One-year functional outcomes of naturalistically treated patients with schizophrenia

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ABSTRACT

Against the background of the growing evidence that the patient's functioning significantly influences the course and outcome of schizophrenia, the aims of this analysis were to examine what proportion of patients achieve functional outcome criteria after 1 year, and to identify clinical and sociodemographic predictive factors for functional remission. Patients with the diagnosis of schizophrenia who were treated as inpatients at the beginning of the study were examined within a naturalistic follow-up trial. The present study reports on the time frame from admission to discharge of an inpatient treatment period and the 1-year follow-up assessment. The Global Assessment of Functioning (GAF) Scale and Social and Occupational Functioning Assessment Scale (SOFAS) were evaluated with respect to functional outcome, whereas Positive and Negative Syndrome Scale (PANSS) scores were rated as psychopathological outcome measures. Functional remission thresholds were defined according to a GAF score of ≥61 points and a SOFAS score ≥61 points. Symptomatic remission criteria were applied according to the remission criteria of the Schizophrenia Working Group. The Strauss–Carpenter Prognostic Scale (SCPS), the Phillips Premorbid Adjustment Scale, medical history, sociodemographic and psychopathologic parameters were evaluated in order to find valuable predictors for functional remission. One year after discharge from inpatient treatment, 211 out of 474 patients were available for analysis according to both rating scales used to assess functional remission (GAF and SOFAS). Forty-seven percent of patients fulfilled criteria for functional remission (GAF and SOFAS) at discharge and 51% of patients at the 1-year follow-up visit. With regard to symptomatic remission criteria, the corresponding remitter rates were 61% of patients at discharge and 54% at the 1-year follow-up visit. Forty-two percent of patients fulfilled both remission criteria at discharge and 37% at the 1-year follow-up visit. A significant association was found between functional and symptomatic remission at discharge and at the 1-year follow-up visit. The strongest predictors for functional remission at the 1-year follow-up visit were: a higher SCPS total score at admission, a lower number of previous hospitalizations, a status of employment, lower scores in all PANSS subscales at discharge, a better premorbid social adjustment, the occurrence of a first psychotic episode, a younger age, a lower PANSS negative subscore at admission, a status of being an early responder, a shorter duration of inpatient treatment, a later age of onset, and female gender.

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1. Introduction

Traditionally, treatment conceptions in schizophrenia have emphasized the reduction of psychotic symptoms. At least since the development of second-generation antipsychotics (SGAs), however, the targets of therapeutic efforts have been extended. Additional positive effects of SGAs on depressive or cognitive symptoms contribute to improvements in quality of life or in social and occupational functioning of patients. Recently, symptomatic remission criteria have been proposed by the Remission in Schizophrenia Working Group concurrently acknowledging that their definition for remission requires further examination of its validity and utility, as well as future refinement, particularly in relation to psychosocial functioning and cognitive dysfunctions (Andreasen et al., 2005). The importance of functional outcome parameters in patients with schizophrenia was acknowledged in 1980 with its formal inclusion as one of the five axes of patient clinical status in the Diagnostic and Statistical Manual of Mental Disorders, Third Edition (DSM-III) classification system (American Psychiatric Association, 1987), which was retained in the subsequent DSM-IV (American Psychiatric Association, 2000). Impairments in patient functioning can lead to decreased medication adherence, increased risk of hospitalization, and diminished ability to either engage in relationships or to maintain employment, which can further impact the disease progression (Leucht and Heres, 2006; Lieberman et al., 2006; Leifker et al., 2009).

Furthermore, schizophrenia is associated with considerable economic burden due to the loss in productivity as well as the costs of

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treatment, hospitalization and rehabilitation. Regarding prognostic factors of functional outcome, the neurocognitive performance of patients with schizophrenia is closely correlated with several key outcome domains such as the development of new social skills and the ability to function independently in the community (Kirkpatrick et al., 2006; Murphy et al., 2006). Additionally, patients with more pronounced negative symptoms, especially in the early course of the disease, have been shown to exhibit worse long-term social and occupational functioning (Ventura et al., 2009; Shamsi et al., 2010). In a large 3-year follow up study of schizophrenic patients Haro et al. observed that those with a better social functioning (living independently, in paid employment, socially active or having a partner) at baseline and a shorter duration of illness had a more favorable functional outcome (Haro et al., 2008). Other significant predictors for functional outcome described in the literature were medication adherence (Ascher-Svanum et al., 2006; Bachmann et al., 2008) and premorbid adjustment measured by the Premorbid Adjustment Scale (Harrigan et al., 2003). The duration of untreated psychosis (DUP) was consistently described as a strong predictor of symptomatic as well as functional outcome (Bottlender et al., 2003; Harrigan et al., 2003; Harris et al., 2005; Boden et al., 2009). Recent data have demonstrated that the most substantial change in psychiatric symptoms occurs early during the course of treatment with antipsychotic drugs (Agid et al., 2003, 2006; Leucht et al., 2005; Lipkovich et al., 2009) and that even changes within the first 2 weeks of treatment might hold predictive value for subsequent outcomes incorporating both symptomatic and functional domains (Correll et al., 2003; Kinon et al., 2010). There is a broad consensus that symptomatic treatment response is a necessary condition for improvement in functional outcome. This is underlined by study results showing that the fulfillment of the symptomatic remission criterion seems to be a strong predictor of a sustained functional remission (Helldin et al., 2007; Boden et al., 2009). However, e.g. Karow et al. assessed symptoms, functional outcome as well as subjective well-being in 131 patients with schizophrenia and found that symptomatically remitted patients still showed areas of low functioning comprising mainly social relations, work and daily life activities (Karow et al., 2011). These results indicate that symptomatic and functional dimensions are somehow distinguishable concepts and that there is a need to define outcome domains beyond symptomatic improvement (Lambert et al., 2010). Despite its rising attention in the literature and obvious implications for research and clinical practice, the development of remission criteria for functional in comparison to symptomatic disability remains somewhat more challenging. Apart from studies which applied a more complex rating approach (Helldin et al., 2007; Harvey and Bellack, 2009; Novick et al., 2009; Bottlender et al., 2010) in most studies functional outcome was defined according to scales based on the DSM-IV with a more general scope (Harrison et al., 2001; Whitehorn et al., 2002; Bachmann et al., 2008; Menezes et al., 2009). An example is the Global Assessment of Functioning (GAF) Scale, which was introduced as a measure of global severity of illness in the Diagnostic and Statistical Manual of Mental Disorders version III-R first published in 1987 (American Psychiatric Association, 1987). Another widely used assessment tool for functional dimensions in schizophrenia is the Social and Occupational Functioning Assessment Scale (SOFAS). It differs from the Global Assessment of Functioning (GAF) Scale due to the fact that it focuses exclusively on the individual's level of social and occupational functioning in specific domains and is not directly influenced by the overall severity of the individual's clinical symptoms (American Psychiatric Association, 1987). In the present study we applied a combined threshold of both the GAF and SOFAS scales to clearly provide a useful global measure covering functional outcome. The aim was to examine what proportion of patients achieve functional and concurrently symptomatic outcome criteria and to identify psychopathological and sociodemographic predictive factors for functional remission.

2. Methods

2.1. Subjects

Within a multicenter follow-up program (German Research Network on Schizophrenia) at 11 psychiatric university hospitals and three psychiatric district hospitals all patients admitted between January 2001 and December 2004 suffering from schizophrenia (paranoid, disorganized, catatonic or undifferentiated subtype), schizophreniform or schizoaffective disorder according to DSM-IV criteria were included according to in- and exclusion criteria. To prevent centrum effects and other potential factors of interference, the patients included in statistical analyses were randomly selected via computer software. Patients were aged between 18 and 65 years. A clinical diagnosis of head injury in the history, major medical illness and alcohol or drug dependency were defined as exclusion criteria. An informed written consent had to be provided prior to inclusion. The study was approved by the local ethics committees and followed the declaration of Helsinki.

2.2. Assessments

DSM-IV diagnoses were assessed by clinical researchers on the basis of the German version of the Structured Clinical Interview for DSM-IV (American Psychiatric Association, 1994). During interviews with patients, relatives and care providers' sociodemographic and course-related variables were collected using a standardized documentation system (BADO) (Cording, 1998).

Symptom severity was assessed biweekly with the Positive and Negative Syndrome Scale for Schizophrenia (PANSS) (Kay et al., 1988) from baseline to discharge and again at the one year follow-up time-point.

The following instruments were applied at admission, discharge and at the one year follow-up time-point on the patient's current level.

The Global Assessment of Functioning Scale (GAF) (American Psychiatric Association, 1994), which comprises the axis V of the DSM-IV. This scale was introduced as a measure of global severity of illness including the patient's psychological, social and occupational functioning. The furthermore applied SOFAS, developed by the American Psychiatric Association for the DSM-IV to operationalize functioning, improved on the GAF by incorporating the impact of psychological and general medical symptoms on patient functioning (American Psychiatric Association, 1987). The validity and reliability of these scales were verified (Patterson and Lee, 1995; Roy-Byrne et al., 1996). Sociodemographic variables (partnership, employment state) and course-related variables like age of onset, age of first hospitalization, duration of illness, number of previous hospitalizations, duration of hospitalization and episodes of illness or presence of preceding stressors were recorded using the standardized documentation system BADO (Cording, 1998). Other potential prognostic factors were assessed with the 21-item version of the Strauss–Carpenter Prognostic Scale (Kokes et al., 1977) at admission. This scale is an observer rating scale which comprises several areas of functioning, e.g. employment state, social class, family history of psychiatric hospitalization, age of onset and psychopathological symptoms. It represents a multidimensional attempt to predict long-term outcome which is well-documented in previous studies (Möller et al., 1986; Handel et al., 1996). Premorbid social adjustment was rated according to the second factor of the abbreviated version of the Phillips Scale (Harris, 1975). All assessments were performed by well experienced psychiatrists. Psychopathological and functional interactive video based rater-training sessions were regularly performed throughout the study period in every participating hospital to establish and maintain a high interrater reliability (ANOVA-ICC > 0.8).

Concerning functional remission thresholds traditional definitions from the literature were followed; a GAF score of ≥61 points and a SOFAS score ≥61 points (Harrison et al., 2001; Bachmann et al., 2008; Menezes et al., 2009). Symptomatic remission criteria were applied according to Andreasen et al. (2005). These criteria comprise a PANSS rating of ≤3 of the following items: delusions (P1), unusual thought contents (G9), hallucinatory behavior (P3), conceptual disorganization (P2), mannerism/posturing (G5), blunted affect (N1), social withdrawal (N4) and lack of spontaneity (N6) for a time period of six months (Andreasen et al., 2005). Complete remission is defined as a combined fulfillment of symptomatic and functional remission criteria. Early response was defined as ≥20% improvement in PANSS total scores within the first two weeks of inpatient treatment.

2.3. Statistical analysis

For group differences the Wilcoxon and t-tests as well as the Fisher's exact test were applied. Two different methods were used to select the most important predictors for remission: 1. univariate tests 2. logistic regression model and 3. CART (classification and regression trees) analysis. Starting with the univariate tests including clinical and sociodemographic variables [duration of inpatient-treatment, study discontinuation rate, number of previous hospitalizations, duration of illness, duration of current episode, living situation, education, employment status] a backward–forward method based on the Akaike information criterion (AIC) was used to identify the relevant baseline predictors. The final model computed only these predictors. The discriminative ability of the regression model was evaluated using a receiver-operating characteristic (ROC) curve. The area under the curve (AUC) was calculated, which is a measure of the overall discriminative power. A value of 0.7–0.8 is considered reasonable