears to have a greater impact on patients' perceived QoL even in a sustained period of euthymia, as demonstrated by the present study. The

fact that bipolar II patients had mean scores on several subscales of the SF-36 that were equal to those expressed by subjects with RMD, moreover, supports the view of depressive symptoms as the primary determinants of HRQoL, as already reported in the literature.[6–8,20] It is also possible, however, that patients with bipolar II disorder perceive their QoL as poorer than it really is during euthymic periods because they base "normality" on how they feel during hypomanic episodes, and this might not be true for bipolar I individuals.

This study had several limitations. First, HRQoL was evaluated cross-sectionally, although during a euthymic state, as in the majority of the studies investigating QoL in bipolar disorder. Since bipolar disorder is a chronic illness with not only multiple episodes of mania and depression but also fluctuating residual symptoms, it will be important to conduct more studies to assess HRQoL over extended periods of euthymia. Euthymic patients are not necessarily asymptomatic, in fact, as many have mild subsyndromal symptoms, and even residual depressive symptoms can be strongly associated with impaired QoL. Although in the present study it was required that all patients have a HAM-D score < 8 at intake, which excludes the presence of residual depressive symptoms, we cannot exclude fluctuations of subsyndromal symptoms during the euthymic phase, and this could differently impact on HRQoL in the 2 subgroups of bipolar disorder patients. A second limitation of the present investigation is the self-report assessment of QoL: some researchers have pointed out that self-report ratings for HRQoL may be suspect due to the characteristic psychopathology of bipolar disorder.[21] Moreover, the instrument used in the present study, the SF-36, is a generic measure of HRQoL not specifically designed for use in bipolar patients. However, instruments derived from the Medical Outcomes Study, such as the SF-36, the SF-20, and the SF-12, were the most widely used in studies[1,2] that conducted QoL assessments in bipolar patients. The SF-36, moreover, appears to possess acceptable psychometric properties and yield detailed normative data, and its use allows comparisons of HRQoL measures in different patient samples; taken together, these characteristics make the SF-36 one of the recommended scales[3] for the measurement of HRQoL in patients with bipolar disorder, and are the reason we chose this instrument in the present investigation.

Another limit of our study is that we recruited patients who were able to achieve a period of at least 8 weeks with a HAM-D score < 8 and a YMRS score < 6, and HRQoL was measured in this sample; our results may then only apply to a subgroup of subjects with bipolar I, bipolar II, or major depressive disorder. For instance, our results do not apply to patients who are unable to achieve and maintain euthymia and do not reflect potential differences in HRQoL observed during the acute phase.

Notwithstanding the limitations, this study provides additional evidence that bipolar type II is associated with poorer HRQoL compared to type I even during sustained periods of euthymia and excluding residual symptoms. Interventions targeting rehabilitation and/or functional enhancement may be helpful to improve HRQoL, especially among subjects with bipolar II disorder. It would also be of interest to compare in future studies bipolar I and II patients in euthymic states with no mood-stabilizing treatment.

Disclosure of off-label usage: The authors have determined that, to the best of their knowledge, no investigational information about pharmaceutical agents that is outside U.S. Food and Drug Administration–approved labeling has been presented in this article.

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