



Prognostic Value of Affective Symptomatology in First-Admitted Psychotic Patients

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Abstract: Objective: to analyze the predictive value of affective symptomatology in a first psychotic episode sample followed up during three and five years, regarding to hospitalization, relapses, suicidal behaviour, working level, social activity and global functioning. Method: 112 inpatients with a first psychotic episode were included in a longitudinal-prospective study followed up during three (N=91) and five-year (N=82). Assessments included the YMRS and HRDS-21, the GAF, the Strauss-Carpenter prognostic scale, the PANSS and the Phillips premorbid adjustment scale. We used descriptive and logistic analysis to determine the predictive factors associated to the number of relapses, hospitalizations and suicide attempts; depressive, manic, activation and dysphoric dimensions as covariables. Results: 91.46% of relapses and 21% of suicide attempts at fifth year. The GAF discriminated among prognostic groups from the third year (p 0.020), with the poorest prognosis in the schizophrenia group, while bipolar disorders and the rest of the diagnoses achieved an intermediate prognosis. The Strauss-Carpenter scale, specifically working, social activity and global functioning items, discriminated among three diagnostic groups and between affective and non-affective psychosis (p < 0.05); while schizophrenia scored the poorest outcome, bipolar disorder scored the highest. Depressive dimension was significantly associated with a lower number of relapses and hospitalizations (p= 0.045 and p=0.012) and manic dimension with more relapses (p=0.023). Conclusion: The depressive dimension presents the best prognosis. On the contrary, the activation dimension, in general, gives a more favourable prognosis with regards to functionality (social) and unfavourable with respect to relapses. Finally, the manic dimension is associated with a worse evolution regarding relapses. Only the dysphoric dimension is not associated with syndromic and/or functional prognosis.

Keywords: prognostic, affective, dimension, first psychosis.

1. Introduction

First episode psychosis includes a heterogeneous population which represents an extensive number of diagnoses. Today's classifications systems are every time more focused in the inclusion of dimensions versus categories in psychiatry, and the clinical definition of psychosis may involve only one part of the total psychosis phenotype¹.

Little is studied about the influence of affective symptomatology in functional psychosis and results are frequently controversial. Moreover, these studies are nearly non-existent in first psychotic episode, and only a few of them used a dimensional approach. Therefore, dimensional representations would be useful to predict the clinical course and treatment needs in first episode psychosis.

Crow² and van Os³ suggested the hypothesis of the psychopathological continuum where different diagnostic categories share dimensional which could refer factors to similar neurobiological mechanisms for each of the dimensions regardless of the type of psychosis. Dimensions are not diagnostic-specific and have been reasonably replicable in psychosis, stable solutions in a variety of settings, diagnostic groups and patient samples ⁴. Initial work was done on schizophrenia, finding a three-factor solution, with positive, negative and disorganized dimensions ⁵. Afterwards, Cassidy ⁶, Serretti ⁷ and Disalver⁸ examined the factor structure of the bipolar disorder. González-Pinto et al. 9 obtained a five-factor solution in a 103 bipolar disorder sample. Later, samples included the full spectrum of psychosis, and five-factor solutions were found, including manic and depressive dimensions ¹⁰⁻¹⁵. Finally, factor structure analyses were targeted to first psychotic episode samples ^{4,16-21}.

Regarding to the influence of the affective symptomatology in psychosis, some authors found that affective symptomatology associates good prognosis ^{17,22-25}; some of them associated the better prognosis specifically with the depressive dimension ²⁶; others, like Paillére-Martinot ²⁷ associated the better prognosis to a higher score on the GAF (Global Assessment of Functioning) ²⁸. Both van Os ¹⁷ and Allardyce et al.⁴ associated the manic dimension with a good outcome; the first one specified fewer symptoms and their lesser severity, while the latter associated it with being married and working; McIntosh et al.¹⁹ also found a good outcome related to depression dimension.

However, others researchers found a negative association between depression and outcome: Geddes et al²⁹ found early relapse and more time in hospital; Birchwood ³⁰ found early relapse; Meng et al. ³¹ also associated it with a poor prognosis. Thara et al.³² associated longer time with symptoms with manic descompensation. Power et al.³³ associated affective symptoms with more hospitalizations. Finally Sipos et al.³⁴ also associated it with a poor outcome.

In conclusion, our **objective** was to study the predictive value of affective symptomatology in a first psychotic episode sample followed up during three and five years, using a dimensional approach. We studied outcome in terms of hospitalization, relapses, suicidal behaviour,

2. Results and Discussion

Patient Sociodemographic and Clinical Characteristics

A total of 112 patients with a first psychotic episode were included in the study at baseline. Of these 112 patients, 91 (81.25%) and 82 (73.2%) patients were available for analysis at 3 and 5 years' follow-up. At baseline, the mean age of the total sample was 28.8 years (SD = 10.3) and 75 (67%) were men. Initial DSM-IV diagnosis at baseline included bipolar disorder (23.2%), schizophrenia (15.2%) and other diagnosis (61.6%). Sociodemographic and clinical baseline characteristics are describe in a previous work⁵⁰.

There were no differences between patients followed or not followed with respect to the following baseline variables: age (U= 1023, p=0.62), sex (χ 2 =0.30, p=0.58), marital status (Fisher, p= 0.69), socioeconomic level (Fisher, p=0.27) and tobacco use (Fisher, p= 0.53).

Diagnostic Categories

The patient sample was classified both into three diagnostics groups: (1) those with schizophrenia diagnosed; (2) those with bipolar disorder diagnosed; and (3) those with other psychosis, and two diagnostic groups: affective psychosis (bipolar disorder, depressive disorder) and non-affective psychosis (the rest of the psychosis).

Of the 91 patients at 3-year follow-up, 25 (27.47%), had a diagnosis of schizophrenia, 34 (37.36%) bipolar disorder and 32 (35.17%) were classified as other psychosis. Final diagnosis at fifth year were: 34.14% of the patients have

working level, social activity and global functioning.

schizophrenia, 37% bipolar disorder and 29.26% other psychosis.

Prognostic Groups

Of the 91 patients, 20.9% had a good prognosis (GAF \geq 71), 51.6% intermediate prognosis (GAF 51-70) and 27.5% (GAF \leq 50) had a bad prognosis at 3-year. And of the 82 patients at fifth year, 23.7% had a good prognosis, 51.3% intermediate prognosis and 25% bad prognosis. See table 1 for Strauss-Carpenter.

Affective Dimensions

As previously reported, factor structure analysis⁹ produced a five-factor solution explaining 60.8% of the total variance in a sample of patients with bipolar disorder. In the present study, we analysed four of these affective dimensions. The *depressive dimension* at baseline included symptoms of depressed mood, suicidal thoughts, feeling of guilt, obsessive and compulsive symptoms, and anxiety, and had a mean score of 3.92 (SD = 3.65). The *dysphoric* dimension at baseline included disruptiveaggressive behaviour, irritability, and lack of insight, and had a mean score of 8.55 (SD = 4.89). The manic dimension at baseline included appearance, sexual interest, elevated mood and reduced sleeping, and had a mean score of 5.27 (SD = 3.44). Finally, the *activation dimension* at baseline included speech difficult to understand, increased motor activity-energy and languagethought disorder, and had a mean score of 5.37 (SD = 4.78).

Clinical Characteristics at Follow-up

Of the 91 patients at third year: 80.2% had relapses, 61.5% hospitalizations and 19.8% suicide attempts during the follow up. Of the 82 at fifth year: 91.46% have relapses, 73.17% hospitalizations and 21% suicide attempts along the total follow-up period.

Outcome by GAF and Diagnostic Categories

The GAF discriminated among prognostic groups from the third year of the follow up (X2 11.725; p 0.020): the poorest prognosis in the schizophrenia group, while bipolar disorders and the rest of the diagnoses achieved an intermediate prognosis, with the bipolar disorder group as having a slightly better prognosis. <u>Figure 1.</u>

Outcome by Strauss-Carpenter and Diagnostic Categories

The Strauss-Carpenter scale, specifically working item (X2=10.551; p 0.032 / X2=8.661; p 0.013), social activity item (X2= 16.231; p 0.003 / X2=6.237; p 0.044) and global functioning item (X2=12.742; p 0.013 / X2=11.443; p 0.003) discriminated among three diagnostic groups and between affective and non-affective psychosis (X2=8.611; p 0.013 for hospitalization item; X2=6.237; p 0.044 for working activity item and X2=11.443; p 0.003 for social activity item) at fifth year. At work functioning: in schizophrenia, 53.6% have a bad prognosis, 28.6% intermediate prognosis and 17.9% a good one; in bipolar disorder. 41.2% bad prognosis, 5.9% intermediate and 52.9% good prognosis; for the rest of psychosis, 45% bad, 15% intermediate and 40% a good prognosis. At social functioning: in schizophrenia, 35.7% bad, 35.7% intermediate and 28.6% good prognosis; in bipolar disorder,

20.6% bad, 11.8% intermediate and 67.6% good prognosis; and for the rest of psychosis, 15% bad, 5% intermediate and 80% good prognosis. At global functioning: in schizophrenia, 42.9% have bad prognosis, 50% intermediate and 7.1% good prognosis; in bipolar disorder, 17.6% bad, 35.3% intermediate and 47.1% good prognosis; and finally, for the rest of psychosis, 25% bad, 45% intermediate and 30% good prognosis. Therefore, while schizophrenia scored the poorest outcome at work functioning, social activity and global functioning, bipolar disorder scored the highest. Figures 2, 3, 4

Diagnostic Predictive Value of Affective Dimensions

The predictive value of affective symptomatology was also determined by analysing the influence of dimensions on hospitalizations, relapses, suicidal behaviour, working activity, social activity and global functioning, using regression models.

With respect to the depressive dimension, we observed that it significantly associated with a lower number of relapses at fifth year and hospitalizations at 3-year (β coef -0,03, 95 % CI 0,94 0,99, p 0.045 and β coef -0,08, 95 % CI 0,87 0,98, p 0.012), meanwhile manic dimension was significantly associated with more relapses (Coef. \beta 0,04, 95 \% CI 1,01 1,08, p 0.023) at fifth year. Finally, activation dimension was significantly associated with the presence (OR 1,13; 95 % CI 1 1,27, p 0.050) and higher number of relapses (OR 1,10, 95 % CI 1 1,22, p 0,050) and with a more benign illness in terms of social activity in Strauss-Carpenter (Coef. β 0,03, 95% CI 1.01 1,06, p 0.016) at fifth year. However, dysphoric dimension was the unique dimension not significantly associated with any of the tested variables. Table 2.

Strauss-Carpenter	Prognosttic groups	Third	Fifth vear
	Good prognosis (punctuation: 4)	year 62,6 %	year 92,7 %
Hospitalization	Intermediate prognosis (punctuation:2 and 3)	36,3 %	4,9 %
	Bad prognosis (punctuation:0 and 1)	1,1 %	2,4 %
	Good prognosis (punctuation:4)	31,9 %	37,8 %
Work activity	Intermediate prognosis (punctuation:2 and 3)	36,3 %	15,9 %
	Bad prognosis (punctuation: 0 y 1)	31,9 %	46,3 %
	Good prognosis (punctuation: 4)	35,2 %	57,3 %
Social activity	Intermediate prognosis (punctuation: 2 and 3)	38,5 %	18,3 %
	Bad prognosis (punctuation:0 and 1)	26,4 %	24,4 %
	Good prognosis (punctuation:4)	16,5 %	29,3 %
Global functioning	Intermediate prognosis (punctuation:2 and 3)	62,6 %	42,7 %
	Bad prognosis (punctuation:0 and 1)	20,9 %	28 %

Table 1. Frequencies in % in respect to Strauss-Carpenter at third and fifth years by prognostic groups.



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44%	□ 43,80%
Bipolar disorder	r
^{6%}	□ 26,5%
	6%





Figure 2. Working activity prognosis by diagnostic groups, at 5th year.



Figure 3. Social activity prognosis by diagnostic groups, at 5th year.



Figure 4. Global functioning prognosis by diagnostic groups, at 5th year.

3. Materials and Methods

Study Design and Participants

This was a prospective, longitudinal study of 112 patients presenting with a first episode of psychosis between January 1996 and December 1997, and who were admitted to the only psychiatric inpatient unit in the Vitoria-Gasteiz region of Spain. First episode psychosis was defined as the first time a patient presented with psychotic symptomatology, consisting of the presence of one or more of the following symptoms: delusions, hallucinations, grossly disorganized behaviour and marked thought disorder.

Patients, aged 16-65 years, were included in the study if they met the diagnostic criteria of the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders³⁵ (DSM-IV) for schizophreniform disorder. schizoaffective disorder, schizophrenia, delusional disorder, brief psychotic disorder, atypical psychosis or psychotic disorder not otherwise specified, bipolar I or II disorder, or major depressive disorder with psychotic symptoms (American Psychiatric Association, 1994). The DSM-IV axis I diagnosis was made using the Structured Clinical Interview for DSM-IV³⁶ (SCID-I) (Spitzer et al., 1996); the same interviewers for baseline and follow-up assessments. Subjects with mental retardation, organic brain disorders and substance-induced psychotic disorders as their main diagnosis were excluded from the study.

The study was approved by the ethics committee of the hospital and all participants provided informed consent.

Assessments

Assessments were made at baseline and at 3 and 5 years of follow-up. The baseline assessment was performed within 24 hours of hospitalization for the first psychotic episode and reflected the patient's clinical status during the previous week. After hospital discharge, subjects attended their corresponding mental health care centre.

collected included Data patient sociodemographics and clinical characteristics. Patients were assessed by different raters from those who assessed the diagnosis, using the following scales: Young Mania Rating Scale (YMRS) (Young et al., 1978)³⁷, Hamilton Depression Rating Scale (HDRS-21) (Hamilton, 1960) ^{38,39}, Global Assessment of Functioning (GAF) (American Psychiatric Association, 1987) ⁴⁰. Phillips Rating Scale of Premorbid Adjustment in Schizophrenia (Phillips) (Phillips, 1953)⁴¹, Strauss-Carpenter Scale (Strauss and Carpenter, 1972)⁴² and the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1986) ⁴³. Additional information provided by family informants and from staff observations was incorporated into the rating process. All interviews were carried out independently by one psychiatrist and one psychologist who demonstrated good inter-rater reliability for SCID diagnoses ($\kappa = 0.88$), YMRS ($\kappa = 0.90$), HDRS-21 ($\kappa = 0.93$), GAF ($\kappa = 0.94$), Phillips (κ = 0.80), Strauss-Carpenter (κ = 0.81) and PANSS $(\kappa = 0.82).$

The affective dimensions used in the present study were based on a previous factor structure analysis using the YMRS and HDRS-21 in 103 patients with bipolar disorder^{9.} This gave a fivefactor solution and the component symptom loadings obtained for each of the affective dimensions (depressive, dysphoric, manic, psychosis and activation) is summarised in a previous work (González-Pinto et al., 2003) ⁹. Factor structure analysis has been widely used for research purposes and in clinical trials for studying the symptom dimensions of psychosis ^{4,11,14, 16-19, 34, 44}. In the present study, we analysed four affective dimensions (depressive, dysphoric, manic and activation; baseline scores); the psychosis factor was not used because all patients presented with psychosis symptoms.

The patient sample was classified both into three diagnostics groups: (1) those with schizophrenia diagnosed; (2) those with bipolar disorder diagnosed; and (3) those with other psychosis, and into two diagnostic groups: affective psychosis (bipolar disorder, depressive disorder) and non-affective psychosis (the rest of the psychosis).

In respect to the GAF Scale, the followings groups were considered to describe outcome among diagnostic categories (schizophrenia, bipolar disorder and the rest of the psychosis): good prognostic for the punctuation \geq 71, intermediate prognostic for 51-70 and bad prognostic for \leq 50.

Likewise, for the Strauss-Carpenter Prognostic Scale, a good prognostic group when 4 punctuation was scored in all the items evaluated, an intermediate prognostic group for 2 and 3, and finally a bad prognostic group for 1 and 0.

Statistical Analysis

Statistical packages used for the analyses were SAS, SPSS and R 2.5.1.

Baseline characteristics of the total study sample were described using summary statistics (means and standard deviations (SD) or median and range, as appropriate, for continuous variables, and frequencies for categorical variables). Statistical comparisons between groups were performed using the χ^2 test (or Fisher's test where $n \le 5$) for categorical variables and the Student's *t* test or Mann-Whitney *U* test (depending on the distribution of the sample) for continuous variables.

The prognostic value of affective dimensions was examined using regression models, with number of hospitalizations, relapses, suicidal behaviour, working level, social activity and global functioning as the dependent variable. A logistic regression model including all four affective dimensions as independent variables was used to identify which dimensions were predictive of the evolution of first-admitted psychotic patients. Logistic regressions were adjusted by age and gender, negative symptoms (PANSS-N) and premorbid state (Phillips Rating Scale of Premorbid Adjustment) according to the method used by other researchers since it is known these variables influence the outcome. Effect sizes are expressed as odds ratios (ORs) and 95% confidence intervals (CIs) with P Poisson regressions effect sizes are values. expressed as β coefficient, 95% confidence intervals (CIs) with P values. Associations were considered significant when $P \leq .05$.

We established three cut-points for GAF for statistical purposes: 70, which, in our opinion, divided the sample in two groups, related to a complete recovering or not; 60 ^{25,34,45}; and finally, 50, following criterions of other researchers ²⁶.

In the case of the Strauss-Carpenter scale, the cut-points were the followings: 4 vs the rest of the values for the hospitalization item ^{25,46,47}, working activity item ^{48,49}and the global functioning item²⁵; we considered 0 and 1 vs the rest of the values for the social activity item, considering that this cut-point divided patients in two completely different groups ⁴⁹.

4. Discussion

This prospective, longitudinal study of the predictive diagnostic value of affective symptomatology in a sample of hospitalized first-episode psychosis patients followed-up over 5 years shows that affective dimensions (manic, activation, dysphoric and depressive) have different kind of influence in the prognostic of psychosis.

Regarding number of relapses, our percentage is high, 80.2%-91.46%. While Robinson et al.⁵¹ also found a high percentage of relapse (86.2% at fifth year), most authors ^{27,30,52-54} find 58-78%. Diverse definitions of the "relapse term" may be considered; besides, our patients are hospitalized and their severity is higher. In our study, manic and activation dimensions are associated with higher number of relapses, while depressive dimension protects against them.

In respect to the number of hospitalizations, while 61.5% of the total samples were hospitalized sometime in the first three years, 73.17% were hospitalized at the end of the following period; Power et al.³³ confirmed this percentage. Means of both periods are similar and identical to Sipos et al.³⁴. Some authors find higher number. This point depends on a variety of factors: organization of both intra and extra mental services and accessibility. In our study, depressive dimension protects against hospitalizations.

With regard to the number of suicides, 19.8% at third year and 21% at fifth year, our percentages are identical to Birchwood et al.³⁰, van Os et al.¹⁷, Verdoux et al.⁵⁵ and Robinson et al.⁵¹, and the mean is similar in both periods. Two patients committed suicide in the last two years (2.4%); unfortunately, not for being the first years of the illness, suicide risk is disminished ³⁰.

Additionally, and with respect to the outcome assessed by the Strauss-Carpenter Prognostic Scale: this scale discriminates among the threediagnostic groups, schizophrenia, bipolar disorder and other psychotic disorders, for working and social activity at third and fifth year and for global functioning at fifth year; also discriminates among affective and non-affective psychosis. Prognosis gets better within time of evolution. While schizophrenia scored the poorest outcome at work functioning, social activity and global functioning, bipolar disorder scored the highest.

Furthermore, the GAF discriminates among prognostic groups from the third year of the follow-up: while the schizophrenia has the poorer prognosis ²⁶, the bipolar disorder has the best ²⁴⁻²⁵; the rest of the psychosis have an intermediate prognosis in the outcome. Considering the three diagnostic groups, the majority of the patients are in the group of intermediate prognosis.

In summary, prognosis improved along time of evolution. Although the percentage of relapses is high in our sample, many patients maintained a good level of functioning. Tohen et al.²⁴ and Swaran et al.²⁵ pointed out the importance of both sindromic and functional outcome, separatedly.

Additionally, and concerning the prognostic value of affective dimensions, the depressive dimension is significantly associated with fewer relapses and hospitalization at fifth and third years respectively; therefore, it conferres a good prognosis. Many authors confirm a better outcome ^{14,19,25-27,56} in the presence of depressive symptomatology. Lindenmayer and Kay ⁵⁷ nevertheless, question themselves about the influence of negative symptoms in that result. We obviously took this problem into account, since our statistical analyses were adjusted by

baseline negative symptomatology. Also Peralta et al.⁵⁸ found that depressive dimension was associated to negative factors. So, we used assessment tools which are specifically designed for rating affective rather than negative symptomatology. There are also both authors who do not find an association between depressive dimension and outcome^{17,32,47,53,59} and some who describe a worse course ^{10,29,31,60}.

manic The dimension is significantly associated with a higher number of relapses at the end of the follow-up period. The activation dimension is also associated with the presence of relapse at the third year and a higher number of relapses at the fifth year. It is also significantly associated with better social functioning. Therefore, the activation dimension is related to the outcome in two ways: better social adjustment, but increased relapse risk. Consequently, both manic and activation dimensions are related to a poorer symptomatic outcome; activation dimension, nevertheless, confers a good functional prognostic. Tohen et al.²⁴ agree with this afirmation.

Sipos et al.³⁴ and Gift et al.⁵⁹ also find a major risk for hospitalization and Erickson et al.²² and Allardyce et al.⁶¹ confirmed the better social outcome for manic dimension. On the contrary, Murray et al.¹⁴, McIntosh et al.¹⁹ and van Os et al.¹⁷ described a better symptomatic outcome.

Besides, manic dimension was associated with the absence of suicide attempts as a tendency. In the opinion of the majority of the researchers the depressive dimension is the one which is associated with poorer outcome regarding this subject ^{14,62,63}.

The activation dimension was also nearly significantly associated with a better work level at the third year, which agrees with Allardyce et al.⁶¹.

Finally, the dysphoric dimension was not associated with any of the variables described above and it do not discriminate among all groups.

The fact that these results have been adjusted by negative symptomatology and premorbid adjustment make the results consistent.

In summary, only one of the dimensions is not associated with syndromic and/or functional dysphoric dimension. prognosis, the The depressive dimension presents the best prognosis. On the contrary, the activation dimension, in general, gives a more favourable prognosis with regards to functionality (social) and unfavourable with respect to relapses. Finally, the manic dimension is associated with a worse evolution regarding relapses.

Our results suggest that the affective symptomatology gives a determined prognosis to the evolution of the psychotic illness. Therefore, the systematic evaluation of affectivity will permit us to reach important conclusions regarding the prognosis. The intervention on the patients with manic and activation syndrome could be beneficial in decreasing relapses in the first episodes.

It is of maximum interest to point out that our original contribution is the using of affective dimensions obtained from a bipolar disorder sample and their application to a sample with functional psychosis.

We also would like to mark the representativeness of the sample as our unit is the unique one for acute inpatients in our region. Besides, our study is longitudinal and includes an heterogeneous sample. It also includes a large time of follow-up.

Nevertheless, some limitations must be considered. First, a number of patients were taking medication; we tried to overcome this limitation assessing them within 24-48 hours of hospitalization. Secondly, patients with more severe conditions are probably overrepresented; thus, the results generalization is limited to patients who are hospitalized. Nevertheless, more than 80% of first psychotic episodes are hospitalized. Also, a few of the assessments had been done by telephone when coming was not possible for them. Finally, the main limitation is that we have not adjusted results by drugs; cannabis use is frequent in this kind of patients and we know its influence in psychotic episodes. Therefore, we will choose this issue for future studies. It have not been possible to introduce one more variable for statistical reasons; we adjusted by age, sex, negative symptomatology and premorbid adjustment following the method of most of the authors.

Despite these limitations, definitively our results suggest that affective symptomatology confers a certain prognosis to the course of the illness, so that systematic evaluation of affectivity will make possible conclusions to be obtained in regard to prognosis. Also, intervention in patients with manic and activation syndrome could be benefitial to disminish relapses in first psychotic episodes. The fact that these results were obtained after controlling the analyses by the presence of negative symptoms and premorbid adjustment and, therefore, basal functionality, makes the data be consistent.

Of course, the evolutions of determined variables do not have any reason to reflect the general evolution as was clarified through an evolution study by the World Health Organization ⁶⁴; the variables that determine the global evolution are different and varied. This affirmation is in harmony with that mentioned previously with respect to the need to differentiate between the syndromic and functional recovery. One must take into account that this differentiation has its value when proposing the prevention and improving the prognosis of the patients with real possibilities of recovery.

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