# A prospective cohort study of the incidence and determinants of post-stroke depression among the mainland Chinese patients

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Background: Post-stroke depression is a common consequence of stroke and can negatively affect the rehabilitation process in patients. This work was undertaken to examine the incidence, demographic factors and clinical determinants of post-stroke depression in 3 months after ischemic stroke in mainland Chinese patients.

Methods: One hundred and sixty-five patients with acute ischemic stroke were included in the present work. The *Diagnostic and Statistical Manual of Mental Disorders* (fourth edition) diagnosis of post-stroke depression was evaluated by the World Health Organization Composite International Diagnostic Interview during the follow-up exam at 3 months after the stroke. The demographic factors and clinical variables at the time of stroke onset and 14 days after stroke were also examined.

Results: The 3 month cumulative incidence of post-stroke depression was 27·3% in this patient population. The univariate analysis suggests that the female gender, past history of depression, marital status and level of handicap at 14 days after stroke were factors associated with the development of post-stroke depression. In the multivariate model, female gender [$p$=0·0040; odds ratio (OR)=3·550; 95% confidence interval (CI): 1·499–8·408], past history of depression ($p$=0·0010; OR=5·225; 95% CI: 1·959–13·940) and level of handicap at 14 days after stroke ($p$=0·0066; OR=1·607; 95% CI: 1·141–2·262) were further confirmed as demographic and clinical factors that correlate with the development of post-stroke depression.

Conclusion: The present work suggests that female gender, history of depression and level of handicap at 14 days after stroke are three independent determinants of post-stroke depression occurrence during the first 3 months after ischemic stroke in mainland Chinese patients.

**Keywords:** Post-stroke depression, risk factors, determinants, WHO Composite International Diagnostic Interview

## Introduction

Post-stroke depression (PSD) is the most common and important affective disorder following stroke[1–3]. It may exert significantly negative impacts on patient's rehabilitation progress from their neurological dysfunctions, prolong their hospital stay, impair their quality of life and increase economical burdens on the society and patient's family. Importantly, PSD also increases the disability and mortality rates in stroke patients[4–6]. Despite its high prevalence in mainland China, PSD has often been unrecognized or overlooked by stroke survivors and physicians. Unfortunately, the importance of an early identification and medical intervention of PSD has also been underestimated or neglected by most physicians[2,3].

In order to achieve an earlier identification and a better treatment for PSD, especially in Chinese patients with ischemic stroke, it is essential to gain a better understanding of the epidemiology of PSD in this patient population. To our knowledge, there has been no reported study focusing on the epidemiology and determinants of PSD in mainland Chinese patients with ischemic stroke. In addition, some previous studies may have significant methodological drawbacks (e.g. inappropriate diagnosis and measurements of depression), which could lead to potential pitfalls in data interpretation and inconsistent findings across studies[7–9]. To avoid this problem, we used version 3.0 of the World Health Organization (WHO) Composite International Diagnostic Interview, a fully structured lay-administered interview, as the diagnostic criteria of depression and the psychometric measurement[10]. This method has been proven to be effective and reliable for diagnosing PSD and fits the needs of the present work[11,12]. The present work therefore was

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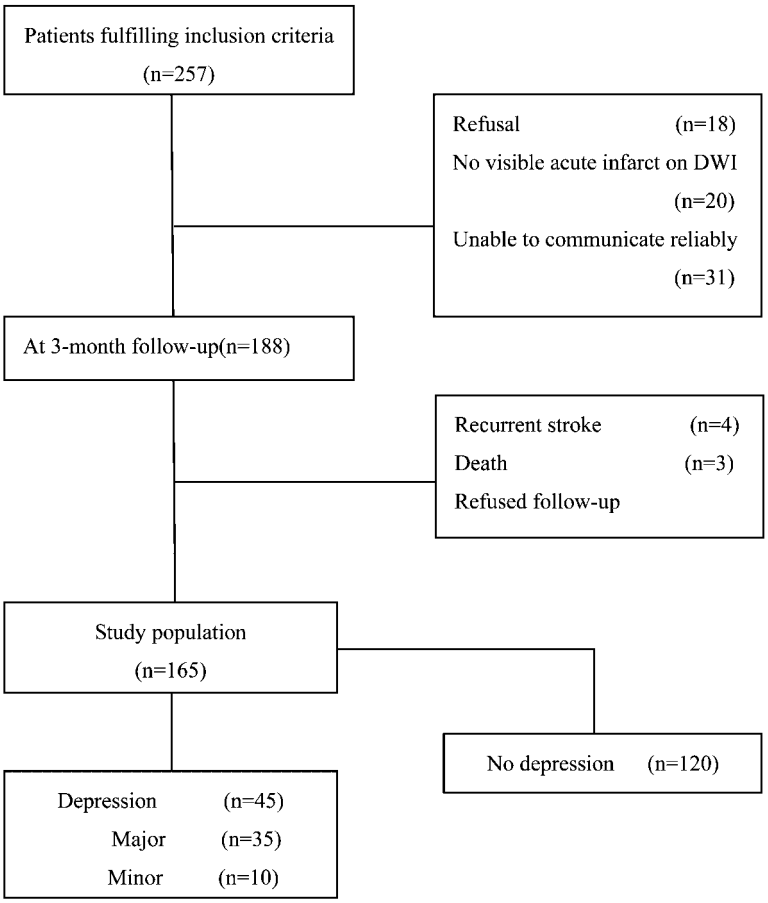


**Figure 1 Patient selection and recruitment: DWI=diffusion-weighted imaging**

undertaken to investigate the incidence, the demographic factors and the clinical risk factors for PSD in mainland Chinese patients in 3 months after ischemic stroke.

## Subjects and methods

### *Subjects*

A total of 257 consecutive ischemic stroke patients admitted to the Department of Neurology, Beijing Tiantan Hospital, Capital Medical University (Beijing, China), were screened for the present work. According to the WHO criteria, ischemic stroke was defined as 'rapidly developing clinical signs of focal (or global) disturbance of cerebral function, with symptoms lasting 24 hours or longer, with no apparent cause other than of vascular origin' in which a brain computed tomography (CT) or magnetic resonance imaging (MRI) scan did not show intracranial hemorrhage[12]. Patient was excluded from the present work if he/she: (i) is over 85 years or below 18 years; (2) is not living in Beijing; (3) has a history of dementia or other neurological disease known to affect cognition; (4) is currently an alcohol or drug abuser; (5) has communication problems that preclude him from a psychiatric interview [exclusion of patient who was unable to communicate reliably (e.g. due to reduced level of consciousness, severe hearing or visual impairment, severe aphasia or dysarthria and severe cognitive dysfunction) was based on combined clinical judgment and a mini-mental state examination (MMSE) score that is <12]; (6) has no visible acute brain infarct on diffusion-weighted MRI sequence. Patients who had a recurrent stroke within 3 months of the index stroke onset were also excluded ($n$=4). There were three patients who died from the index stroke during the period, and 16 patients refused receiving the follow-up exam at 3 months after stroke. Thus, a total of 165 stroke patients were employed in this work and were evaluated both at 14 days and 3 months after stroke by means of face-to-face interviews and physical and cognitive examinations (*Figure 1*). All patients included in this work were given the informed consent. The work was approved by the Medical Ethics Committee of Beijing Tiantan Hospital, the Capital Medical University.

### *Clinical characteristics*

The following patient information was collected in 14 days after stroke onset: demographics (age, gender, residence, education history, marital status and medical insurance coverage); history of depression or previous stroke; current medications; and stroke risk factors (e.g. hypertension, diabetes, alcohol consumption and smoking). Pre-stroke disability was defined by a retrospective modified Rankin Scale (mRS) score >1. Smoking status and alcohol consumption were classified as current, ex-smoker or drinker or never. Stroke severity in all patients was assessed on the admission day and at 14 days after stroke onset by board-certified neurologists using the National Institute of Health Stroke

Scale (NIHSS). The cognitive function, the level of handicap and severity of depressive symptoms in these patients were also examined with MMSE, mRS and 17-item version of Hamilton Depression Rating Scale (HDRS), respectively, by full-time raters from our department.

### *Follow-up at 3 months*

At 3 months after stroke, all patients underwent assessment of level of handicap (mRS), severity of depressive symptoms (HDRS) and cognitive function (MMSE). Data on concurrent medication use were also recorded. The mRS is derived from an ordinal six-point scale in which two consecutive scores can be considered to represent equal increase in the level of handicap. The severity of depression was categorized as absent ($<8$), mild ($\geq 8$), moderate ($\geq 18$) or severe ($\geq 24$) by HDRS score.

### *Diagnostic assessment of depression*

The diagnosis of PSD was considered by the WHO Composite International Diagnostic Interview, which generates diagnosis according to the definitions and criteria of both *International Classification of Disease and Related Health Problems* (tenth revision) and *Diagnostic and Statistical Manual of Mental Disorders* (fourth edition) diagnostic systems[10]. Our work only used the *Diagnostic and Statistical Manual of Mental Disorders* (fourth edition) criteria. All interviews were conducted in a private room at our outpatient clinic center by the same interviewer who was blind to the clinical and radiological data of the patients. The interviewer had been trained at Beijing University Institute of Mental Health, the only official Composite International Diagnostic Interview training center in China authorized by WHO, and obtained the trainer certificate. This institution is also in charge of inputting Composite International Diagnostic Interview data and generating diagnoses of depression with specialized computer programs. It needs to be noted that (1) patients who previously had a depressive episode before the index stroke onset, but without receiving a previous diagnosis from the doctors, were identified in the present work from the lifetime and 12 month prevalence of depressive disorder in conjunction with the first age of onset by the Composite International Diagnostic Interview; (3) the depressed patients without any recent psychosocial stress factors except for stroke were defined as having the stroke-related depression.

### *Statistical analysis*

Statistical analyses were performed with SAS 9·0 (SAS Institute Inc., Cary, NC, USA). Quantitative data were presented as median [inter-quartile range (IQR)]. Group differences between patients with and without PSD were examined with Wilcoxon test. Factors that potentially relate to the occurrence of PSD were examined using the $\chi^2$ tests or Fisher's exact test (as appropriate). Multivariate analysis using stepwise logistic regression was undertaken to adjust for confounding factors to explore whether or not the existing conditions affect the occurrence of PSD with a 5% significance level. All variables with $p<0{\cdot}1$ in the univariate analysis were entered in the multivariate model simultaneously. $p<0{\cdot}05$ was considered significant (two-sided).

## Results

In 165 patients at 3 months after the stroke onset, the incidence of PSD was 27·3% ($n=45$). Cross-sectionally, the incidence rates were 20% ($n=33$) at 1 month and 7·3% ($n=12$) at 3 months after stroke. There were 35 patients (21·2%) diagnosed with major depression and ten (6·1%) diagnosed with minor depression by the WHO Composite International Diagnostic Interview method, based on the *Diagnostic and Statistical Manual* (fourth edition) criteria (data not shown). There were 23 patients (65·7%) who developed major depression within the first month and an additional 12 (34·3%) at 3 months after the index stroke. Major depression tended to occur within 1 month after the event.

The demographic characteristics and clinical baseline data of the PSD and non-PSD stroke patients are presented in *Table 1*. Only one of the 165 patients was left-handed. There were no statistically significant differences between the two patient groups in age, education, history of previous stroke, medical insurance, the pre-morbid mRS, cerebral vascular disease risk factors (e.g. smoking and alcohol consumption) and co-morbid diseases (e.g. hypertension and diabetes), respectively. Likewise, no difference existed in the severity of stroke between the two groups, as indicated by NHISS, on admission. Although none of the 165 patients had a self-reported history of depression, 28 patients were diagnosed with depressive disorder occurring before the index stroke on the basis of the WHO Composite International Diagnostic Interview. The univariate analysis suggested that female gender ($p=0{\cdot}0014$), depression history ($p=0{\cdot}0006$) and marital status ($p=0{\cdot}0149$) are factors that may be closely related to the development of PSD.

The physical status and psychiatric assessment performed at 14 days and 3 months after ischemic stroke, respectively, were compared between the PSD and non-PSD groups (*Table 2*). Of the 165 patients examined, 13 (7·9%) used antidepressant medication at 3 month follow-up and 11 of them belonged to the PSD group (45 patients). The level of handicap (mRS) at 14 days after stroke positively correlated with PSD (i.e. there were more patients with a high score of 4 or 5 in PSD group than that in non-PSD group). Specifically, 19 (43·2%) of PSD patients and 69 (58%) of non-PSD patients showed no significant residual neurological disability ($\text{mRS} \leqslant 1$) at 3 months after stroke. The remainders in each group showed either mild to moderate (mRS2–3; PSD group, 34·1%; non-PSD group, 27·7%) or severe disability ($\text{mRS} \geqslant 4$; PSD group, 22·7%; non-PSD group, 14·3%). In patients with PSD, the median HDRS scores were 10 (IQR5–14) and 14 (IQR10–20), respectively, at 14 days and 3 months after stroke onset. The median HDRS score was 5 (IQR2–9) at these time points in patients without PSD. There was a significant difference in HDRS score between PSD

and non-PSD group ($p<0{\cdot}001$). The percentage of patients with severe depressive symptoms at 3 months after stroke was significantly higher than that at 14 days after stroke in PSD group. Neither the stroke severity (NIHSS) nor the cognitive function (MMSE) was associated with the development of PSD at 14 day time point. In addition, neither mRS nor MMSE appeared to correlate with the PSD at 3 month time point.

We put those variables with $p<0{\cdot}1$ from the univariate analysis into a stepwise multilogistic regression model to find the independent demographic and clinical correlates of PSD. According to the multiple logistic regression analyses, female gender [$p=0{\cdot}0040$; odds ratio (OR)=3·550; 95% confidence interval (CI): 1·499–8·408], history of depression ($p=0{\cdot}0010$; OR=5·225; 95% CI: 1·959–13·940) and level of handicap at 14 days after stroke ($p=0{\cdot}0066$; OR=1·607; 95% CI: 1·141–2·262) were three independent risk factors for PSD, whereas others (e.g. marital status and hypertension) were not (*Table 3*). In other words, the risks of developing PSD were 3·550 and 5·225 times greater in female patients and in patients with depression history, respectively, than that in male patients and patients without depression history. In addition, the risk for a patient to develop PSD would be 1·607 times greater, with each increment of his/her mRS score of 1, yet the correlation between the level of handicap and PSD was relatively less remarkable than the other two factors.

## Discussion

Over a quarter of ischemic stroke patients included in the present work were diagnosed for PSD at 3 months after stroke. The incidence of PSD (27·3%) in this cohort of mainland Chinese patients is comparable to that from previous studies conducted in Western countries [3,4,13,14]. However, it is worth noting that there were considerable variations in the frequency of PSD among these studies (20–65%), which is likely due to differences in patient populations, psychiatric assessment methods, as well as the diagnostic criteria used. These differences also make the cross-study comparison difficult and a misinterpretation of previous data possible. For example, some studies used HDRS or the Center for Epidemiology Studies Depression as the solo diagnostic instrument. Since these methods were designed exclusively for assessing the presence and severity of depressive mood in patients within a short time period (e.g. 2 weeks) after stroke, they may lead to an inaccurate conclusion about the incidence of PSD if applied to other patient populations (e.g. patients in 3 months after stroke)[1]. Accordingly, these rating scales should be used in conjunction with other diagnostic criteria and structural measurements[15]. For this reason, we used version 3.0 of WHO Composite International Diagnostic Interview for the present work, as it generates diagnosis of major and minor depressive disorders according to the definitions and criteria of both the *International Classification of Disease and Related Health Problems*

**Table 1 Clinical characteristics of patients with and without post-stroke depression**

| | Non-PSD ($n=120$) | PSD ($n=45$) | |
|---|---|---|---|
| Variables | *N* (%) | *N* (%) | *p* value |
| Gender | | | |
| Female | 18 (15·0) | 17 (37·8) | 0·0014* |
| Male | 102 (85·0) | 28 (62·2) | |
| Living alone | 3 (2·5) | 2 (4·55) | 0·5222 |
| Marital status | | | |
| Single | 0 (0) | 3 (10·0) | 0·0042* |
| Married | 103 (96·3) | 26 (86·7) | |
| Widowed/divorced | 4 (3·7) | 1 (3·3) | |
| Having medical insurance | 103 (86·6) | 36 (80·00) | 0·2974 |
| Past history of stroke | 20 (16·7) | 10 (22·2) | 0·6083 |
| Past history of depression | 13 (10·8) | 15 (33·3) | 0·0006* |
| CVD risk factors | | | |
| HBP | 78 (67·9) | 33 (82·5) | 0·0762 |
| DM | 30 (26·1) | 12 (27·9) | 0·8177 |
| Smoking | | | |
| Never | 37 (31·4) | 20 (46·5) | 0·1872 |
| Ex-smoker | 11 (9·3) | 4 (9·3) | |
| Current | 70 (59·3) | 19 (44·2) | |
| Alcohol consumption | | | |
| Never | 62 (53·0) | 26 (57. 8) | 0·4765 |
| Ex-drinker | 6 (5·1) | 4 (8·9) | |
| Current | 49 (41·9) | 15 (33·3) | |
| Pre-morbid mRS (>1) | 3 (2·5) | 3 (6·7) | 0·4200 |
| | Median (IQR) | Median (IQR) | |
| Age (years) | 57 (51–65) | 59 (50–69) | 0·4775 |
| Years of education, median (IQR) | 9 (9–12) | 9 (6–12) | 0·5124 |
| NIHSS on admission, median (IQR) | 4 (2–7) | 5 (2–9) | 0·2386 |

IQR, interquartile range; CVD, cerebral vascular disease; HBP, hypertension; DM, diabetes mellitus; mRS, modified Rankin Scale; NIHSS, National Institute of Stroke Scale. Values are expressed as number (%) or median (IQR).
*Indicates statistical significance.

**Table 2 A comparison of the physical status and psychiatric assessment at 14 days and 3 months after ischemic stroke between patients with and without depression**

| | Non-PSD | | PSD | | |
|---|---|---|---|---|---|
| **Variables** | ***N* (%)** | **Median (IQR)** | ***N* (%)** | **Median (IQR)** | ***p* value** |
| At 14 days | | | | | |
| NIHSS | | 2·5 (1–4) | | 3 (2–7) | 0·1243 |
| mRS | | 2 (1–3) | | 2 (1–4) | 0·0242* |
| 0–1 | 50 (41·7) | | | 5 (16·7) | 0·0263* |
| 2–3 | 54 (45·0) | | | 18 (40·0) | |
| 4–5 | 15 (14·02) | | | 13 (43·3) | |
| MMSE | | 28 (26–29) | | 27 (26–29) | 0·1178 |
| Hamilton Depression Rating Scale | | 5 (2–9) | | 10 (5–14) | <0·001* |
| <8 | 86 (71·7) | | 16 (35·6) | | <0·001* |
| ⩾8 | 30 (25·0) | | 20 (44·4) | | |
| ⩾18 | 4 (3·3) | | 8 (17·8) | | |
| ⩾24 | 0 (0·0) | | 1 (2·2) | | |
| At 3 months | | | | | |
| mRS | | 1 (0–3) | | 2 (1–3) | 0·1613 |
| 0–1 | 69 (58·0) | | 19 (43·2) | | 0·2094 |
| 2–3 | 33 (27·7) | | 15 (34·1) | | |
| 4–5 | 17 (14·3) | | 10 (22·7) | | |
| MMSE | | 28 (25–29) | | 27 (25–29) | 0·1162 |
| HDRS | | 4 (2–8) | | 12·5 (10–23) | <0·001* |
| <8 | 81 (67·5) | | 6 (13·3) | | <0·001* |
| ⩾8 | 33 (27·5) | | 23 (51·1) | | |
| ⩾18 | 6 (5·0) | | 8 (17·8) | | |
| ⩾24 | 0 (0·00) | | 8 (17·8) | | |

MMSE, mini-mental state examination; HDRS, Hamilton Depression Rating Scale.
Values are number (%) or median (IQR).
*Indicates statistical significance.

(tenth revision) and *Diagnostic and Statistical Manual* (fourth edition) diagnostic systems[10]. Another advantage of using Composite International Diagnostic Interview is that both the lifetime and 12 month prevalence of depressive disorder can be determined, which allow us to identify patients who already had a depressive episode before the index stroke onset. To our knowledge, there were only three separate studies of PSD that employed WHO Composite International Diagnostic Interview for diagnosing depression[11,13,16]. Among those studies, only Morris and Robinson[16] employed a similar methodology as that used in the present work. According to their work from sampling a smaller patient population ($n$=99) than the current one ($n$=165), the prevalence of PSD was around 35% in patients at 2 months after stroke. Based on the majority of studies that sampled patients in Asia including Hong Kong area[17], Taiwan area[18], Japan[19], Malaysia and Thailand[17], the overall incidence of PSD was lower in Asian patients than in patients from Western countries (e.g. countries in Europe and America), especially of the major depression. According to the work of Kulkantrakorn and Jirapramukpitak[20], the lower incidence of PSD in Asian patients was partially due to the popular social networks in Asia and a higher level of psychological support to the elderly patients from their family members, which may help to reduce the incidence of PSD. In addition, negative life events and psychosocial stressors were also less common in Asian patients than that in Western patients. Yet, the phenomenon could also be due to differences in the social and cultural influences on the diagnosis of PSD in the two populations, as Asian patients tend to be less willing to admit abnormal mood symptoms than Western patients.

Our work suggests that some sociodemographic and clinical factors may correlate with the development of PSD. Consistent with several previous findings[17,21–23], female gender was found to be significantly associated with PSD and was an independent risk factor in the present work. Although this finding contradicts some previous observations[1,3], it agrees with a recent systematic review, which showed that the prevalence of depression was higher in women than that in men in 78% of the studies reviewed[9]. Reasons for the gender difference in PSD are not clear yet, but may include both genetic factors (e.g. differences in brain functioning and organization) and psychosocial factors.

Our work also suggests that a history of depression could predispose stroke patients to PSD. Indeed, a history of pre-stroke depression was identified as the strongest risk factor for PSD among all the variables included in our regression analysis. This finding strongly supports that observed by Storor and Byrne[11] and indicates that social–psychological factors may play a very important role in the pathogenesis of PSD. In order to identify the

**Table 3 Logistic regression analyses for predictive variables**

| Variables | *p* value | OR | 95% CI |
|---|---|---|---|
| Female gender | 0·0040 | 3·550 | 1·499–8·408 |
| Past history of depression | 0·0010 | 5·225 | 1·959–13·940 |
| mRS score at 14 days | 0·0066 | 1·607 | 1·141–2·262 |

OR, odds ratio; 95% CI, 95% confidence interval.

susceptible patient population for PSD, it would be meaningful for clinicians to use specific measurements (e.g. WHO Composite International Diagnostic Interview) to determine whether stroke patients had a history of depression or other similar psychiatric disorders. The depressed patients were also more severely handicapped at their early post-stroke period, as estimated from the mRS score in the present work. This finding is in line with those observed by others[24–26]. According to the logistic regression model, the level of handicap at 14 days after stroke was a predictor for the development of depression during the subacute period of ischemic stroke, yet the low stroke severity in patients included in the present work prevented us from detecting any association between the stroke severity and the development of PSD. In our work, depression tended to be more common in single, widowed or divorced patients than in married patients, indicating that social support from spouse is important and beneficial to stroke survivors.

At the 3 month follow-up exam, we found that only 24·4% of patients with PSD were taking antidepressant medication. Therefore, the importance of psychiatric examination to post-stroke patients should be emphasized, especially to female stroke patients and patients with either a significant disability or a history of prior depressive episodes. The psychiatric exam will help physicians to identify PSD early and to initiate prompt treatment to improve stroke outcomes.

Several potential limitations should also be addressed. First, we did not collect data from patients who had been excluded from the present work. This may give rise to the possibility of a subject selection bias. Second, factors that are also likely to influence the incidence of depression[25,27], including social support, pre-morbid personality and subcortical atrophy, were not controlled. Third, the exclusion of stroke patients with global aphasia, cognitive impairment or severe handicap limited our sample size and reduced the power of statistic analysis. Since a relatively small sample size for epidemiology study may limit the value of logistic modeling, a larger population cohort study in the future will help to consolidate current findings.

In conclusion, the present work from examining mainland Chinese patients with ischemic stroke suggests that (1) the 3 month cumulative incidence of PSD was 27·3%; (2) female gender, past history of depression and the level of handicap at 14 days after the stroke were three independent risk factors for PSD during the first 3 months after stroke; (3) PSD tended to be more common in single, widowed or divorced patients than in married patients.

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