Winner of Resident Paper Award 2018

Borderline Personality Features in Inpatients with Bipolar Disorder: Impact on Course and Machine Learning Model Use to Predict Rapid Readmission

Background: Earlier research indicated that nearly 20% of patients diagnosed with either bipolar disorder (BD) or borderline personality disorder (BPD) also met criteria for the other diagnosis. Yet limited data are available concerning the potential impact of co-occurring BPD and/or BPD features on the course or outcome in patients with BD. Therefore, this study examined this comorbidity utilizing the standardized Borderline Personality Questionnaire (BPQ).

Methods: This study involved 714 adult patients with a primary diagnosis of BD per DSM-IV criteria who were admitted to the psychiatric unit at an academic hospital in Houston, TX between July 2013 and July 2018. All patients completed the BPQ within 72 hours of admission. Statistical analysis was used to detect correlations between severity of BD, length of stay (LOS), and scores on the BPQ. A machine learning model was constructed to predict the parameters affecting patients’ readmission rates within 30 days.

Results: Analysis revealed that the severity of certain BPD traits at baseline was associated with mood state and outcome measured by LOS. Inpatients with BD who were admitted during acute depressive episodes had significantly higher mean scores on 7 of the 9 BPQ subscales ($P < 0.05$) compared with those admitted during acute manic episodes. Inpatients with BD with greater BPQ scores on 4 of the 9 BPQ subscales had significantly shorter LOS than those with lower BPQ scores ($P < 0.05$). The machine learning model identified 6 variables as predictors for likelihood of 30-day readmission with a high sensitivity (83%), specificity (77%), and area under the receiver operating characteristic curve of 86%.

Conclusions: Although preliminary, these results suggest that inpatients with BD who have higher levels of BPD features were more likely to have depressive rather than manic symptoms, fewer psychotic symptoms, and a shorter LOS. Moreover, machine learning models may be particularly valuable in identifying patients with BD who are at the highest risk for adverse consequences including rapid readmission. (Journal of Psychiatric Practice 2019;25:279–289)

KEY WORDS: bipolar disorder, borderline personality disorder, Borderline Personality Questionnaire (BPQ), predictive analytics, artificial intelligence, machine learning

There is considerable overlap in symptoms between bipolar disorder (BD) and borderline personality disorder (BPD). Features such as impulsivity, mood instability, inappropriate anger, suicidal behavior, and unstable relationships are shared between BD and BPD, although patients with BPD tend to show higher levels of impulsiveness and hostility than patients with BD. In the largest published review related to BD and BPD, Paris et al analyzed data
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from over 145 reports and concluded that up to 20% of the patients diagnosed with either BD or BPD met criteria for both diagnoses. There are also substantial data supporting shared risk factors between BD and BPD.\(^5\)\(^-\)\(^7\) Despite the fact that both BD and BPD are severe psychiatric disorders associated with chronic clinical courses, significant functional impairment, and long-term treatment, fewer data are available concerning the potential impact of comorbid BPD on the course and/or prognosis of BD. Most of the reported studies have suggested that the presence of comorbid BPD has a negative impact on the course of BD, including an earlier age of onset, longer episodes, less time euthymic, and increased rates of substance abuse, suicidality, and aggression.\(^6\)\(^-\)\(^7\) However, because most patients with BD (~80%) do not meet full criteria for BPD, investigation of the potential impact of borderline personality features on the course of illness in BD may prove to be more helpful. Fonseka et al.\(^8\) reported that high rates of certain borderline personality spectrum symptoms in adolescents with BD were associated with greater severity of mood symptoms and functional impairment. Riemann and colleagues\(^9\) recently conducted the largest reported study examining the potential impact of individual borderline personality features on prospective illness course in patients with BD (\(N = 375\)). They found that the presence of greater borderline personality features in general was associated with an unfavorable illness course of BD. Moreover, 3 individual borderline personality features (affective instability, impulsivity, and self-mutilation/suicidality) were associated with both rapid cycling BD and BD.\(^9\)

The study described in this article utilized the Borderline Personality Questionnaire (BPQ), a standardized scale, to examine the comorbidity and potential impact of BPD features on course and outcome in psychiatric inpatients with BD. The BPQ is an 80-item self-report measure that assesses borderline personality traits as defined by DSM-IV criteria.\(^10\) The BPQ has 9 separate subscales for each BPD criterion: Impulsivity (I), Affective instability (AI), Abandonment (A), Relationships (R), Self-Image (SI), Suicide/Self-mutilation (S/SM), Emptiness (E), Intense anger (IA), and Quasi-Psychotic (Q-P). The BPQ has demonstrated internal consistency and convergent and divergent validity in both general and clinical populations and has been found to be a useful tool in screening for borderline personality traits in numerous studies.\(^10\)\(^-\)\(^12\)

In addition to examining the prevalence of BPD in BD, this study was designed to examine the potential impact of BPD as well as borderline personality features (as defined by the individual BPQ subscales) on the clinical course of patients with BD hospitalized for acute mood episodes. While clinical course can be assessed using numerous variables, length of hospital stay (LOS) and readmission rates are generally accepted as the most critical measurable outcomes in inpatient settings.\(^13\) LOS is a considered a reliable measure of the amount of resources utilized.\(^14\)\(^-\)\(^17\) Earlier research has also demonstrated a significant association between LOS and psychiatric diagnosis,\(^\)\(^18\)\(^-\)\(^20\) with some data suggesting that a psychosis diagnosis is responsible for the highest LOS,\(^21\)\(^-\)\(^23\) whereas other studies have reported that affective disorder diagnoses were more reliable predictors of LOS.\(^24\)\(^-\)\(^26\) Substance use disorder diagnoses were negatively correlated with LOS in another study.\(^27\) Although personality disorders are rarely the primary diagnosis in inpatient settings, there are relatively few data concerning their potential impact as a comorbid diagnosis on LOS. The study described here used conventional statistical analyses to investigate the prevalence of BPD in inpatients with BD as well as the potential relationships among BD severity, the BPQ total and subscale scores, and outcome as measured by LOS.

Because 30-day readmission rates have become one of the most popular parameters for assessing quality and efficacy of psychiatric inpatient care, the identification of factors that may prove useful in identifying patients at high risk for rapid readmission represents a compelling target for research efforts.\(^28\)\(^-\)\(^30\) Given these issues related to readmissions, this study also examined whether a machine learning model could be successful in using clinical, sociodemographic, and BPQ data to successfully predict which patients with BD would be at high risk for readmission within 30 days.

**METHODOLOGY**

**Study Design and Population**

This study involved 714 adults (18 y of age and older) patients with a primary diagnosis of BD per DSM-
IV criteria admitted to the same psychiatric unit at an inner-city academic hospital in Houston, TX between July, 2013 and July, 2018. All subjects in the study completed the BPQ within 72 hours of admission. All study participants were interviewed and examined by a board-certified physician (T.P.) and had a primary diagnosis per DSM-IV-TR criteria of bipolar I disorder (BD I), bipolar II disorder (BD II), or BD not otherwise specified (BD-NOS). Baseline demographic data and information on clinical outcomes were obtained during hospital assessment and from review of electronic medical records. The study was approved by the institutional review board (IRB) of the University of Texas Health Science Center, Houston. Individual consent was waived by the IRB as data were being collected through retrospective chart reviews. Patients with diagnoses of intellectual deficit disorder, dementia, significant cognitive dysfunction, and/or other comorbid psychiatric diagnoses were excluded from study participation. In addition, patients who were illiterate or had less than a third-grade education were also excluded.

**Assessment**

Demographic information was collected for all participants including age, sex, and race. The BPQ consists of 80-items that assess the severity of 9 subscales: Impulsivity (I), Affective instability (AI), Abandonment (A), Relationships (R), Self-Image (SI), Suicide/Self-mutilation (SSM), Emptiness (E), Intense anger (IA), and Quasi-Psychotic (Q-P). Total BPQ scores as well as individual scores on each of the 9 severity subscales were calculated for all participants.

**Statistical Analysis**

Analyses were conducted for all patients who completed the BPQ. Between-group differences were compared using Pearson $\chi^2$ tests for categorical variables, and $t$ tests for continuous variables presented as means $\pm$ SDs. Demographic data were analyzed using $\chi^2$ and analysis of variance tests. Regression analyses were used to test the correlations between BPQ scores and length of stay (LOS) and 30-day readmission rates. All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS), version 22.

**Machine Learning**

The 714 inpatients with BD who were included in the analysis were randomly split into a training set ($n = 499$) and a testing set ($n = 215$). Scores on the 9 subscales of the BPQ (I, AI, A, R, SI, SSM, E, IA, Q-P) and 5 clinical variables (sex, age, diagnosis, LOS, number of admissions at BPQ baseline) acted as features—“independent/input variables”—to the model, while 30-day readmission status acted as the target “dependent/output” variable. The online freely available Python software version 2.7 was used for coding the algorithm. Synthetic minority oversampling technique (SMOTE) was applied to the testing set to ensure an equal class distribution of the readmission output variable. A support vector machine (SVM) classifier was trained with the training set utilizing the top 6 features determined by analysis of variance $F$-score feature selection. The SVM classifier was then evaluated with the testing set.

**RESULTS**

**Demographic Data**

Table 1 presents the demographic data for the BD study sample ($n = 714$). There were 375 females (52.5%) and 339 males (47.5%). The mean age was 33.04 years (SD: 10.55 y). The BD sample was comprised of 402 (56%) Caucasians, 254 (36%) African Americans, 41 (6%) Hispanics, 14 (2%) Asians, 2 (0.3%) Native Americans, and 1 (0.1%) Other. The most common primary diagnosis was BD I ($n = 471$, 66%) followed by BD-NOS ($n = 207$, 29%) and BD II ($n = 36$, 5%). In terms of mood state at admission, the inpatients with BD-I were more likely to be in a manic ($n = 247$, 52%) or mixed ($n = 122$, 26%) episode than in a depressed episode ($n = 102$, 22%). The mean total BPQ score was $30.63 \pm 18.7$. On the basis of the BPQ criteria for BPD (total BPQ score $\geq 56$), ~14% ($n = 99$) of the entire BD inpatient sample also met criteria for BPD. No significant effects of age, sex, or ethnicity were identified on the BPQ total or subscale scores in the BD inpatient sample.

**BPD in BD Subgroups, Borderline Personality Features, and Mood State in BD**

Approximately 16% ($n = 34$) of the 207 inpatients with a primary diagnosis of BD-NOS, ~13% ($n = 59$) of...
the 471 inpatients with a primary diagnosis of BD I, and ~17% (n = 6) of the 36 inpatients with a primary diagnosis of BD II also met criteria for BPD per the BPQ criteria (total BPQ score \( \geq 56 \)). In addition, those with a primary diagnosis of BD-NOS had significantly higher (\( P < 0.05 \)) total BPQ scores (mean ± SD: 32.68 ± 19.5) compared with the BD I group (29.35 ± 18.3). Analysis of the individual BPQ subscales revealed that the BD-NOS group had significantly greater (\( P < 0.05 \)) borderline personality features as measured by 3 of the 9 BPQ subscales: Suicide/Self-mutilation (mean ± SD: 2.9 ± 2.2 vs. 2.5 ± 2.2), Emptiness (3.9 ± 3.2 vs. 3.2 ± 2.9), and Intense anger (4.2 ± 3.2 vs. 3.6 ± 2.9) (Fig. 1).

Prevalence rates for BPD based on total BPQ scores were also examined by mood state (manic, mixed, or depressed) as well as by the presence or absence of psychotic symptoms in the BD I group. As noted above, most (52.4%) of the patients with BD I were admitted during a manic episode, compared with 26% and 22% admitted during a mixed or depressive episode, respectively. Of the patients with BD I, 11.1% of the 247 patients admitted during a manic episode also met criteria for BPD, compared with 9.1% of the 122 patients admitted in a mixed episode and 9.8% of the 102 patients admitted in a depressed state. Analysis of variance of total BPQ scores also revealed that patients admitted in a depressive state had significantly higher mean BPQ scores than those admitted in a manic state (mean ± SD: 38.5 ± 19.8 vs. 24.8 ± 16.4, \( P < 0.05 \)). In addition, scores on 7 of the 9 BPQ subscales were significantly higher in the patients with BD I admitted in a depressive state compared with those admitted in a manic state: Affective instability (6.38 ± 3.3 vs. 4.21 ± 3.2), Abandonment (4.88 ± 3.4 vs. 3.15 ± 2.8), Suicide/Self-mutilation (3.43 ± 2.3 vs. 2.02 ± 2.0), Self-Image (3.6 ± 2.6 vs. 1.8 ± 1.9), Emptiness (4.78 ± 3.2 vs. 2.53 ± 2.6), Intense anger (4.65 ± 3.1 vs. 3 ± 2.6), and Quasi-Psychoticism (2.71 ± 1.9 vs. 1.76 ± 1.7) (Fig. 2).

**Psychosis and BPD Prevalence and Features**

Psychotic symptoms were very common (84%, \( n = 396 \)) in the inpatients with BD I regardless of mood state and appeared to be associated with a decreased risk that the patients would also meet criteria for BPD. That is, patients admitted in a manic state without psychotic symptoms were more likely to also meet criteria for BPD than those admitted in a manic state with psychotic symptoms (16.7% vs. 6.4%). Similarly, comorbid BPD was more common in patients admitted in a mixed state without psychotic symptoms (30.8%) than with psychosis (11.5%) and in patients admitted in a depressed state without (24.3%) than with psychosis (21.5%) (Table 1 and Fig. 3).

Further stratification and analysis of the mean BPQ scores in the BD I group identified an inverse relationship between psychosis and BPQ scores; that is, in general, the patients with psychotic symptoms had significantly lower BPQ scores than those without psychosis (mean ± SD: 28.28 ± 17.7 vs. 35.03 ± 20.1, \( P < 0.05 \)).

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**TABLE 1. Demographic Data and Clinical Characteristics of the Sample (N = 714)**

<table>
<thead>
<tr>
<th>Sex [n (%)]</th>
<th>Females 375 (52.5)</th>
<th>Males 339 (47.5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age [mean (SD) = 33.04 y of age (10.55 y) [n (%)]]</td>
<td>18-29 y 319 (44.7)</td>
<td>30-39 y 222 (31.1)</td>
</tr>
<tr>
<td>Ethnicity [n (%)]</td>
<td>Caucasian 402 (56.3)</td>
<td>African American 254 (35.6)</td>
</tr>
<tr>
<td>Bipolar subtypes [n (%)]</td>
<td>BD I Manic with psychosis 235 (32.9)</td>
<td>BD I Manic without psychosis 12 (1.7)</td>
</tr>
<tr>
<td>Length of stay (LOS) (mean ± SD) (d)</td>
<td>8.14 ± 5.2</td>
<td></td>
</tr>
<tr>
<td>30 d readmissions [n (%)]</td>
<td>Yes 63 (8.8)</td>
<td>No 651 (91.2)</td>
</tr>
</tbody>
</table>

*BD indicates bipolar disorder; BD-NOS, bipolar disorder not otherwise specified.*
Multiple regression analysis was conducted to analyze any potential relationship between borderline personality features and outcome as measured by LOS. There was a significant inverse relationship identified between the mean BPQ total score and LOS. Greater BPQ scores were associated with shorter LOS ($\beta = -0.023, P = 0.03, F = 4.737, R^2 = 0.007, R^2_{\text{adjusted}} = 0.005$). Subsequent stepwise analysis of each of the BPQ subscales
identified 4 subscale scores that were negatively associated with LOS: Affective instability ($\beta = -0.167$, $P = 0.003$, $F = 8.702$, $R^2 = 0.012$, $R^2_{\text{adjusted}} = 0.011$), Relationships ($\beta = -0.188$, $P = 0.035$, $F = 4.485$, $R^2 = 0.006$, $R^2_{\text{adjusted}} = 0.005$), Suicide/Self-mutilation ($\beta = -0.285$, $P = 0.001$, $F = 10.498$, $R^2 = 0.015$, $R^2_{\text{adjusted}} = 0.013$), and Intense anger ($\beta = -0.129$, $P = 0.046$, $F = 4.013$, $R^2 = 0.006$, $R^2_{\text{adjusted}} = 0.004$). Of these subscales, the Suicide/Self-mutilation subscale had the most significant relationship ($F = 10.498$, $P = 0.001$).

Machine Learning Model and 30-Day Readmission Rates

While most of the patients in this sample were not rapidly readmitted to our facility, 63 patients (8.8%) did require readmission within 30 days. Using a machine learning model, we found that 6 variables (total number of admissions, the BPQ Suicide/Self-mutilation Subscale, the BPQ Self-Image Subscale, LOS, sex, and age) predicted 30-day readmission with calculated $F$-scores of 30.2, 11.9, 8.0, 7.8, 7.7, and 7.4, respectively (Fig. 4). Spearman correlation analysis of the model revealed that younger age ($r = -0.03$), reduced LOS ($r = -0.02$), a higher score on the BPQ Suicide/Self-mutilation Subscale ($r = 0.05$), a higher score on the BPQ Self-Image Subscale ($r = 0.06$), female sex ($r = 0.05$), and a greater number of previous admissions ($r = 0.2$) were associated with a greater risk for readmission at 30 days. In fact, the SVM classifier demonstrated high sensitivity (0.83), good specificity (0.77), and an area under the receiver operating characteristic curve of 0.86. These results indicate that our machine learning model was able to accurately identify 6 key variables for rapid readmission with “good” predictive validity (Fig. 5).

A separate conventional statistical analysis was also conducted to further investigate the potential relationship between 30-day readmission and number of previous admissions. Regression analysis demonstrated that a greater number of previous admissions was associated with an increased risk of 30-day readmission ($\beta = 0.099$, $P = 0.003$, $F = 25.682$, $R^2 = 0.011$, $R^2_{\text{adjusted}} = 0.025$). Individual analysis of the receiver operating characteristic area under the curve for the 3 strongest variables (previous admissions, BPQ Suicide/Self-mutilation Subscale, and BPQ Self-Image Subscale) demonstrated a good predictive validity.
Subscale, and BPQ Self-Image Subscale) associated with 30 day readmission as identified by the machine learning model revealed predictive values of 0.68, 0.55 and 0.56, respectively (Fig. 6).

DISCUSSION
The prevalence of BPD (14%) found in this study of inpatients with BD was on the higher end of the range reported in previous studies (in which prevalence ranged from 5.6% to 16.1%), but our study was limited to an inpatient setting, whereas the other studies included other clinical settings. This difference in prevalence may reflect the greater clinical severity required for treatment in an inpatient setting. In fact, 84% of patients in our BD I group had psychotic symptoms. The prevalence of BPD in our inpatients with BD II (almost 17%) was at the upper end of the range reported in previous studies (in which prevalence ranged from 8% to 19%)31–38; however, our sample size

/-SM indicates the Suicide/Self-mutilation Subscale; S-I, Self-Image Subscale; LOS, length of stay; S, sex; Admit # at BPQ, number of admissions at baseline when the borderline personality questionnaire was administered.


Confusion matrix, without normalization

Receiver operating characteristic curve

ROC curve indicates receiver operating characteristic curve.
was relatively small (n = 36) especially compared with the size of our BD I (n = 471) and BD-NOS (n = 207) groups. Interestingly, we found that the BD-NOS group was more likely than the BD I group to have comorbid BPD. Although the criteria for DSM-IV BD-NOS specified that the patient does not meet criteria for BD I or BD II, it does allow for diagnosis of a BD with atypical presentations or when differentiation from a substance-induced mood disorder or mood disorder due to general medical condition is not possible. As such, the underlying factors contributing to BD-NOS are generally accepted as being distinct from those in other BD subgroups.39,40 Moreover, comorbid substance abuse disorders are common in all patients with BD including those with BD-NOS.41-43

This study utilized the BPQ, a standardized self-report measure comprised of subscales corresponding

![ROC curves for top 3 features determined by the machine learning model.](image)
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to the 9 DSM-IV BPD criteria. Since its development by Poreh et al in 2006,10 the BPQ based on DSM-IV criteria has been considered a very useful tool in screening for borderline personality traits in both general and clinical populations.44 Multiple studies have demonstrated that the BPQ has a high degree of validity and reliability, with a few exceptions, in particular the Quasi-Psychotic States Subscale.12 When compared with the Minnesota Multiphasic Personality Inventory (MMPI), BPQ showed significantly high convergent validity with a high coefficient (r = 0.85).12 Other studies have concluded that the BPQ has the optimal mix of characteristics, with moderate sensitivity (68%), high specificity (90%), and high negative predictive value (91%).45 Compared with the McLean Screening Instrument for Borderline Personality Disorder (MSI-BPD), the BPD items from the International Personality Disorder Examination Screening Questionnaire, and the BPD items from the Structured Clinical Interview for DSM-IV Axis II disorders (SCID-II), the BPQ had the highest overall diagnostic accuracy of 85%.45

In the sample of inpatients with BD I in this study, psychotic symptoms were very common (84%, n = 396) regardless of mood state. Our original hypothesis in planning the study was based on the suggestion that mood states complicated by psychotic symptoms would have higher rates of comorbid BPD. However, further analysis of mean total BPQ scores indicated that greater levels of borderline personality features were associated with significantly fewer psychotic symptoms. This finding may suggest that the presence of borderline personality features rather than symptoms that meet full criteria for BPD may represent more of a trait than a state phenomenon. In other words, our findings suggest that the presence of some borderline personality traits, even if not sufficient for a full diagnosis of BPD, are likely to be associated with the presence of fewer psychotic symptoms, with a larger number of traits trending toward a full diagnosis of BDP being associated with an increasingly smaller number of psychotic symptoms.

In addition to examining the prevalence of BPD in inpatients with BD, this study also examined the potential impact of BPD as well as borderline personality features (as defined by the individual BPQ subscales) on the clinical course of patients with BD hospitalized for acute mood episodes. LOS and 30-day readmission rates were used to assess clinical outcome. Not only were higher scores on the

BPQ associated with a shorter LOS in our study, but higher scores on certain borderline personality traits (BPQ subscales of Affective instability (AI), Relationships (R), Suicide/Self-mutilation (S/SM), and Intense anger (IA) were also associated with shorter LOS.

The promise of using artificial intelligence in medicine to enhance diagnostic and prognostic accuracy may well prove limitless.46 Given the complex heterogenous pathophysiology underlying psychiatric disorders, machine learning models may provide the best chance for developing novel statistical approaches capable of extrapolating patterns across different data sets (cross-validation) en route to the pursuit of personalized psychiatry.47–49 Unlike conventional statistical methods, machine learning techniques can harness the general principles of underlying complex observations without making undo assumptions. In addition, machine models allow the data to self-represent while managing extensive amounts of heterogeneous data resulting in multiclass predictions.50,51

In this study, the machine learning algorithm demonstrated 86% accuracy in predicting 30-day readmissions in inpatients with BD using 6 variables: total number of admissions, the BPQ Suicide/Self-mutilation Subscale, the BPQ Self-Image Subscale, LOS, sex, and age. Specifically, the model demonstrated that lower age, reduced LOS, a higher score on the BPQ Suicide/Self-mutilation Subscale, a higher score on the BPQ Self-Image Subscale, female sex, and a greater number of previous admissions could be used with 86% accuracy to predict patients at high risk for readmission within 30 days.

Limitations

The limitations of this study included use of a self-report measure for diagnosis of BPD. The study also used a retrospective study design, which introduces multiple potential biases, including incomplete documentation, missing data, difficulty interpreting information found in the documents, and problematic verification of information. The study was also limited to patients treated in an inpatient setting, which may reduce the generalizability of the results to other clinical settings. In addition, machine learning models have known limitations and
challenges such as reproducibility; small sample sizes may also exacerbate data noise and lead to over-fitting (over-estimation), and the variable course of psychiatric illness may further complicate disease trajectories.

**CONCLUSIONS**

Although preliminary, the results presented here suggest that inpatients with BD with greater levels of BPD features were more likely to have depressive rather than manic symptoms, fewer psychotic symptoms, and a shorter LOS. A machine learning model identified 6 variables, including 2 subscales on the BPQ, that were highly predictive of readmission within 30 days of discharge. Given that inpatient treatment is one of the largest direct costs associated with the treatment of BD, machine learning models may be particularly valuable in identifying patients with BD who are at the highest risk for adverse consequences, including rapid readmission.

**REFERENCES**


