An up to 12-year follow-up of mortality-adjusted diagnostic stability of psychotic depression, schizoaffective disorder and psychosis NOS

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Abstract

Change in the diagnosis is not uncommon among patients suffering from severe psychiatric disorders. Psychotic depression has shown an intermediate stability, whereas the results are conflicting concerning schizoaffective disorder. To have clinically useful predictive power a diagnostic description should have satisfactory stability. This follow-up study of psychiatric inpatients treated in Satakunta hospital district aimed to describe the stability of diagnosis in psychotic depression, schizoaffective disorder, depressive subtype and psychosis NOS, and to study factors associated with a change in diagnosis. Out of the 181 subjects in the study, 119 (65.7%) had a readmission during a minimum follow-up of eight years. The adjusted incidence of change in diagnosis in psychotic depression was 4.56-fold compared to schizoaffective disorder ($p<0.001$). Most patients (88.0%) with schizoaffective disorder retained their diagnosis, while more than two-thirds (68.7%) of those with psychotic depression had remained, although not psychotic, within the group of major depressive disorders. A non-affective schizophrenia group psychosis was the most common eventual diagnosis among the patients with a change in diagnosis.

Introduction

When evaluating the validity of a diagnostic category, the stability of diagnosis during the course of illness is one relevant phenomenon to observe. The degree diagnoses are retained from one assessment to another may depend on several factors concerning: 1. the diagnostic process, 2. the differential presentation of symptoms throughout the course of illness and 3. the reliability and validity of diagnostic

categories. The diagnosis can be based on insufficient or unreliable information and the symptoms may fluctuate or be modified by effects of treatment or other disorders (1). For descriptive diagnoses to be valid and reliable in clinical settings the stability of these diagnoses is an important issue. One must also remember that, especially in naturalistic settings, the stability of diagnosis is influenced by the amount of contacts with healthcare providers (2).

Significant variation has been found in the stability of different diagnostic categories of first-episode psychosis patients. In several studies schizophrenia has shown a high level of stability (1,3-10) and affective psychoses, including psychotic depression, an intermediate stability (1,4-5,9,11-13). As one might expect, undefined psychosis has appeared as a very unstable diagnosis (1). Previously, there have been inconsistent findings regarding the stability of schizoaffective disorder, with some studies showing high stability rates (1,8,14) and others relatively low ones (5,9,11). Furthermore, the existence of schizoaffective disorder has been called into question due to lack of any boundary with schizophrenia (15).

It has been suggested that psychotic depression should be viewed only as a provisional diagnosis, questioning the validity of psychotic depression as a diagnostic entity (12). One factor probably affecting the diagnostic trajectory of psychotic depression is age at illness onset. Young age may predict shift to bipolar disorder (16). At an old age, vascular depression and Alzheimer's disease could manifest first with a clinical picture of psychotic depression. Additionally, psychotic depression has been associated with increased mortality (17) and the diagnosis seems to be more stable in those patients with medical comorbidity (13). Therefore, the possible confounding influence of potentially discriminating mortality on the rates of change in diagnosis must be considered.

The follow-up periods have varied dramatically between different studies ranging from less than 2 years to above 25 years, which may partly explain dissimilarities in the results. Likewise, number of hospitalizations may influence change of diagnosis. If no readmissions take place due to death or other reasons, no change can be found. High number of hospitalizations may also decrease inter-rater reliability if clinicians of varying skills and experience assess the patient during the course of illness (2). The diagnostician may have problems interpreting or detecting valid information. In the early phases of schizophrenia, affective disorders are common (18). First-episodes of psychoses may present with affective symptoms that are no longer present during subsequent episodes, resulting in a clinical diagnosis of schizophrenia.

The aim of the present study was to: 1. describe the stability of diagnosis in psychotic depression, schizoaffective disorder and undefined psychosis, 2. to investigate the effects of number of readmissions and mortality as confounds to change in diagnosis and 3. to study factors predicting a change in the diagnosis. The Ethics Committee of the Hospital District of Satakunta approved the study. The national registers require special authorization for the right to use their data. The permissions were applied for and granted before retrieving the register data.

Subjects and methods

Study design

All the cases with the diagnoses (diagnosis codes: F32.3, F33.3x, F25.1x, F29) in the focus of this study were extracted from the local hospital register. Only the patients with a first ever inpatient treatment episode between 1996 and 2000 in Satakunta hospital district were included in the study. Patient records of the study subjects were reviewed, completed in 2011, and data on gender, age, educational level, marital status and diagnoses were collected. A review of DSM-IV-TR symptoms of major depression and psychosis described in the patient records (entered by residents/psychiatrists and nurses) was made to study the distribution of specific symptoms in the diagnostic groups under study.

Diagnoses of schizoaffective and psychotic depression were chosen, because: 1. these diagnoses could be easily confused, 2. they would be suitable for comparison regarding diagnostic stability, and that 3. if a change in diagnosis would be evident, there might be a drift towards less affective symptoms, i.e. schizophrenia. Diagnosis of undefined psychosis implies either a diffuse clinical picture or not having enough information for an accurate diagnosis. It was used as a marker of possible instability of a diagnostic category.

Data from national registers (hospital discharge register including all hospitalization due to all illnesses and causes of death) were collected from 1995 and followed until 31.12. 2008. For the follow-up, we collected the date and cause of any hospitalization for all participants who were treated in a hospital between January 1,

1995 and December 31, 2008. The baseline for hospital register data was 1.1. 1995 to find out if there had been recent inpatient episodes elsewhere than in Satakunta hospital district. None were found. The Hospital Discharge Register (HDR) collects information on all episodes of inpatient care in hospitals (since 1969). The register contains information on the patient's background, hospitalization period, procedures, and the main diagnosis and up to two other diagnoses by ICD code (ICD-9 in 1987 through 1995 and ICD-10 in 1996 through 2007). All hospitals send their data electronically to the National Institute for Health and Welfare in charge of HDR. A 1986 data quality study reported that 99% of hospitalizations relating to mental disorders were registered under the correct ICD chapter and 98% of the main diagnoses had been correctly reported at the three-digit ICD code level (19). The causes of death were obtained from the death certificates issued by the physicians and annually collected by Statistics Finland (20). In the case of suicide, the certificate is based on a forensic autopsy. The data filed in Statistics Finland also comprise information on sex, age, and region where the deceased lived, as well as various other demographic data. The initial diagnoses of the patients came from a local register and follow-up diagnoses from the national register.

Statistical analysis

Cross tables were used to analyse differences in background variables between men and women, between readmitted and non-readmitted patients, and between patients whose diagnoses had changed and those who had no change. Mean values were counted using ANOVA or Kruskal-Wallis test. Poisson regression analysis was used to calculate differences between the diagnostic groups in: 1. incidence of readmissions and 2. incidence of change, i.e. the number times a change in the diagnosis was made, in the diagnosis adjusting for the duration of follow-up, gender, number of readmissions, initial diagnosis, psychiatric symptoms, comorbidity and mortality during the follow-up starting from 1.1. 1995. Data was coded binomial (0 vs. 1).

Results

Sample characteristics

Altogether, the sample included 181 subjects, 70 men (38.7%) and 111 women (61.3%). The mean age at time of first admission was 58.8 years (SD=18.0). The mean age of patients with schizoaffective disorder was 49.8 (SD=5.97), with psychotic depression 60.1 (SD=3.52) and psychosis NOS 36.5 (SD=6.98) ($p<0.001$, Kruskal-Wallis). Out of the whole sample, at baseline 17.1% (N=31) had a diagnosis of schizoaffective disorder, 23.8% (N=43) a diagnosis of psychosis NOS and 59.1 % (N=107) a diagnosis of psychotic depression. The clinician had diagnosed a comorbid condition in 16.6 % (N=30) of the cases. Mean number of depressive symptoms was 4.7 (SD=4.7) in schizoaffective disorder, 7.2 (SD=1.5) in psychotic depression and 5.5 (SD=2.3) in psychosis NOS ($p<0.001$, Kruskal-Wallis). Mean number of psychotic symptoms was 6.0 (SD=3.1) in schizoaffective, 3.5 (SD=3.0) in psychotic depression and 7.0 (SD=3.1) in psychosis NOS ($p<0.001$, Kruskal-Wallis). Those with psychotic depression were significantly more commonly widowed (40.2 % vs. 9.3-16.7%, $p<0.001$). Patients with either psychotic depression or schizoaffective disorder were significantly more commonly on pension or disability pension (63.6% and 51.6%, respectively) than patients with psychosis NOS (14.0%) ($p<0.001$) (Table 1).

Hospitalization and mortality

About two-thirds of the patients (N=119) had at least two treatment episodes. Patients with schizoaffective disorder had an average of 4.03, psychotic depression an average of 3.3 and psychosis NOS an average of 2.86 hospitalizations ($p=0.18$). None of the background factors, initial diagnoses or symptoms described in the patients' records predicted the risk of readmission. There were no statistically significant differences in the adjusted incidence of readmissions between patients with schizoaffective disorder and psychotic depression, but patients with schizoaffective disorder and psychotic depression had a significantly higher incidence of readmissions than those with a psychosis NOS (1.92-fold and 1.66-fold respectively, $p<0.001$, Table 2).

During the follow-up, altogether 75 cases (42.0%) had died and 34.7% (N=26) of the deceased had never been readmitted. Among the deceased patients 72% (N=54) had an initial diagnosis of psychotic depression, 20% (N=15) a schizoaffective disorder and

8% (N=6) psychosis NOS diagnosis ($p<0.001$). Cardiovascular diseases (CVD) were the most common cause of death and accounted for 48.0% (N=36) of the mortality, but there were no statistically significant differences in mortality due to CVD between the diagnostic categories.

Changes in diagnoses

A change in the diagnosis of a patient from the first episode to the last during 8 to 12 years of follow-up was observed in 34 (28.6%) out of 119 readmitted subjects. Men had significantly more commonly had a change in their diagnosis (40.9%) compared to women (21.3%) ($p<0.05$). There were no statistically significant differences in mean age of patients, between groups of employment, groups of educational attainment, marital status, or groups of depressive and psychotic symptoms regarding a change in diagnosis. Those with a change in diagnosis had on average more hospitalization episodes compared to those with no change (5.5 vs. 4.2, $p<0.05$).

The adjusted incidence of change in diagnosis in psychotic depression was 4.56-fold compared to schizoaffective disorder ($p<0.001$, Table 3). A multivariate analysis of factors predicting a change in diagnosis did not indicate any statistically significant predictors. Patients with schizoaffective disorder had mostly retained their diagnosis (88.0%, N=22), while in psychotic depression the stability was lower, because about two-thirds had retained a diagnosis of the major depressive group (68.7 %, N=46). Only one case with psychosis NOS had retained the diagnosis and the rest of the cases were either not readmitted (N=16) or had switched to a different category (N=26). The most common eventual diagnosis in psychosis NOS was schizophrenia (N=11, 40.7%), and in psychotic depression a schizophrenia group diagnosis other than schizoaffective disorder (N=9, 13.4%). In schizoaffective disorder, two patients ended up with a major mood disorder and one with schizophrenia diagnosis. As for other cases (N=12) with a change in diagnosis, their eventual diagnoses were too heterogeneous to categorize.

Table 1. Background factors and first-episode diagnoses.

	Schizo-affective disorder	Psychotic depression	Psychosis NOS	Total	Chi-square p-values
Female	18 (16.2%)	69 (62.2%)	24 (21.6%)	111 (61.3%)	
Male	13 (18.6%)	38 (54.3%)	19 (27.1%)	70 (38.7%)	
Total	31 (33.7%)	107 (59.1%)	43 (23.8%)	181 (100%)	0.565
Age group					
55 < years	21 (67.7%)	36 (33.6%)	38 (88.4%)	95 (52.5%)	
> 55 years	10 (32.3%)	71 (66.4%)	5 (11.6%)	86 (47.5%)	
Total	31 (100%)	107 (100%)	43 (100%)	181 (100%)	<0.001
Employment status					
Employed	10 (32.3%)	23 (21.5%)	16 (37.2%)	49 (27.1%)	
Unemployed	5 (16.1%)	16 (15.0%)	21 (48.8%)	42 (23.2%)	
Disability pension/ Pension	16 (51.6%)	68 (63.6%)	6 (14.0%)	90 (49.7%)	
Total	31 (100%)	107 (100%)	43 (100%)	181 (100%)	<0.001
Marital Status					
No relationship	14 (46.7%)	23 (21.5%)	24 (55.8%)	61 (33.9%)	
Married/ common law marriage	11 (36.7%)	41 (38.3%)	15 (34.9%)	67 (37.2%)	
Widowed/divorced	5 (16.7%)	43 (40.2%)	4 (9.3%)	52 (28.8%)	
Total	30 (100%)	107 (100%)	43 (100%)	180 (100%)	<0.001
Educational attainment					
Basic level	13 (41.9%)	54 (50.9%)	19 (44.2%)	86 (47.8%)	
Vocational education	16 (51.6%)	47 (44.3%)	21 (48.8%)	84 (46.7%)	
College/University	2 (6.5%)	5 (4.7%)	3 (7.0%)	10 (5.5%)	
Total	31 (100%)	106 (100%)	43 (100%)	180 (100%)	0.874
Total	31 (100%)	107 (100%)	43 (100%)		

Table 2. Incidence of readmissions.			
Category comparison	**RR for incidence**	**95% CI**	**p-value**
Schizoaffective disorder vs. Psychosis NOS	1.92	1.46 - 2.52	<0.001
Psychotic depression vs. Schizoaffective disorder	1.15	0.90 - 1.50	0.268
Psychotic depression vs. Psychosis NOS	1.66	1.27 - 2.17	<0.001

Table 3. Incidence of change in diagnosis.			
Category comparison	**RR for incidence**	**95% CI**	**p-value**
Schizoaffective disorder vs. Psychosis NOS	2.74	1.11 - 6.58	0.024
Psychotic depression vs. Schizoaffective disorder	4.55	1.86 - 11.12	<0.001
Psychotic depression vs. Psychosis NOS	0.60	0.32 - 1.03	0.063

Discussion

Overview

In this study, we found a higher incidence of change in diagnosis among patients with psychotic depression compared to those with schizoaffective disorder. The patients with psychotic depression were older than patients with other diagnoses and had a higher mortality rate. We also found that the patients who had a change in diagnosis were hospitalized more often, but the readmission rate was not statistically different between psychotic depression and schizoaffective disorder. Background factors, including age at first admission, were not found to predict a change in diagnosis. However, between the index episode and the last hospital episode, men seemed to have a change in diagnosis more often. The distribution of symptoms within the diagnostic groups was in line with expectations giving some support to the validity of conclusions on the diagnosis.

Previous studies

The number of hospitalizations has been observed to associate with diagnostic instability (2), though not in all studies (4). In our study, there were more readmissions in the group of patients whose diagnosis had changed, but the number of readmissions did not predict the change in the multivariate analysis. Age at illness onset did not predict a change in diagnosis, which may partly be explained by a high average age (72% were above 50 years of age in the psychotic depression group). We found that men seemed to have more diagnostic change compared to women. This result conflicts with some previous studies (6,13). The mean age of patients with schizoaffective disorder was high (49.8) considering that this was their first hospitalization. One reason could be that these patients were previously treated in outpatient care with a different diagnosis.

Our finding of a somewhat low diagnostic stability of psychotic depression during follow-up is in line with several previous studies with, however, shorter follow-up than in our study (1,9). Compared to a study with a rather similar follow-up period of ten years, our study showed higher diagnostic consistency (68.7% vs. 45.0%) (12). That study has been criticized due to its very young sample with a high proportion of males (21). Another recent study with a long follow-up also found a low diagnostic stability

in psychotic depression (11). However, the average age of the patients in this study was also significantly lower. Psychotic depression may be a more stable diagnosis when the onset of the illness is at an older age. Young age of a patient with psychotic depression has been found to associate with conversion to bipolar disorder (16). We did not find a drift towards bipolar disorder. Age at index episode and diagnostic practices may have influenced the scarcity of conversion to bipolar disorder in our sample. Initial diagnoses were set at a time when bipolar disorder was much more commonly missed than today. If the symptom profile during the course of illness had retained psychotic and affective symptoms, the diagnosis that was set previously could have been set during further episodes due to convention rather than due to its validity as a description of the patient's disorder. Moreover, diagnosis of hypomania is difficult and could have been missed during later treatment episodes.

Previous studies with a similar long follow-up as in our study have found conversion to schizophrenia common (4,11). Likewise, we found a drift towards either schizophrenia or schizophrenia group diagnosis. The studies regarding diagnostic stability of schizoaffective disorder have found conflicting results with widely varying stability rates. Our study found schizoaffective disorder to be a stable diagnosis (88.0%) over time. There are similar findings in studies with short follow-up periods (1,8). Yet, during a long follow-up, the diagnostic stability of schizoaffective disorder has been found considerably lower (11). The high average age of patients with schizoaffective disorder at baseline in our study is likely to be one reason for the observed stability.

We cannot rule out that the low rate of diagnostic change in the schizoaffective disorder group could be a result of clinician- and institution-related factors such as diagnostic convention in clinical assessments. However, schizoaffective disorder as defined in ICD-10 seems to have provided the clinicians a reliable description of the patient's condition. Anyhow, there may be less need for the clinician to assess critically and change the diagnosis in naturalistic settings when he/she is already dealing with a schizophrenia spectrum disorder. We cannot, of course, take stock of the validity of the diagnoses in the present study. Our study reflects the use of clinical diagnoses and not as such the true disorders of the patients.

Strengths and weaknesses

The major strength of our study was that all patients with these diagnoses could be traced from the local register, making the review of all hospital records possible, and that our sample was not biased by drop-outs since the national registers of hospital discharge cover all possible hospitalizations, and causes of death register, likewise, cover all deceased cases during the follow-up. The study also had a long follow-up period from 8 up to 12 years. One weakness of the study is that the diagnoses of the index episode were confirmed through reviewing the patient records instead of structured clinical interviews, and the same limitation applies to follow-up where diagnoses were gathered from national registers. The sample size is a limitation that may have influenced statistical significance of the findings, for instance, in factors predicting readmissions. The mean age of the sample was quite high, but to an extent this may be a result of some patients possibly having had a previous treatment episode outside Satakunta before 1995. The patient records, however, include information on previous episodes, but there may be variability in the reliability of the self-reports.

Conclusions

The diagnosis of schizoaffective disorder has shown variable stability previously, probably partly due to differences in diagnostic systems and partly due to length of follow-up periods. We found schizoaffective disorder a highly stable diagnosis in our study. Psychotic depression showed intermediate diagnostic stability. It is interesting, in the light of discussion on the validity of schizoaffective disorder, that this diagnosis might actually be more reliable. Studies on patients at-risk for psychosis have found that depression often precedes full-blown psychotic states. This, in addition to conversion to bipolar disorder, may explain the lower stability of psychotic depression found in several studies. Future studies with large samples should focus on the role of age, incipient vascular depression and progression to schizophrenia in psychotic depression.

High proportions of diagnostic drift over time in first-episode psychotic patient samples highlight the problems of a clinician assessing a patient’s symptoms in a complex situation with varying signal to noise ratios. Diagnoses are set in diverging

settings with differing skills to interpret and match the findings to the descriptions and definitions of the diagnostic categories. Moreover, diagnoses are indexes of illnesses the patients suffer from and sometimes indexes do not function ideally.

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