ORIGINAL RESEARCH

Impact of psychiatric comorbidity on the severity, short-term functional outcome, and psychiatric complications after acute stroke

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Background and purpose: The comorbidity of psychiatric disorders and cerebrovascular disease appears to be complex with underlying bidirectional influences. Hitherto, research has focused mainly on the evaluation of stroke risk in particular psychiatric disorders; only a few studies have assessed their role in the acute natural history of stroke. The aim of this study was to provide a perspective on psychiatric premorbidity and its impact on stroke severity, psychiatric complications during the initial treatment phase, and the short-term functional outcome of stroke.

Patients and methods: We retrospectively studied the impact of a predocumented psychiatric diagnosis (PDPD) on stroke severity, short-term functional outcome, and psychiatric complications in a sample of 798 patients consecutively admitted for acute ischemic or hemorrhagic stroke by performing a chart review. Group comparisons (PDPD vs non-PDPD) with adjustment for covariates were carried out either using multivariate analysis of variance or logistic regression analysis.

Results: More severe strokes (ie, mean National Institute of Health Stroke Scale score on admission 10.1±7.9 vs 7.5±7.4; F(10,796)=18.5, $p<0.0001$) and higher prevalence of poor outcome (73.7 vs 54.9%; OR: 2.6, standard error: 0.5, z=4.82, $p<0.0001$) was found in patients with a documented psychiatric diagnosis at the time of stroke, as well as a higher rate of psychiatric complications during the initial treatment phase (46.7 vs 28.9%; OR: −0.78, z=4.59, $p<0.0001$).

Conclusion: Our data have clinical implications in that they call for identification of psychiatric premorbidity or comorbidity through careful history-taking and particularly close monitoring for psychiatric complications with respect to their potentially negative impact on outcome after stroke.

Keywords: stroke, psychiatric disorder, comorbidity

Introduction

Stroke is one of the major causes of disability and death worldwide.[1–3] Nonmodifiable (eg, age, sex, race or ethnicity, and heredity) and modifiable (eg, diabetes, atrial fibrillation, smoking, dyslipidemia, and arterial hypertension) risk factors for stroke have been extensively studied.[4,5] In addition, a variety of factors impacting on initial stroke severity and prognosis after stroke have been identified: beyond predictors such as age, gender, National Institute of Health Stroke Scale (NIHSS) score at admission, and fever,[6] metabolic and cardiovascular comorbidities – diabetes, prior stroke, and atrial fibrillation in particular[3,7,8] – negatively influence long-term functional outcome in stroke survivors.

Depression, anxiety, psychosis, or dementia are frequent and relevant comorbidities of stroke. Poststroke depression, for example, affects nearly a third of all stroke

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survivors within five years following stroke,[9] and post-stroke depression severity predicts the extent of impairment in activities of daily living after stroke.[10] Pre-existing affective disorder, on the other hand, has been demonstrated to predict more severe strokes on admittance and to negatively impact functional and cognitive outcomes after stroke.[11,12] Recent data from a large Swedish register study indicate that patients with prestroke psychosis showed a poorer outcome and poorer utilization of secondary pharmacological prevention after stroke.[13] While prevalence data regarding the occurrence of poststroke delirium vary between 13 and 48%, this condition leads to prolongation of hospital stay, poorer functional outcome, and increased risk for developing dementia. Dementia affects approximately 10% of patients after first stroke and 30% after recurrent stroke,[14] stressing the causal relevance of stroke per se for the development of dementia independently of underlying vascular risk factors.

Apart from a mere co-occurrence due to high prevalence of psychiatric and cerebrovascular disease, shared risk factors or pathomechanisms as well as complex causative relationships may be invoked to explain their coexistence. To begin with, delirious or depressive syndromes may ensue from cerebrovascular events, with characteristics such as stroke severity, lesion size, and lesion location conferring various degrees of risk for these complications.[10,15,16] Second, there is a large body of research investigating the – presumably bidirectional – relationship between vascular risk factors and psychiatric disorders like affective disorders or schizophrenia.[17–19] There is also evidence for deeper underlying relationships: biological changes associated with affective disorders include, among others, increased inflammation, overactivity of the hypothalamus–pituitary–adrenal axis, and endothelial dysfunction, which in turn may comediate the link to vascular disease and, eventually, stroke.[20,21] Based on data from functional genomic analyses, it has also been suggested that schizophrenia may be a vascular-ischemic and postischemic repair disorder.[22] Finally, aspects related to the treatment of psychiatric conditions may pertain to their co-occurrence with cerebrovascular disease, as an increased risk of stroke has been found in association with antipsychotic pharmacotherapy.[23]

Specific psychiatric disorders such as affective disorders, schizophrenia, and dementia have mainly been studied with a focus on the evaluation of risk for stroke or their role in recovery or longer-term outcome in the wake of a stroke.[19,24–26] Rarely, however, has a general

perspective on psychiatric premorbidity and stroke risk[27,28] or its impact on stroke severity on admission been taken. We aim to elaborate on this issue through a retrospective analysis of stroke patients' documented pre-existing psychiatric diagnoses and severity and short-term functional outcome of stroke.

Methods
Patients
The study was approved by the ethics committee (Ethikkommission II der Universität Heidelberg – Medizinische Fakultät Mannheim) and performed in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki). Written informed consent was obtained from all participants prior to enrolment. We retrospectively analyzed medical data of 798 patients consecutively admitted to the stroke unit of the University Medical Centre, Mannheim, Germany, for acute ischemic or hemorrhagic stroke between January and December 2016. The study was approved by the local ethics committee. Cases of cerebral ischemia or intracranial hemorrhage due to trauma, infection, vascular malformation, or cerebral venous thrombosis were not included in the study.

Measures
The necessary information was obtained through a retrospective chart review. As the predictor variable, a predocumented psychiatric diagnosis (PDPD) was defined. Possible covariates were basic demographic information such as age and sex as well as the prevalence of pre-existing cardiovascular risk factors and the premorbid modified Rankin Scale (mRS) score. Outcome variables were subdivided into variables indicating the clinical severity of the index stroke (NIHSS and mRS scores on admission, "minor stroke" with initial NIHSS score <4, NIHSSS at discharge), variables indicating the short-term functional outcome (mRS score at discharge, death, and "poor outcome" with mRS>2 at discharge), treatment-related outcome variables (duration of hospitalization, acute therapy for ischemic stroke), and variables for the outcome of psychiatric complications during the hospitalization for stroke (defined as newly diagnosed delirium or depressive syndrome – both as judged by the treating physician, new prescription of an antidepressant, antipsychotic, or benzodiazepine, dosage increase of pre-existing psychiatric medication, or requirement for physical restraint).

Any PDPD independent of acuity at the time of hospitalization for stroke was recorded in accordance with the ICD-10: F0x (dementia – delirium was excluded, see below), F1x (substance-associated disorders excluding tobacco, which was recorded separately), F2x (schizophrenia and related disorders), F3x (affective disorders), and F4x (anxiety, somatic–neurotic–stress disorders). We separately noted whether there was a history of delirium. Pre-existing psychiatric medication was classified into antidepressant, antipsychotic, and antidementive medication and benzodiazepines.

Statistical analysis

Unless differently indicated, all values are expressed as mean±SD. Statistics were performed using STATA® (version 11; StataCorp LP, College Station, TX, USA) at a significance level ≤0.05. The Kolmogorov–Smirnov goodness-of-fit test was used to test normality and as the data were normally distributed, parametric tests could be used. The distribution of categorical variables such as demographic variables, vascular risk factors, and psychiatric complications between both groups was compared by chi-square tests, and Fisher's exact test in the case of small cell sizes. Group comparisons of continuous variables such as age were assessed using independent-samples t-tests. Age, sex, and the prevalence of pre-existing cardiovascular risk factors were assumed to be covariates, and thus group comparisons (PDPD vs non-PDPD) for dichotomous outcome variables such as minor stroke, poor outcome, or death were carried out using logistic regression analysis in order to adjust for the covariates. Accordingly, group comparisons for continuous outcome variables such as mean NIHSS or mRS scores were carried out using multivariate analysis of variance to adjust for the covariates mentioned. A subgroup analysis of PDPD patients with the exclusion of patients with dementia was intended, because it could be at least argued to count dementias as neurodegenerative diseases in the category of psychiatric disorders.

Results

Demographic information and predocumented psychiatric diagnoses

798 patients were included in our analysis; 599 were regarded as non-PDPD patients, whereas 199 patients were PDPD patients. Demographic information is summarized in Table 1. PDPD and non-PDPD patients did not differ in terms of age (71.9 vs 71.8 years) or sex (54.8 vs 58.8% male). Differences between the groups were found regarding living circumstances prior to the index stroke, with PDPD patients living significantly more frequently under family ($p<0.0001$) or institutional ($p<0.0001$) care and significantly less frequently at home in an independent manner ($p<0.0001$). In concordance

Table 1 Demographic information and vascular risk factors compared between PDPD and non-PDPD patients

	PDPD patients (n=199)	Non-PDPD patients (n=599)	*p*-value
Demographics			
Age (years), mean (SD)	71.9 (14.5)	71.8 (12.8)	0.972
Sex (male), n (%)	109 (54.8)	352 (58.8)	0.323
Living circumstances prior to index stroke			
Independent at home, n (%)	115 (57.8)	523 (87.3)	**0.001**
Family care, n (%)	41 (20.6)	55 (9.2)	**0.001**
Institutional care, n (%)	43 (21.6)	21 (3.5)	**0.001**
Premorbid mRS score (mean, ± SD)	2.1 (1.8)	1.0 (1.4)	**0.001**
Vascular risk factors			
Hypertension, n (%)	153 (76.9)	496 (82.8)	0.083
Diabetes mellitus, n (%)	58 (29.1)	194 (32.4)	0.417
Dyslipidemia, n (%)	51 (25.6)	194 (32.4)	0.080
Coronary heart disease, n (%)	27 (13.6)	111 (18.5)	0.115
Prior myocardial infarction, n (%)	16 (8.0)	54 (9.0)	0.687
Prior stroke, n (%)	45 (22.6)	119 (19.9)	0.388
Current or past smoker, n (%)	58 (29.1)	108 (18.0)	**0.001**

Note: Bold data indicate statistical significance.
Abbreviations: mRS, modified Rankin Scale; PDPD, predocumented psychiatric diagnosis.

with this, premorbid mRS scores differed between the groups (median mRS scores 2 vs 0; $p<0.0001$).

Concerning vascular risk factors, no differential distribution was found between PDPD and non-PDPD patients except for smoking, where past or present tobacco consumption was more frequent among PDPD patients (29.1 vs 18.0%; $p=0.001$).

In the group of patients with psychiatric comorbidity, the most frequent PDPDs were substance-associated (35.7%) and affective (34.2%) disorders, as well as dementia (34.7%). Table 2 provides a more detailed overview of the PDPDs and of the subclasses of medication recorded in the PDPD. Psychiatric polypharmacy (ie, more than one medication from the classes listed above) was found in 18 PDPD patients.

Index stroke – severity, treatment, functional outcome

All reported group comparison results between PDPD and non-PDPD patients concerning the index stroke are adjusted for age, sex, and vascular risk factors in order to control for potentially confounding factors.

No differences were noted regarding the frequency of ischemic vs hemorrhagic stroke between the groups

Table 2 Predocumented psychiatric diagnosis (PDPD) and psychiatric medication in PDPD patients

PDPD	Patients, n (%)
F0	69 (34.7)
F1	71 (35.7)
F2	8 (4.0)
F3	68 (34.2)
F4	17 (8.5)
History of delirium	14 (7.0)
Medication	
Antidepressant	58 (29.1)
SSRI	45 (22.6)
Tricyclic	19 (9.6)
Benzodiazepine	11 (5.5)
Antipsychotic	33 (16.6)
First generation, high potency	3 (1.5)
First generation, low potency	19 (9.6)
Second generation	14 (7.0)
Antidementive	11 (5.5)

Notes: F0, dementia (delirium was excluded); F1, substance-associated disorders (excluding tobacco, which was recorded separately); F2, schizophrenia and related disorders; F3, affective disorders; F4, anxiety, somatic–neurotic–stress disorders

($p=0.24$) (Table 3). Stroke severity was more pronounced in PDPD patients on admission (mean NIHSS score 10.1±7.9 vs 7.5±7.4; $F_{(10,796)}=18.5$, $p<0.0001$) and on discharge (mean NIHSS score 9.7±12.0 vs 6.3±10.0; $F_{(10,796)}=15.3$, $p=0.0001$). Functional impairment was also more severe in this patient population as evidenced by higher mRS scores on admission (4.1±1.1 vs 3.6±1.3; $F_{(10,796)}=25.6$, $p<0.0001$) and discharge (3.7±1.6 vs 2.9±1.7; $F_{(10,796)}=32.1$, $p<0.0001$), and a larger proportion of poor outcomes (ie, discharge mRS score>2, 73.7 vs 54.9%; OR: 2.6, standard error (SE): 0.5, z=4.82, $p<0.0001$; 95% CI: 1.8–3.9). The extent of recovery during hospitalization estimated by the difference between NIHSS scores at discharge and admission did not differ (0.5±8.8 vs 1.1±0.7.4; $p=0.26$). There was a significantly larger proportion of minor strokes[29] (ie, initial NIHSS score <4) in non-PDPD patients (22.1 vs 41.2%; OR: 0.38, SE: 0.08, z=−4.89, $p<0.0001$; 95% CI: 0.26–0.56). There were no differences regarding acute treatment, in particular the utilization of intravenous systemic thrombolysis (29.4 vs 26.9%; $p=0.51$) or thrombectomy (8.9 vs 10.4%; $p=0.55$) for ischemic stroke between the groups. The portion of PDPD patients discharged home to live independently did not differ from non-PDPD patients (8.0 vs 10.4%; $p=0.29$). Significantly fewer PDPD patients were discharged home with family care (18.1 vs 28.0%; OR: 0.56, SE: 0.12, z=−2.76, $p=0.006$; 95% CI: 0.37–0.84), but more frequently into institutional care (10.0 vs 1.5%; OR: 7.5, SE: 3.4, z=4.48, $p<0.0001$; 95% CI: 3.1–18.1). Eighteen PDPD patients (9.0%) died, which differed significantly from non-PDPD patients, where 27 patients died (4.5%; OR: 2.1, SE: 0.69, z=2.25, $p=0.024$; 95% CI: 1.10–4.02).

Psychiatric complications

In general, we found a higher rate of psychiatric complications during the initial treatment phase in PDPD patients compared to non-PDPD patients (46.7 vs 28.9%; OR: −0.78, SE: 0.2, z=4.59, $p<0.0001$; 95% CI: 0.45–1.12). Delirium and depressive syndromes during hospitalization for acute stroke occurred more frequently in PDPD patients ($p<0.0001$ and $p=0.012$, respectively), as did the initiation of new psychopharmacotherapy of any kind ($p=0.001$), which was mainly due to significantly more newly prescribed antipsychotics and benzodiazepines (Table 4). The need for physical restraint because of imminent danger to self or others did not differ between the groups and was in all 20 cases due to a delirious syndrome. Almost two-thirds of the cases of delirium occurred in patients with dementia (59.7%), followed by patients with a pre-existing substance-associated disorder (33.9%). A

Table 3 Characteristics of the index stroke and the short-term outcome compared between PDPD and non-PDPD patients

	PDPD patients	Non-PDPD patients	p-value
Index stroke			
Ischemic, n (%) vs. hemorrhagic stroke, n (%)	180 (90.4) vs. 19 (9.6)	557 (93.0) vs. 42 (7.0)	0.243
Admission NIHSS score, mean ± SD	10.1 ±7.9	7.5 ±7.4	**0.001**
Discharge NIHSS score, mean ± SD	9.7 ±12.0	6.3 ±10.0	**0.001**
NIHSS score difference D-A, mean ± SD	0.5 ±8.8	1.1 ±.7.4	0.292
Minor stroke (NIHSS<4), n, %	44 (22.1)	247 (41.2)	**0.001**
Admission mRS score, mean ± SD	4.1 ±1.1	3.6 ±1.3	**0.001**
Discharge mRS score, mean ± SD	3.7 ±1.6	2.9 ±1.7	**0.001**
Acute therapy (ischemic strokes only)			
Systemic thrombolysis, n (%)	53 (29.4)	150 (26.9)	0.512
Thrombectomy, n (%)	16 (8.9)	58 (10.4)	0.554
Trial medication, n (%)	2 (1.1)	5 (0.9)	0.681
Duration of hospitalization, days, mean (SD)	10.0 (0.43)	9.8 (0.31)	0.764
Poor outcome (discharge mRS >2), n (%)	146 (73.4)	329 (54.9)	**0.001**
Death (mRS=6), n(%)	18 (9.0)	27 (4.5)	0.016
Survivors			
Home discharge, independent, n (%)	16 (8.0)	62 (10.4)	0.342
Home discharge, family care, n (%)	36 (18.1)	168 (28.0)	**0.005**
Institutional care, n (%)	20 (10.0)	9 (1.5)	**0.001**
Rehabilitation/different hospital, n (%)	109 (54.8)	331 (55.4)	0.905

Note: Bold data indicate statistical significance.
Abbreviations: mRS, modified Rankin Scale; NIHSS, National Institute of Health Stroke Scale; PDPD, predocumented psychiatric diagnosis.

Table 4 Psychiatric complications during hospitalization for acute stroke compared between PDPD and non-PDPD patients

Psychiatric complication	PDPD patients	Non-PDPD patients	p-value
Delirium, n (%)	62 (31.1)	94 (15.7)	**0.001**
Depressive syndrome, n (%)	15 (7.5)	20 (3.3)	**0.012**
Newly prescribed antidepressant, n (%)	15 (7.5)	27 (4.5)	0.097
Newly prescribed antipsychotic, n (%)	46 (23.1)	95 (15.9)	**0.020**
Newly prescribed benzodiazepine, n (%)	29 (14.6)	42 (7.0)	**0.001**
Dosage increase of pre-existing psychiatric medication, n (%)	6 (3.0)	1 (0.2)	**0.001**
Physical restraint, n (%)	8 (4.0)	12 (2.0)	0.115

Note: Bold data indicate statistical significance.
Abbreviation: PDPD, predocumented psychiatric diagnosis.

depressive syndrome occurred in 15 PDPD patients, 12 of whom had a predocumented affective disorder. Both a delirious syndrome and a depressive syndrome were diagnosed in seven patients, five of whom had no PDPD.

Subgroup analysis of PDPD patients without dementia

The exclusion of 69 patients with pre-existing dementia yielded a significant difference in age between patients with a pre-existing psychiatric diagnosis and those without (mean age 67.6 vs 71.8 years, respectively; p=0.001). No significant differences were found regarding gender and

vascular risk factors (hypertension, diabetes, dyslipidemia, KHK, prior myocardial infarction, or stroke – data not shown) except for tobacco consumption (40.0 vs 18.0% of patients; p<0.0001). Initial clinical deficits were more severe in PDPD patients than in non-PDPD patients (mean NIHSS score 9.1±7.5 vs 7.5±7.4; $F_{(10,727)}$=8.55, p=0.0036 and median mRS score on admission 3.9±1.2 vs 3.6±1.3; $F_{(10,727)}$=10.79, p=0.0011), and NIHSS scores at discharge differed significantly (8.7±12.1 vs 6.3±10.0; $F_{(10,727)}$=10.05, p=0.0016), as did mRS on discharge (3.3 ±1.7 vs 2.9±1.7; $F_{(10,727)}$=11.92, p=0.0006). Minor strokes were found more frequently in non-PDPD patients

(41.2 vs 27.7%; OR: 0.48, SE: 0.11, z=−3.29, p=0.001; 95% CI: 0.31–0.74), while poor functional outcome was found more frequently in PDPD patients (61.5 vs 54.9%; OR: 1.73, SE: 0.38, z=2.46, p=0.014; 95% CI: 1.12–2.67). Delirium was equally prevalent in PDPD and non-PDPD patients (19.2 vs 15.7; p=0.17), but more depressive syndromes were diagnosed in PDPD patients (11.5 vs 3.3; OR: 3.09, SE: 1.16, z=3.00, p=0.003; 95% CI: 1.48–6.46).

Discussion

In our retrospective analysis of patients with ischemic and hemorrhagic stroke, we found more severe strokes and a higher prevalence of poor outcomes as well as a higher rate of psychiatric complications during the initial treatment phase in patients with a PDPD than in those without. Moreover, when excluding patients with predocumented dementia, whose categorization as neurodegenerative diseases in the category of "psychiatric diseases" could be argued, a significant age difference between PDPD and non-PDPD patients emerged, corroborating data by Chiu et al[30] who found a higher risk for stroke in adults younger than 45 years of age and with pre-existing mental disorder.[30] At the same time, initial stroke severity was more pronounced and poor outcomes were more frequent in nondemented PDPD patients.

A large body of data supports the notion of mental illness as a – potentially modifiable – stroke risk factor. Patients with bipolar disorder,[26] schizophrenia,[19] alcohol use,[31] and illicit drug use[32] have an increased risk for stroke. Limited data exist on the relation between anxiety disorders and stroke incidence.[33] However, there is a scarcity of studies investigating the relationship between pre-stroke psychiatric morbidity and the severity of stroke or outcome after stroke: two groups demonstrated associations between prestroke depression and stroke severity as well as functional outcome.[11,12] Data on the impact of prestroke dementia on stroke severity and outcome are also consistent in that pre-existing dementia is associated with a higher burden of disability and higher rates of institutionalization after stroke.[34–36] Aron et al[37] found the living situation prior to stroke and ensuing social isolation,[37] which is more frequent in the mentally ill,[38] to contribute to the initial stroke severity. In our cohort, significantly more PDPD patients lived in family or institutional care prior to the index stroke. This does not preclude a relevant influence of social isolation since the quality of social involvement appears to be inadequately reflected by merely considering patients' living situation.[37]

Prieto et al[17] hypothesize that patients with depression lead an unhealthier lifestyle, which in turn may be associated with higher prevalence of other risk factors for stroke.[17] In a study examining diabetic patients, alcohol consumption was identified as a relevant contributor to the severity of stroke and outcome in these patients.[39] In our sample, the prevalence of vascular risk factors did not differ between stroke patients with and without psychiatric premorbidity except for smoking, supporting the well-established fact that smoking is more common in psychiatric patients than in the general population.[40] However, even though cigarette smoking is an established risk factor for stroke,[41] data regarding the contribution of smoking to stroke severity are inconsistent.[42–45] Unfortunately, we did not have information on our patients' body mass index, which would have been valuable in light of the association of obesity and mental health, on the one hand,[46] and obesity and prognosis after stroke, on the other.[47–49] For patients with premorbid psychiatric diagnoses, several studies have demonstrated increased morbidity and mortality from acute medical conditions, such as prolonged hospitalization, worse cardiac adverse events, and mortality after acute coronary syndrome.[50] Liao et al[51] found higher rates of postoperative complications and mortality rates in patients suffering from schizophrenia.[51] Data unadjusted for sociodemographics and comorbidity indicate that mentally ill stroke survivors were more frequently hospitalized for nonpsychiatric reasons prior to and up to one year after their initial stroke.[52] Patients with atrial fibrillation and schizophrenia or severe depression experienced increased rates of stroke and major bleeding compared with matched comparisons,[53] and coagulation control is poorer in mentally ill patients.[54] On a related note, Blackburn et al[55] showed that statins do not lower the risk for cardiovascular disease in psychiatric patients.[55] Insufficient power of that study may be one reason for this finding; however, concomitant psychopharmacotherapy may interact with lipid-lowering agents and diminish their efficacy.[56] Finally, adherence to medication may be problematic in patients with a mental disorder or cognitive impairment,[57] which may impact on prescription practices.[58] A recent meta-analysis investigating the association between cognitive impairment and medication adherence in stroke survivors,[59] however, suggests that it may be useful to differentiate degrees of cognitive impairment with more severely affected patients' adherence actually being improved by their reliance on caregivers. Inequalities regarding the initiation of treatments have also been

noted with respect to acute stroke treatment: a recent study reports lower rates of thrombolysis in patients with a psychiatric diagnosis,[60] a finding we could not support in our sample. In our study, PDPD patients mainly received antidepressant and antipsychotic medication as prestroke psychopharmacotherapy. Prestroke use of antipsychotic medication was found to be associated with a higher risk for severe strokes and higher poststroke mortality,[61] and serotonin reuptake inhibitors also negatively impacted on stroke outcome with a trend-level negative influence on initial stroke severity.[62] Hence, medication may be one factor contributing to more severe strokes in PDPD patients.

Limitations of our study are predominantly tied to its retrospective design where comprehensiveness and quality of the source data are of paramount importance. As a certified stroke unit, the stroke unit of University Medical Centre, Mannheim, Germany has to meet certain standards regarding completeness of data required by the German Stroke Society.[63] Identification of psychiatric premorbidity by patient record and documentation may have missed patients with a psychiatric diagnosis. Psychiatric conditions are frequently under-recognized, misdiagnosed, or under-treated, and nonpsychiatrists' accuracy in recognizing psychiatric disorders does not improve over time without specific training.[64] We furthermore did not distinguish between active versus remote history of psychiatric disorder, and we did not have information regarding the duration of and compliance to current psychopharmacotherapy as well as comprehensive data pertaining to past hospitalizations for psychiatric disorder, which would have been interesting in the context of Zuflacht et al's[28] research showing an association between time of last psychiatric hospitalization and timing of stroke.[28] It would also have been desirable to have standardized follow-up evaluations after seven and 90 days to investigate the longer-term outcome. This would have been particularly informative for stroke survivors discharged to a different hospital or into rehabilitative treatment. Depressive or delirious syndromes during hospitalization for acute stroke were clinically diagnosed, which contrasts with *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition and ICD-10 definitions for a depressive episode and the required minimum of symptom duration. However, on the grounds of clinical impression, antidepressant medication is frequently initiated early after stroke, which has been shown to positively influence short-term mortality in ischemic stroke.[65] We are also well aware that the strategy of conflating patients with different predocumented psychiatric diagnoses into one group may overgeneralize, and thus neglect idiosyncrasies of specific psychiatric disorders regarding their impact on the acute natural history of stroke.

Conclusion

In summary, we found more severe strokes and higher prevalence of poor outcome in patients with a documented psychiatric diagnosis at the time of stroke, as well as a higher rate of psychiatric complications during the initial treatment phase. In the light of a recently identified association between the number of mental disorders and the incidence of nonfatal stroke, it is recommended to obtain a mental health history of stroke patients in order to evaluate extent and persistence of premorbid psychopathology,[27] and patients with a pre-existing psychiatric disorder should be particularly closely monitored for poststroke psychiatric complications.

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Disclosure

The authors report no conflict of interest in this work.

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