

POST STROKE DEPRESSION IN REHABILITATION

Yookarajah UD¹, and Latiff L¹.

¹Department of Rehabilitation Medicine, Faculty of Medicine, University of Malaya, 50603 Kuala Lumpur, Malaysia

Correspondence:

*Uma Devi Yookarajah,
Department of Rehabilitation Medicine,
Faculty of Medicine,
University of Malaya, 50603 Kuala Lumpur, Malaysia
Email: yumadevi@yahoo.com*

Abstract

Depression is a frequent companion of stroke. It is associated with a degree of functional impairment that might adversely affect rehabilitation. A study was carried out to determine the rate of self-reported depression at admission and after six months, and the associated factors, in patients with stroke who were referred for rehabilitation. A multiple binary logistic regression was used to determine the associated factors at six months. Depression was recorded in 45% of patients at admission and in 39% at six months after the stroke. Patients who were employed, those who were depressed at admission, those who did not return to work and those who did not return to driving six months after stroke, were significantly associated with depression.

Keywords: Stroke, Depression, Rehabilitation, Malaysia

Introduction

Stroke, a major cause of death and disability, as defined by the World Health Organization was a clinical syndrome, with rapidly developing clinical signs of focal disturbance of cerebral function lasting more than 24 hours, or with a global disturbance in the comatous, and leading to death in some with no apparent cause other than a vascular origin. The definition would include subarachnoid

haemorrhage, intracranial haemorrhage, and cerebral infarction, but not a transient ischemic attack (TIA) (1).

Depression was a frequent companion of stroke, leading to functional impairment, associated adversely with the rehabilitation process and outcome (2). According to epidemiological studies, nearly 30% of patients with stroke developed depression, either in the early or in the later stages. Although depression could affect the functional recovery and quality of life after a stroke, it was often ignored. Only a minority of patients was diagnosed, and even fewer were treated clinically (3).

Depressive disorders included major depressive disorder, persistent depressive disorder, substance-induced depressive disorder and depressive disorder due to an associated medical condition. Each differed from the others, in duration, timing and aetiology (4). A diagnosis of major depression in an adult would require minimally two weeks of five or more symptoms, including symptoms of a depressed mood that lasted for most of the day or of a loss of interest or pleasure in almost all activities. Further symptoms might include significant weight loss or weight gain, changes in sleep patterns, psychomotor agitation or retardation, fatigue or loss of energy, feelings of worthlessness or inappropriate guilt, diminished ability to think or concentrate, with recurrent thoughts of death or suicide in some. The symptoms could result in clinically significant impairment in functioning socially, occupationally or others and would not be due to the direct physiological effects of a substance or a medical condition (4).

The essential features of depressive disorder due to an associated medical condition would be the presence of a depressed mood or a markedly diminished interest or pleasure in almost all activities that could be attributed to the direct physiological effects of the medical condition. It would also be evident from the history, physical examination or laboratory findings that the disturbance was the direct pathophysiological consequence of the medical condition (4). The study of depression in the research would be based on screening with a self-reported instrument using the Patient Health Questionnaire -9 (PHQ-9).

The potential risks during the handling of corpses

Stroke was one of the top five leading causes of death and one of the top ten causes of hospitalization in Malaysia (5). Local researchers had identified the risk factors for stroke and predictors of survival in stroke, the complications of stroke and the effectiveness of acute stroke management. Most studies had looked into post-stroke depression, and one study demonstrated that depression appeared to be as common among Malaysian stroke patients at three to six months after a cerebrovascular accident as among patients in other countries, there was, however, an absence of studies in a rehabilitation setting for post-stroke depression in Malaysia (5).

The primary objective of the study was to determine the rate of depression among stroke patients referred for rehabilitation, at admission and after six months of the stroke. The secondary objective was to examine the causes of depression after stroke and to identify factors associated with post-stroke depression.

Materials and Methods

Sample collection

A prospective observational study was conducted at the rehabilitation ward, neuro medical ward and rehabilitation clinic at the University Malaya Medical Centre, in Kuala Lumpur. Patients were recruited from March 2017 till December 2017, and the six-month follow-up was completed from September 2017 till June 2018.

Through a convenient sampling method, all stroke patients referred to rehabilitation with either inpatient admission to the rehabilitation ward or early supported discharge from the stroke ward were screened. Patients were recruited who fulfilled the inclusion criteria: a first stroke, a new-diagnosis of stroke, age 25 to 75 years, lesions identified on CT or MRI scan with either an ischemic or haemorrhagic stroke, and clinical evidence of sensory or motor impairment. Exclusion criteria included foreign nationality, dementia, aphasia or communication difficulties, recurrent stroke or TIA, prior psychiatric illness with mood disturbances, history of previous neurologic disease that affected the functional ability before the stroke, and history of substance abuse.

In the study, patients were divided into the age groups according to WHO classification: adults, 25-54 years old; prime working age, 55-64 years old; and mature working age, above 65 years. Subjects older than 75 years were excluded. The Oxfordshire Community Stroke Project classification (OCSP) was generally applied in ischemic stroke, even though its accuracy in discriminating stroke lesions

was debatable (6). The locations of stroke lesions were confirmed by CT or MRI scans.

The National Institutes of Health Stroke Scale (NIHSS) measured stroke severity, monitored the neurological outcome and predicted mortality risks during acute stroke treatment. Stroke severity was graded into the range of scores: 1-4, minor stroke; 5-15, moderate stroke; 16-20, moderate to severe stroke; and 21-42 severe stroke (7). The NIHSS score for the most severe neurological status within 24 hours to the 10th day after the onset of stroke was obtained.

The Modified Barthel Index (MBI) was used to measure the dependency level. The dependency level was graded into the range of scores: 100 independent; 91-99 mild dependency; 61-90 moderate dependency; 21-60, severe dependency; and 0-20 total dependency (8). The MBI scores at admission and six months post-stroke were recorded.

The Mini-Mental Status Examination (MMSE) was a useful cognitive screening tool. A cut-off score of below 27 indicated a person at risk of cognitive decline (9). The MMSE score in the study was calculated at admission following stroke.

The Patient Health Questionnaire (PHQ-9) was used in screening for depression. Two versions were used, the English and the validated Malay version (10). It was reported that the sensitivity and specificity for PHQ-9 were 77% and 94% respectively, to detect depression. Previous studies had shown that the PHQ-9 was a valid diagnostic

tool if used in selected sub-groups of patients with a high prevalence of depressive disorder (11).

A successful return to work was defined as being able to work for one month or more with paid employment either on a full-time or part-time basis (12).

A return to driving post-stroke remained an important issue, as patients who had survived a stroke were frequently eager to resume their previous lifestyle. The decision to return or not to return to driving could be made independently and voluntarily or could be assisted with direct observation and evaluation through a driving assessment. For persons with a stroke who wished to return to driving, many would normally have to complete a driving assessment (13).

Data analysis

Using SPSS version 23, socio-demographic data were analysed through descriptive analysis. A multiple binary logistic regression model analysis was performed to determine the association between the multiple factors for the independent variables; and the Patient Health Questionnaire-9; (PHQ-9) for the dependent variables. Among other factors, the association of a return to driving and a return to work, with PHQ-9 were analysed using the Fisher Exact Test with a statistical significance at $p < 0.05$.

Results

Demographic characteristics of respondents

One hundred and twenty-eight patients, referred to rehabilitation with a first-ever stroke, were identified prospectively for the study and eighty were recruited at admission.

The demographic data and stroke onset characteristics for these patients were summarized in Table 1.

“INSERT TABLE 1 HERE”

Figure 1 showed the admission data. Of these 80 patients, 28 patients (35%) had mild to moderate depression with a PHQ-9 score of 5-14 while eight patients (10%) had moderate to severe depression with a PHQ-9 score of 15-27. At the six-month review, there were 64 patients for analysis as three patients had died, two patients had developed recurrent strokes, while 11 patients were lost to follow-up.

“INSERT FIGURE 1 HERE”

Table 2 showed that at admission, 28 out of 80 patients (35%) had mild to moderate depression with a PHQ-9 score of 5-14 while only eight patients (10%) had moderate to severe depression with a PHQ-9 score of 15-27. Of the 64 patients who were followed-up at six months, 24 patients (37.5%) had mild to moderate depression with a PHQ-9 score of 5-14 and one patient (1.5%) had moderate to severe depression with a PHQ-9 score of 15-27.

Table 3 showed that at admission, 42 out of 80 patients (52.5%) had a moderate dependency level, 30 patients (37.5%) had a severe dependency level, six patients

(7.5%) had a mild dependency level, and two patients (2.5%) had a total dependency level. Upon review at six months, most patients had improved in terms of the dependency level and a majority of them, 31 patients out of 64 patients (48.4%) had a mild dependency level, with an MBI score of 91-99. There were 27 patients (42.2%) with a moderate dependency-level indicated by an MBI score of 61-90. There were reduced numbers of patients with a severe dependency level with an MBI score of 21-60 compared to the patients seen during admission with a count of six patients, 9.4%. None of the patients had a total dependency level (MBI score 0-20).

Of the 35 patients who were not depressed at admission, eight patients (22.8%) became depressed at six months, while 27 patients (77.2%) remained not depressed. On the other hand, of the 29 patients who were depressed at admission, 17 patients (58.6%) remained depressed, but 12 patients (41.4%) became not depressed at six months.

Table 5 showed the logistic regression, performed to assess the factors associated with depression at six months after a first-ever stroke. Patients who were initially employed were more significantly depressed at six months (COR 4.55, p-value = 0.008) than those who were not employed. Patients who were breadwinners were also significantly more depressed at six months (COR 3.18, p-value = 0.030) than those who were not breadwinners. Other factors associated with depression at six months were patients with haemorrhagic stroke (COR 10.41, p-value = 0.005) who were more depressed than those with ischaemic stroke; and patients with

depression at admission (COR 4.78, p-value = 0.005) who became more depressed than those without depression at admission.

Multiple binary logistic regression was used for the significant variables of employment, breadwinner, stroke type, and depression at admission. Using Forward and Backward Logistic Regression, two variables were found to be significant (Table 6). These variables were patients who were employed (AOR 7.50, 95% CI 1.86 – 30.22, p-value = 0.005), and patients with depression at admission (AOR 4.64, 95% CI 1.31 – 16.40, p-value = 0.017).

No significant interaction and multicollinearity were found. Classification table was 76.6% with Nagelkerke R Square of 0.441. Hosmer Lemeshow Goodness of Fit test was not significant with p = 0.334.

Association between a return to drive at 6 six months and depression

Of the 64 patients followed-up at 6 six months post-stroke, there were 51 patients (79.7%) who were driving before the stroke and 13 patients (20.3%) who did not drive before the stroke. At six months post-stroke, of the 51 patients who drove, 12 patients (23.5%) had returned to driving while 39 patients (76.5%) had stopped driving. Table 7 showed that of the 39 patients who did not return to driving six months post-stroke, 20 patients (51.3%) were depressed, and 19 patients (48.7%) were not depressed. However, among the 12 patients who returned to driving, none were depressed.

Using Fisher's Exact test, p -value = 0.001, patients who did not return to driving at six months post-stroke were significantly more depressed than the patients who returned to driving.

Association between return to work at-6 six months and depression

Of the remaining 64 patients at six months after stroke, 35 patients (54.7%) were working, and 29 patients (45.3%) were not working. Of the 35 patients who had been working before the stroke, 12 patients (34.3%) had returned to work while 23 patients (65.7%) had not returned. Table 8 showed that of these 23 patients (65.7%), 18 patients (78.3%) were depressed, and only five patients (21.7%) were not depressed. On the other hand, of the 12 patients who returned to work after six months post-stroke, 11 patients (91.2%) were not depressed, and only one (8.8%) was depressed.

Using Fisher's Exact Test, p -value < 0.001, patients who did not return to work at six months were more significantly depressed than patients who returned to work.

Discussion

This was the first study reported on the frequency of depression among patients with stroke in rehabilitation settings in Malaysia. This study employed the self-reported depression instrument, the Patient Health Questionnaire-9 (PHQ-9).

At admission, 45% of the 80 patients recruited into the study were depressed, and at the follow-up after six months, 39% of the remaining 64 patients were depressed.

These figures were in contrast to the frequency of post-stroke depression of 27% to 55% reported by Gaete et al. (14), in a systematic review of post-stroke depression in rehabilitation, and where the prevalence rates after six months, were similar to those found in the acute stroke phase.

By re-assessing the patients at six months, an improvement in depression could be observed. The moderate rate of depression seen in the study could be associated with the setting of the study itself. The majority of the patients enrolled in the study, at the University Malaya Medical Centre, came to or lived near the city of Kuala Lumpur. The city had more established disability rehabilitation facilities and healthcare services than the other cities in Malaysia. More patients with depression after stroke could be detected and treated compared to those in the other cities and the rural areas, which also lacked rehabilitation and speciality healthcare services.

At admission, the majority of patients had a moderate dependency-level (52.5%), but at six months post-stroke most patients had only a mild dependency level (48.4%). The improvement in the dependency level at six months could explain the drop of depression rate from 45% at admission to 39%.

Of the 45% of patients who were depressed at admission, 35% had mild to moderate depression, and 10% had moderate to severe depression. These findings were similar to an earlier study done by Karamchandani et al. (15), where 35.44% of patients were screened positive for depression with a score > 4 and 12% of patients had moderate to severe depression.

A discrepancy in the rate of depression could also be related to the study methodology. The definition of depression, whether minor or major and the different measures used to diagnose or report depression, could explain the difference in the rate of depression with earlier studies.

Of the 35 patients (54.7%) who were not depressed at admission, eight patients (22.8%) became depressed at six months while 27 patients (77.2%) remained not depressed. These findings were higher compared to the study by De wit et al. (16), where about 7% of those initially not depressed became depressed six months after stroke. Moreover, of the 29 patients (45.3%) who were depressed at admission, 17 patients (58.6%) remained depressed, and 12 patients (41.4%) recovered from their depression at six months. De wit et al. (16) found that 40% of the patients with initial depression remained depressed at six months.

Alajbegovic et al. found that depression after stroke was more frequent in younger patients, female patients, patients with localized stroke in the left hemisphere and patients with a higher disability score (17). Gaete et al. found that emotional lability during the first few days after stroke and social factors, like living alone were associated with depression after stroke (8). Burvill et al. in their study found that living in a nursing home, being divorced and having high alcohol intake pre-stroke were risk factors for depression post-stroke. However, in this study, factors associated with depression at six months were being employed before the stroke and depression at admission. Other factors associated with depression at six months

included the inability to return to driving or work. These factors of employment and a return to driving and work had not been described and explored in the earlier studies. Patients who were previously employed and were unable to return to work could have financial demands and suffer higher economic pressures after stroke, thereby, predisposing them to depression.

The study had several limitations. There were 128 patients initially, but only 80 fulfilled the inclusion criteria and were enrolled. At the review at six months, there were only 64 patients. The high dropout rate could cause a selection bias in the study. However, the number of patients was still comparable to the study by Gaete et al., with 80 patients at admission and 74 patients at a three-month review. Measures were taken in the study to reduce the number of patients lost to follow-up. Patients were seen during their clinic appointments. New replacement dates were given to those who missed their appointments. However, the study was confined only to patients who were referred for rehabilitation and would have missed patients with mild stroke not referred for rehabilitation and who were given an early discharge from the stroke wards. Finally, with the strict eligibility and exclusion criteria of cognition, recurrent strokes, English and Malay-based outcome measures, many patients were excluded leading to a longer duration for the recruitment phase.

Conclusion

The rate of depression in patients with stroke in the study was 45% at admission and 39% at six months after the stroke. Being employed before the stroke, being

depressed at admission, an inability to return to work or driving at six months after stroke were the leading causes of depression.

A definitive psychiatric diagnosis for depression was not a requirement for the study. Instead, the easier and more efficient self-reported depression screening was used in identifying the depressed patients as depression led to a poor prognosis for physical and functional recovery, screening for depression at all stages would be vital for an early detection and appropriate management to improve the quality of life and prevent a further negative impact on the rehabilitation process.

Acknowledgement

Competing interests

The authors declare that they have no competing interests.

Ethical Clearance

We obtained approval from the Medical Research and Ethics Committee (MREC) and the Ministry of Health Malaysia (MOH), registered under NMRR-19-2585-47819.

References

<double check the reference list here, must be cited in the text, vice versa>

1. Feigin VL, Lawes CM, Bennett DA, Barker-Collo SL, Parag V. Worldwide stroke incidence and early case fatality reported in 56 population-based studies: a systematic review. *Lancet Neurol*. 2009;8(4):355-69.
2. El Hussein N, Goldstein LB, Peterson ED, Zhao X, Olson DM, Williams Jr JW, *et al*. Depression Status Is Associated with Functional Decline Over 1-Year Following Acute Stroke. *J Stroke Cerebrovasc Dis*. 2017;26(7):1393-9.
3. Paolucci S. Epidemiology and treatment of post-stroke depression. *Neuropsychiatr Dis Treat*. 2008;4(1):145
4. American Psychiatric Association. Diagnostic and statistical manual of mental disorders (DSM-5®). American Psychiatric Pub; 2013;155-233.
5. Loo KW, Gan SH. Burden of stroke in Malaysia. *Int J Stroke*. 2012; 7(2):165-7.
6. Asdaghi N, Jeerakathil T, Hameed B, Saini M, McCombe JA, Shuaib A, *et al*. Oxfordshire community stroke project classification poorly differentiates small cortical and subcortical infarcts. *Stroke*. 2011;42(8):2143-8.
7. Williams LS, Yilmaz EY, Lopez-Yunez AM. Retrospective assessment of initial stroke severity with the NIH Stroke Scale. *Stroke*. 2000;31(4):858-62.
8. Quinn TJ, Langhorne P, Stott DJ. Barthel index for stroke trials: development, properties, and application. *Stroke*. 2011;42(4):1146-51.
9. O'Bryant SE, Humphreys JD, Smith GE, Ivnik RJ, Graff-Radford NR, Petersen RC, *et al*. Detecting dementia with the mini-mental state examination in highly educated individuals. *Arch Neurol*. 2008;65(7):963-7.
10. Azah MN, Shah ME, Juwita S, Bahri IS, Rushidi WM, Jamil YM. Validation of the Malay Version Brief Patient Health Questionnaire (PHQ-9) among Adult Attending Family Medicine Clinics. *Int Med J*. 2005; 12(4):259-63.
11. Wittkamp KA, Naeije L, Schene AH, Huyser J, van Weert HC. Diagnostic accuracy of the mood module of the Patient Health Questionnaire: a systematic review. *Gen Hosp Psychiatry*. 2007;29(5):388-95.
12. Saeki S, Ogata H, Okubo T, Takahashi K, Hoshuyama T. Return to work after stroke: a follow-up study. *Stroke*. 1995; 26(3):399-401.
13. Marshall SC, Molnar F, Man-Son-Hing M, Blair R, Brosseau L, Finestone HM, Lamothe C, *et al*. Predictors of driving ability following stroke: a systematic review. *Top Stroke Rehabil*. 2007;14(1):98-114.
14. Gaete JM, Bogousslavsky J. Post-stroke depression. *Expert Rev Neurother*. 2008;8(1):75-92.
15. Karamchandani RR, Vahidy F, Bajgur S, Vu KY, Choi HA, Hamilton RK, *et al*. Early depression screening is feasible in hospitalized stroke patients. *PLoS one*. 2015;10(6):e0128246.
16. De Wit L, Putman K, Baert I, Lincoln NB, Angst F, Beyens H, *et al*. Anxiety and depression in the first six months after stroke. A longitudinal multicentre study. *Disabil Rehabil*. 2008;30(24):1858-66.
17. Alajbegovic A, Djelilovic-Vranic J, Alajbegovic S, Nakicevic A, Todorovic L, Tiric-Campara M. Post stroke depression. *Med Arch*. 2014;68(1):47.

Online article:

1. Eric BT. Cardiomyopathy workup. Theheart.org on Medscape. 2019. Available at: <https://emedicine.medscape.com/article/1513631-workup>. Accessed 19 May 2020.

2. World Health Organisation. Broken hearts don't self-heal. 2017. Available at: <https://www.abdn.ac.uk/news/10884/>. Accessed 19 May 2020.
3. Thailand International Cooperation Agency, Ministry of Foreign Affairs. Sufficiency economy philosophy. 2019. Available at: <http://www.tica.thaigov.net/main/en/information/7107>. Accessed 12 August 2020.

Journal article:

1. Said M, Saygili S, Rana ER, Genz O, Hahn C, Bali J, *et al.* **Cardiomyopathy: what we have learned in the last 25 years? A comparative literature review.** *Curr Cardiol Rev.* 2016;12(4):291-7.
2. Sachdev E, Merz CN, Mehta PK. Takotsubo Cardiomyopathy. *Eur Cardiol.* 2015;10(1):25-30.

Book:

1. Uppu RM, Murthy SN, Pryor WA, Parinandi NL. Free Radicals and Antioxidant Protocols. 2nd Ed. Mumbai, India: Humana Press. 2010.
2. Castles S, Miller MJ. **The Age of Migration: International Population Movements in the Modern World.** 5th Ed. London, England: Macmillan. 1998.

Author. Book title. Edition. City, State/Country: Publisher. Year.

Book Chapter

1. Benton G, Gomez ET. **Belonging to the nation: generational change, identity and the Chinese diaspora.** In: Gomez ET, Benton G, eds. **Belonging to the Nation: Generational Change, Identity and the Chinese Diaspora.** New York, United States: Routledge. 2015:1-14.
2. Joly D. Introduction. In: Danièle J, ed. International Migration in the New Millennium: Global Movement and Settlement. Burlington, VT: Ashgate. 2004:1-11.
3. Harris N. **The economics and politics of the free movement of people.** In: Pècoud A, De Guchteneire P, eds. **Migration without Border: Essays on the Free Movement of People.** 1st Ed. New York, USA: UNESCO. 2007:33-50.

Author. Chapter title. Editors. Book title. Edition. City, State/Country: Publisher. Year:page number.

Thesis

1. Wang Y. Roles of macrophage mitochondrial oxidative stress and mitochondrial fission in atherosclerosis. Thesis. Columbia: Columbia University Libraries. 2014.

Table 1: Demographic data and stroke onset characteristics

	Frequency	Percentage
Demographics	n = 80	
Age groups		
25-54	30	37.5
55-64	31	38.8
65-75	19	23.8
Gender		
Male	50	62.5
Female	30	37.5
Ethnic group		
Malay	34	42.5
Chinese	29	36.3
Indian	15	18.8
Others	2	2.5
Marital status		
Single	12	15.0
Married	62	77.5
Divorced/Widower	6	7.5
Educational level		
Primary	14	17.5
Secondary	55	68.8
Tertiary	11	13.8
Employment status		
Employed	47	58.8
Unemployed	33	41.3
Bread winner		
Yes	38	47.5
No	42	52.5
Stroke type		
Ischemic	66	82.5
Haemorrhagic	14	17.5
Stroke location		
Left hemisphere	36	45.0
Right hemisphere	40	50.0
Posterior circulation	4	5.0
Stroke severity (NIHSS)		
Mild to moderate (1-15)	67	83.8
Moderate to severe (16-42)	13	16.3
Dependency level (MBI)		
Mild (91-99)	6	7.5
Moderate (61-90)	42	52.5
Severe (21-60)	30	37.5

Total dependency (0-20)	2	2.5
Cognition (MMSE)		
Normal (27-30)	42	52.5
Mild (21-26)	38	47.5
Do you drive prior to stroke		
Yes	51	79.7
No	13	20.3
Do you work prior to stroke		
Yes	35	54.7
No	29	45.3
Depression at admission (PHQ-9)		
No depression (1-4)	44	55.0
Mild to moderate depression (5-14)	28	35.0
Moderate to severe depression (15-27)	8	10.0

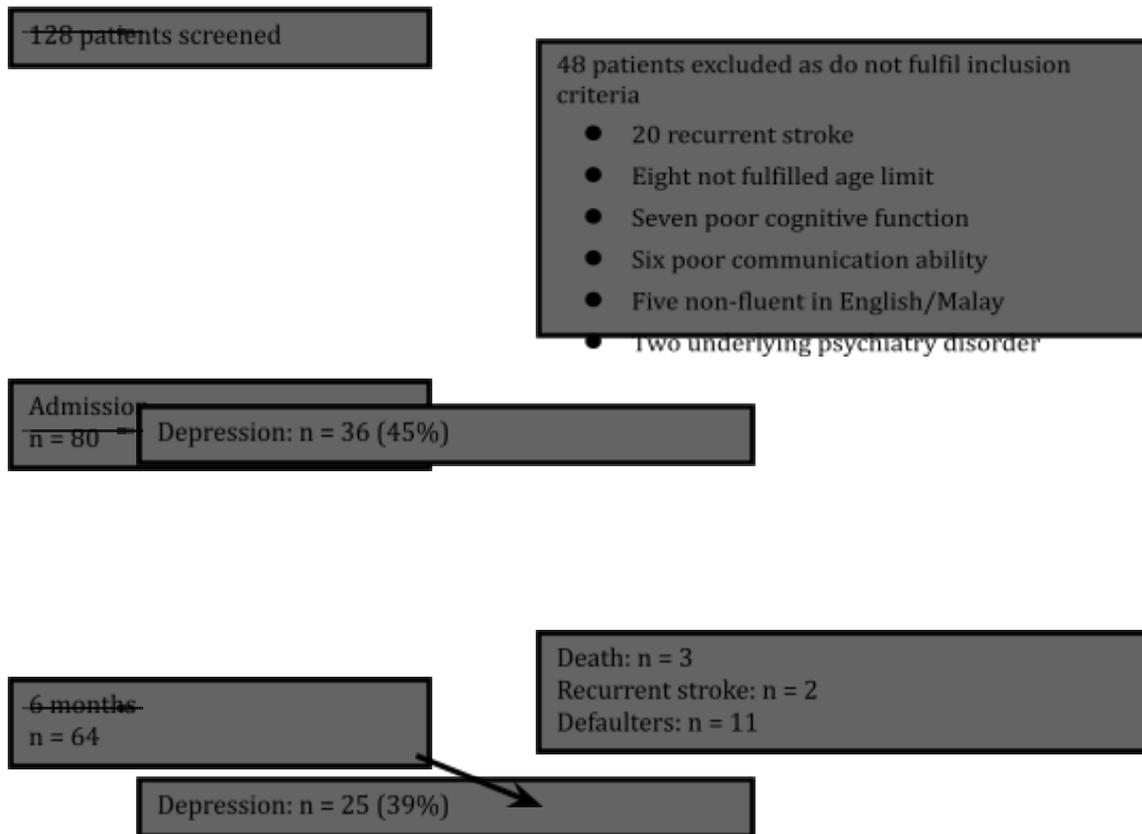


Figure 1: Flow chart showing the number of patients and outcomes at each follow-up