J. López Castromán[1]
E. Baca García[1]
C. Botillo Martín[1]
J. Quintero Gutiérrez del Álamo[1]
R. Navarro Jiménez[1]
M. Negueruela López[1]
M. M. Pérez Rodríguez[2]
I. Basurte Villamor[1]
A. Fernández del Moral[3]
M. A. Jiménez Arriero[4]
J. L. González de Rivera[1]

Diagnostic errors and temporal stability in bipolar disorder

[1] Psychiatry Department
Hospital Universitario Fundación Jiménez Díaz
Madrid (Spain)
[2] Psychiatry Department
Hospital Universitario Ramón y Cajal
Madrid (Spain)
[3] Mental Health Center of Central District
Madrid (Spain)
[4] Mental Health Center of the District of Arganzuela
Madrid (Spain)

Introduction. The diagnosis of bipolar disorder is frequently modified during the course of the illness.

Material and methods. Diagnostic changes and associated errors are described for 1,153 patients diagnosed as bipolar disorder, aged over 18 years and with at least ten follow-up visits. Data was extracted from a clinical registry of out-patient care specialized in Psychiatry and psychiatric hospitalizations of 25,152 patients representative of an urban area of 240,000 inhabitants. Limit for diagnostic stability was established as the maintenance of the bipolar disorder diagnosis in at least 75% of the visits.

Results. A total of 158 (46.1%) out of 342 patients diagnosed as having a bipolar disorders in the first visit kept this diagnostic constant in subsequent evaluations. Infradiagnostic initial error was committed with 108 stable patients who were not diagnosed in the first visit. 184 patients diagnosed in the first visit with bipolar disorder had less than 75% concordant diagnosis along the follow-up and could be considered as initial overdiagnosis. Two hundred and nine out of the 443 patients who were diagnosed as bipolar disorder in their last visit did not keep stability criteria in their follow-up and could be considered therefore as final overdiagnosis. Thirty two stable patients not diagnosed in their last visit could be considered as infradiagnosis final error. Diagnosis from schizophrenia spectrum (F2) appears in one of every four psychiatric visits of the patients included in this study. Overlap was seen in three other categories: anxiety disorders (F4), personality disorders (F6) and substance abuse disorders.

Conclusion. Initial course of bipolar disorder causes difficulties in the diagnosis.

Key words:
Bipolar disorder. Stability. Diagnosis. Course.

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Correspondence:
Jorge López Castromán
Fundación Jiménez Díaz
Av. de los Reyes Católicos, 2
28040 Madrid (Spain)
E-mail: jorgecastroman@gmail.com

Errores de diagnóstico y estabilidad temporal en el trastorno bipolar

Introducción. El diagnóstico de trastorno bipolar se modifica con frecuencia a lo largo de la evolución de la enfermedad.

Material y métodos. Se describen los cambios de diagnóstico y error asociado de 1.153 pacientes mayores de 18 años diagnosticados de trastorno bipolar y con un seguimiento mínimo de 10 visitas en base a un registro clínico de atención ambulatoria especializada en psiquiatría y hospitalizaciones psiquiátricas de 25.152 pacientes representativos de un área urbana de 240.000 habitantes. Se usó como criterio de estabilidad diagnóstica mantener el diagnóstico de trastorno bipolar en al menos el 75% de las visitas.

Resultados. De los 342 pacientes diagnosticados de trastorno bipolar en la primera consulta, el 46,1% mantuvieron el diagnóstico estable. Se cometió un error inicial de infradiagnóstico con 108 pacientes estables no diagnosticados en la primera visita. Ciento ochenta y cuatro de los 342 pacientes diagnosticados en la primera visita obtuvieron posteriormente al menos un 25% de diagnósticos diferentes de bipolar y podrían ser considerados como sobrediagnóstico inicial. Doscientos nueve de 443 pacientes diagnosticados como bipolares en la última visita no mantuvieron criterios de estabilidad en su evolución y podrían, por tanto, considerarse como sobrediagnóstico final. Treinta y dos pacientes estables no diagnosticados en la última visita constituirían el error final de infradiagnóstico. Diagnósticos del espectro de la esquizofrenia (F2), aparecen casi en una de cada cuatro visitas al psiquiatra de los pacientes del estudio. Otras tres categorías presentan solapamiento: los trastornos de ansiedad (F4), los trastornos de personalidad (F6) y los trastornos por consumo de sustancias.

Conclusión. El trastorno bipolar es un trastorno de difícil diagnóstico en su evolución inicial.

Palabras clave:
Trastorno bipolar. Estabilidad. Diagnóstico. Evolución.

INTRODUCTION

The concept of diagnostic stability began to take on importance with the article published by Robins and Guze in 1970, where it was related with predictive validity of the diagnoses in psychiatry for the first time[1]. This concept has been defined as the measure in which a diagnosis is confirmed in consecutive evaluations[2]. Different methods have also been proposed to strengthen the stability of a diagnosis although none of them assure the reliability of the result. These methods would include: longitudinal observation or evaluation[3,4], but also more advanced diagnostic studies such as genetic type one, monitoring of the response to treatment[5] or the evaluation of the effects of the disease on the psychosocial function.

There are many factors that can cause instability in the psychiatric diagnosis. The course of the mental diseases, and specifically of bipolar disorder, often makes it difficult to differentiate the clinical disease from the pictures. In addition, lack of complete information on the course of the disease and possible previous diagnostic errors may also give rise to a bias in the evaluation.

In the specific case of bipolar disorder, the diagnostic difficulties seem to be especially relevant at the onset of the disease and the diagnosis is frequently assured only with the long-term follow-up of the patients. In fact, bipolar disorder is longitudinally one of the diagnoses that is most frequently modified before becoming definitely stabilized. On many occasions, changes occur in its classifications during the course of the disorder, above all towards diagnoses on the schizophrenia spectrum[6,7].

The concept of bipolar disorder currently includes a large variety of clinical pictures with a similar prevalence in the different ethnic groups. These vary from 0.5% to 7.5% of the population according to the different studies published. However, most of the experts on this disorder coincide in stating that the current data probably underestimate the real prevalence of the disease. According to the last version of the international classification of diseases[8], bipolar disorder is defined by the appearance of repeated episodes, that is at least two, in which the mood state and activity levels of the patient are significantly altered. This alteration may be two types: elevation of mood state and increased energy and activity level that would correspond with manic or hypomanic phases of the disorder or decrease of mood state and decreased energy and activity that would correspond to depressive phases. Complete recovery would occur between the isolated episodes. The incidence is similar in both genders.

Few studies have investigated the diagnostic change in bipolar disorder or the relationships between the different diagnoses in their course up to now[9]. We have only found one author[7] in the bibliographic search who analyzes diagnostic stability of bipolar disorder using the ICD-10 criteria for the classification of the patients. Other authors have made studies based on the DSM-IV classification, but using a lower number of patients or significantly reducing the follow-up period[3]. Several different studies have approached the problematic of diagnostic stability after first psychotic episodes[2,6,10-12]. In our study, we have tried to approach these aspects using a significant population of patients diagnosed of bipolar disorder who have had a maintained follow-up for 11 years, which allows us to adequately evaluate the course of their diagnoses during this time[13].

METHODOLOGY

A clinical registry that included all the medical acts conducted in the psychiatric out-patient clinics for a population of approximately 240,000 persons was used. This database corresponds to two Mental Health Care Sites (MHC) and also includes the medical acts made in both the Emergency Department and in the short hospitalization unit of the tertiary hospital. These resources cover a heterogeneous zone in the center of the city of Madrid where there is a high percentage of immigration, which corresponds to about 21.7% of the current population[13,14]. A total of 25,152 patients were attended from January 1, 1992 to December 31, 2004. The total number of visits made by patients with any diagnosis of bipolar disorder and at least 10 recorded visits was 71,543. The diagnoses assigned in each clinic are detailed in table 1.

Because of the wide range of the inclusion period, the nosological codes used have varied to a certain degree during the study. The clinicians assigned the diagnoses using ICD-10 and DSM-IV criteria[8,15] although they were coded at ICD-9[16] for administrative reasons. For our analysis, all the diagnoses were previously and automatically converted to ICD-10.

Those patients who had been diagnosed of F31 (bipolar disorder) according to the ICD-10 and who had been attended at least 10 times in the health care sites of the area during the period mentioned were considered. Ten different

Table 1 Classification of the diagnoses based on frequency reported during the medical visits of the patients registered in the study

Diagnosis	%
Bipolar disorder	31.6%
Schizophrenia	23.9%
Anxiety disorders	9.1%
Chronic depression	6.8%
Personality disorders	3.7%
Substance consumption	2.2%
Psychosomatic disorders	0.8%
Depression	0.5%

evaluations guarantee a minimum period of follow-up of five months, counting an interval between visits of 15 days. In this way, the risk that the evaluations have been made by different specialists and that the shortness of the follow-up would condition the diagnosis is reduced. A total of 10,025 patients were seen on at least 10 occasion and 1,153 of them were diagnosed of F31 at least once.

Kappa index was used as a measure of agreement between the first and last diagnosis for the analysis of the data[17,18]. Those patients who had received the diagnosis of bipolar disorder in 75% of the visits at least were considered as patients correctly diagnosed from the point of diagnostic stability[17,18]. Confidence interval of the different percentages was calculated using the Wald method[19].

RESULTS

We found that 23.1% (266/1153) out of the total of 1,153 subjects who had been diagnosed of bipolar disorder (BD) at least once maintained it in 75% of the visits. The 1,153 patients analyzed received a mean of 62 attendances. Of these, 342 patients were diagnosed of bipolar disorder in the first visit with a prospective consistency (coincidence grade in the last visit recorded) of 49.4% and 443 patients were diagnosed of bipolar disorder in the last visit with a retrospective consistency (coinciding with the first visit) of 38.1%. The agreement between the first and last diagnosis (kappa = 40.0), both being bipolar disorder, stands out. We did not find any differences between the data from the attendance in clinic visits and those from the hospitalization unit or from care given in the Emergency department or in relationship with the duration of the follow-up.

Figure 1 shows the difference in the evolution of the bipolar disorder diagnosis between the first and last visit recorded for the study patients. Only 158 out of a total of 342 patients diagnosed of bipolar disorder in the first consultation maintained the F31 diagnosis in at least 75% of the visits during the follow-up. Thus 59.4% of the 266 patients considered stable along the follow-up were diagnosed in the first visit (158/342, 95% CI: 40.9-50.1). The 108 stable patients who were stable but who had not been diagnosed in the first clinic visit would constitute an initial error (31%, 108/266; 95% CI: 26.6-36.5). In this first visit, 184 of the 342 patients diagnosed subsequently received at least 25% of diagnoses other than F31 and could be considered as initial overdiagnosis or false positives (FP). They would correspond with 53% of the initially diagnosed (184/342; 95% CI: 48.5-59.0).

The number of diagnoses of bipolar disorder increased considerably in the last visit. A total of 234 out of the 443 patients who obtained F31 classification in this visit corresponded with the 266 patients who were stable during the follow-up (88 %). However, the 209 patients (47.2 %, 209/443; 95% CI 42.5-51.8) diagnosed as bipolar in this last visit had not maintained stability criteria during their evolution and could thus be considered as final overdiagnosed (FP). We consider that the 32 stable patients not diagnosed in this visit would constitute the final error in the diagnosis (12%, 32/266; 95% CI: 8.1-15.9).

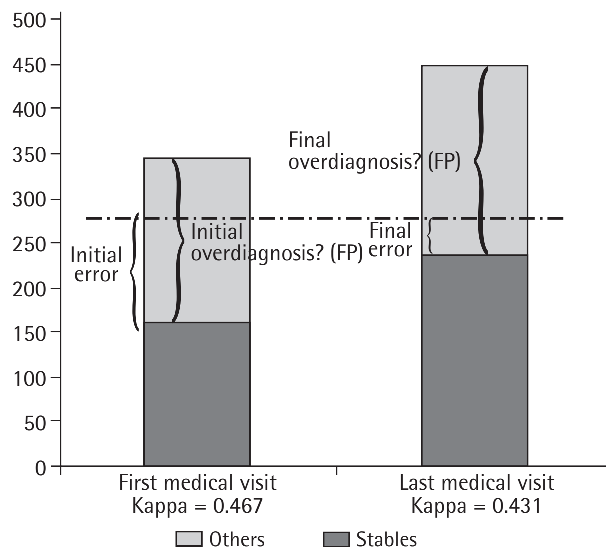

Figure 1 *Comparison of bipolar disorder diagnoses (F31) between the first and last medical visit. The red line represents the number of patients who have maintained this diagnosis in more than 75 % of the medical visits.*

We can observe that there is great variability over time for these patients. There is a wide range of categories that could act as confounding factors in the diagnosis of bipolar disorder. But this is especially true in the case of the schizophrenia spectrum (F2), diagnosis that finally appears in almost one out of every four visits to the psychiatrist of the patients included in the study. In spite of this, there are very few cases in which these patients finally fulfill the criterion of diagnostic stability established in our study for schizophrenia or other similar disorders. In a lesser degree the confusion is also consistent with three other categories: anxiety disorders (F4), personality disorders (F6) and substance abuse disorders. As was expected, most of the diagnoses that remained stable during the follow-up correspond with bipolar disorder.

The F3 category is broken down into its different categories in figure 2. In this way, it can be observed that although most of the diagnoses correspond to F31 of bipolar disorder, many of these patients were included at some time within the F33 category (recurrent depressive disorder) and even, with some frequency, in the last visit recorded. However, they did not fulfill stability criteria for most of these patients.

CONCLUSIONS

The diagnostic difficulties of bipolar disorder stand out in the first contact with the specialist, either because it is dif-

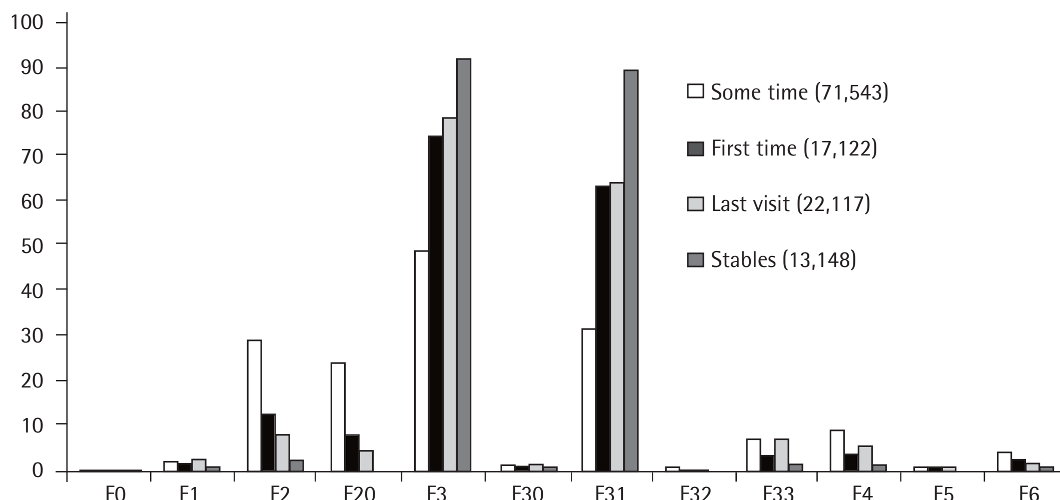

Figure 2 *Diagnoses given to the 1,153 patients who were evaluated as bipolar disorder at some time.*

ficult to recognize the initial symptoms or due to the «masked» presentation due to toxic abuse, to the initial depressive symptoms or transitory psychotic symptoms[7]. In our study, we found that diagnostic stability is low, since fewer than 25% of the patients maintained the diagnosis in their evolution and fewer than 60% of these were diagnosed in their first contact with the specialist. We also found frequent diagnostic oscillations within our study group. These oscillations occurred more frequently towards or from diagnoses such as schizophrenia or acute psychotic episodes but also with disorders related with the use of psychoactive substances, anxiety disorders or personality disorders. The main confounding factor, therefore, and in agreement with previous works, seems to be related with the diagnoses of the schizophrenia spectrum.

Several aspects differentiate our study from others conducted previously. In the first place, the registry included evaluations for three different scenarios: out-patient clinics, hospital emergency departments and acute hospitalization unit. The diagnoses were assigned by psychiatrists who were unaware of the study procedures and their diagnoses were made within the usual clinical practice while in other studies made, the evaluation was often made by structured interviews or using other diagnostic methods. In this way, the study may be of importance since it reflects the routine functioning of the psychiatric classifications in use and better adjusts to the clinical reality. The high representativeness of the sample and long follow-up period also favors the study results.

Temporal consistence of bipolar disorder is less in our study than in others conducted previously[3,7]. This could be explained because in some of these studies, the follow-up period was shorter[6,11]. In any case, the instability in the diagnoses of bipolar disease is outstanding considering the probable bias present in the evaluations because the clinicians had previous references of the patients and often with the clinical record. The disease course itself could partially explain the diagnostic difficulties due to its variability, but it is possible that the current clinical evaluation methods require new revisions to assure their reliability.

Similarly, current research studies (above all, in chronic diseases such as bipolar disorder) are based to a large degree on short-term follow-up studies that may affect their validity as the time is not sufficient to achieve stabilization of the diagnoses. The prevalence and incidence studies may also be influenced by the stability of the diagnoses investigated. The degree that this occurs must still be determined.

The results stress the need for a longitudinal diagnostic process and new diagnostic tools with greater accuracy[13]. New studies that analyze the factors related with diagnostic instability could establish their predictive favors. For example, this could be done by examining the relationship between the different semiological presentations of the disease in its onset and subsequent evolution.

In regards to the limitations of our study, in the first place, the probable underestimation of the instability of the diagnostic because the evaluations conducted before its onset are not included if the patient had been evaluated previously by a psychiatrist stands out. The absence of data on the activity of private specialists and the populational or cultural bias due to the importance of the immigrant population in our area are also added difficulties in the study. In order to assure an adequate study of diagnostic stability in the bipolar disorder, a registry over a longer time period with a larger number of patients should be made so that the historic evolution of the diagnoses of each patient, including the onset of the disorder, could be investigated.

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