



## INTERNATIONAL JOURNAL OF RESEARCH SCIENCE & MANAGEMENT ASSOCIATION BETWEEN HEMISPHERE LESION LOCATION AND LEVEL OF DEPRESSION IN ISCHEMIC STROKE PATIENTS

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### Abstract

**Introduction:** Depression is a common post-stroke complication. Nearly 30% of post-stroke patients can develop depression, either in the early or late stages. Specific locations of lesions in the brain, including hemispheric lesions is said to have a close relationship with the occurrence of post-stroke depression.

**Aim:** To determine the relationship between the location of hemispheric lesions in ischemic stroke patients and level of post-stroke depression.

**Methods:** This cross-sectional study was conducted at Adam Malik and USU Hospital in November 2018 to January 2019 consecutively for 40 ischemic stroke patients who met inclusion criteria. Patients were subjected to history and assessment of depression levels based on DSM -V and BDI-II questionnaire. Data was analyzed using Chi-square and Annova tests.

**Results:** Of 20 right hemisphere lesions patients, 9(45%) had mild, 7(35%) moderate, and 4(20%) severe depression. While 20 left hemisphere lesions patients, 3(15%) had mild, 5(25%) moderate, and 12(60%) severe depression. There was a significant relationship between location of hemispheric lesions and level of depression in ischemic stroke patients where left hemisphere lesions were at higher risk for more severe depression ( $p=0.026$ ).

**Conclusion:** Left hemisphere lesions can be a predictive factor in the occurrence of severe post-stroke depression in ischemic stroke patients.

### Introduction

Depression is a mood disorder characterized by depressive mood, losing of enthusiasm, experiencing cognitive distortions such as decreased self-confidence, feelings of guilt and uselessness, thoughts about a bleak future, pessimistic, hesitant, impaired memory, and bad concentration. Depression related to stroke is called post-stroke depression. The prevalence of post-stroke depression ranges from 11-68%, far higher than the prevalence of depression found in the general population.

Stroke is the leading cause of death in the world after ischemic heart disease. The Indonesian Ministry of Health obtained data on 987.205 subjects from 258.366 households in 33 provinces showed that stroke was the leading cause of death at age more than 45 years old (15.4% of all deaths)[1]. There are several factors that determine the prognosis of ischemic stroke, one of which is the location of the lesion or infarction.[2]

There are several theories regarding post-stroke depression. The first theory states that post-stroke depression is a psychological reaction to the clinical consequences caused by stroke. Whereas the second theory states that post-stroke depression occurs due to specific lesions in the brain.[3] In this study, the authors aim to study the relationship between the location of ischemic stroke hemisphere lesions and the degree of post-stroke depression.



## Methods

### Data Collection

By using cross-sectional study, the study was conducted at tertiary care hospital, Adam Malik General Hospital and USU (University of Sumatera Utara) General Hospital in Medan, Sumatera Utara, Indonesia from November 2018 to January 2019. Outpatients aged over 18 years old who had prior ischemic stroke minimal within 2 weeks of onset were included in the study. Based on lesion location of ischemic stroke, patients were divided into 2 group equally, left hemispheric lesion and right hemispheric lesion. The two groups were then interviewed based on the Diagnostic of Statistical Manual of Mental Disorder Fifth (DSM-V) to assess depressive symptoms and were given a Beck Depression Inventory (BDI-II) questionnaire to assess the degree of depression. Only depressive patients were included and grouped into three categories based on severity: mild (BDI-II score 14-19), moderate (score 20-28), and severe (score 29-63). The exclusion criteria were patients with impaired consciousness at the time of examination, with a history of previous depression prior the onset of stroke, and who cannot understand the contents of the BDI-II questionnaire. The relationship of hemispheric lesion location and level of depression were analyzed. The study was approved by the institutional ethics committee and all subjects gave written informed consent. Demographic characteristics of the patients are shown in Table 1.

### Statistical Analysis

All data were analyzed using statistical package SPSS (version 25, SPSS, Chicago, IL, USA). Baseline characteristics were described as number and percentage for categorical data; and as mean and standard deviation for numerical data with normal distribution; and median with minimal to maximum range for numerical data without normal distribution. The relationship between variables (demography data, lesion location) and level of depression were tested with chi-square test for categorical data and one-way Anova for numerical data. A  $p < 0.05$  was considered to indicate statistical significance.

## Results

### Characteristics of research subjects

Of all stroke patients who went for outpatient care at H. Adam Malik General Hospital and USU Hospital, Medan in the period November 2018 to January 2019, 40 ischemic stroke patients were found to have met the inclusion criteria and were included in the study. Out of 40 subjects, there are 19 men (47.5%) and 21 women (52.5%). All subjects had an age range of 29-80 years, with an average age of 61.35 years  $\pm$  9.936 SD. Most subjects were married (77.5%), Bataknese ethnic group (70.0%), had high level of education (high school 50%), housewives or government employees (37.5%, 20% respectively).

According to BDI-II questionnaire, median BDI score was 25.5, ranging from 14 to 35. Depression levels based on BDI-II scores were found to be 12 subjects with mild (30.0%), 12 subjects with moderate (30.0%), and 16 subjects with severe depression (40.0%). Based on the location of the hemisphere, the proportions are divided equally. Meanwhile, based on CT-scan results most lesions were found in the basal ganglia (47.1%), parietal lobes (20.8%), periventricular (15.1%), temporal lobes (11.3%), occipital lobes (3.8%) and frontal lobes (1.9%). None other lobes or specific location were mentioned on CT-scan results. Based on the number of lesions, 21 respondents (52.5%) had multiple lesions (regarding  $\geq 2$  lobes involved) and 19 respondents (47.5%) had single lesion (regarding 1 lobe involved). Researchers did not calculate the extent of infarction lesions.

*Table 1. Baseline characteristics of post-stroke depression patients*

Variable	n=40	(%)	p-Value
Gender			0.539
Male	19	(47.5)	
Female	21	(52.5)	
Age (years) <sup>a</sup>	61,3	$\pm$ 9.936	0.073
Marriage status			0.625
Single	1	(2.5)	

*Table 1. Baseline characteristics continue*

Variable	n=40	(%)	p-Value
Widower	8	(20.0)	
Married	31	(77.5)	
Ethnic group			0.625
Bataknese	28	(70.0)	
Javanese	9	(22.5)	
Nias	1	(2.5)	
Acehnese	2	(5.0)	
Level of education			0.111
Elementary school	3	(7.5)	
Junior school	4	(10.0)	
High school	20	(50.0)	
College	13	(32.5)	
Occupation			0.111
Government employees	8	(20.0)	
Private employees	1	(2.5)	
Entrepreneur	5	(12.5)	
Retired	5	(12.5)	
Housewife	15	(37.5)	
Farmer	3	(7.5)	
Unemployed	3	(7.5)	
BDI <sup>b</sup>	25.5	(14-35)	
Depression level			
Mild	12	(30.0)	
Moderate	12	(30.0)	
Severe	16	(40.0)	
Lesion location based on hemisphere			
Right hemisphere	20	(50.0)	
Left hemisphere	20	(50.0)	
Lesion location based on CT scan			
Temporal lobe	6	(11.3)	
Basal ganglia	25	(47.1)	
Parietal lobe	11	(20.8)	
Frontal lobe	1	(1.9)	
Periventricular	8	(15.1)	
Occipital lobe	2	(3.8)	
Number of lesions			
Single (1 lobe)	19	(47.5)	
Multiple ( $\geq 2$ lobes)	21	(52.5)	

<sup>a</sup> mean  $\pm$  standard deviation<sup>b</sup> median (minimum – maximum range)



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**Association between lesion location and number of lesions with depression level in ischemic stroke patients**

A chi-square test was performed to assess the association between the level of depression and the location of the lesion based on the hemisphere, affected lobes, and number of lesions. P results obtained for each value of 0.026; 0.742; and 0.664. It can be concluded that there was a significant association between the location of the affected hemisphere and the level of depression of post-stroke patients, but there were no association between affected lobes and number of lesions with depression level of the patients.

**Table 2. Association between lesion and depression level**

Variable	Mild		Moderate		Severe		p-Value
	n	%	N	%	n	%	
<b>Lesion location based on hemisphere</b>							
Right hemisphere	9	45.0	7	35.0	4	20.0	0.026*
Left hemisphere	3	15.0	5	25.0	12	60.0	
<b>Lesion location based on CT scan results</b>							
Temporal lobe	3	50.0	1	16.7	2	33.3	0,742
Basal ganglia	6	24.0	9	36.0	10	40.0	
Parietal lobe	5	45.5	1	9.1	5	45.5	
Frontal lobe	0	0	1	100	1	100	
Periventricular	3	37.5	2	25.0	3	37.5	
Occipital lobe	0	0	1	50.0	1	50.0	
<b>Number of lesions</b>							
Single (1 lobe)	5	23.8	7	33.3	9	42.9	0,664
Multiple ( $\geq 2$ lobes)	7	36.8	5	26.3	7	36.8	

\* p-value is significant  $<0.05$

**Multiple comparison within groups of depression level with hemisphere location**

In this study, the Anova test was carried out to find the association between the depression level and lesion location based on the hemisphere. The results show that there was a statistically significant relationship between the level of depression and the affected hemisphere ( $p = 0.025$ ). The test was continued with post hoc Bonferroni to compare between the depression level groups (mild, moderate, severe depression) with the affected hemisphere. On table 3, there was a significant relationship between mild and severe depression on the location of hemisphere lesions ( $p = 0.025$ ). However, there was no association between mild-moderate depression and moderate-severe depression with the location of the hemisphere ( $p = 1.000$ ;  $p = 0.213$ ).

**Table 3. Multiple comparisons within groups of depression level**

Depression Level	p-Value
Mild – moderate	1,000
Mild – severe	0,025*
Moderate – severe	0,213

\* The mean difference is significant at the 0.05 level.

**Discussion**

In this study, the average age of post-stroke depression patients was 61.3 years  $\pm$  9.936 (elderly). Chi-square test results showed that there was no significant age difference between mild, moderate and severe depression. These results are in line with the DESTRO study[4], where the average age of post-stroke depressed patients was 67.35  $\pm$  12.13 years and age was not a significant factor in the severity of post-stroke depression. Age is a risk factor for stroke that cannot be manipulated. One hypothesis that is increasingly being developed today is the concept of vascular depression in which chronic ischemic damage is an important cause of depression in geriatrics. This concept initially arose from the findings of patients with slow onset depression having higher levels of encephalomalacia or hyperintensity observed with MRI compared with patients with early onset



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depression. Hickie et al.[5] and Alexopoulos et al.[6] hypothesized that cerebrovascular disease could be a predisposing factor, precipitation of depressive syndrome at an older age.

This study found no significant relationship between ethnicity, marital status and education level with the level of depression. Burvil et al.[7] stated that the proportion of depressed individuals was higher in divorce status (40%) or separation (33%) compared to those who were single (21%), married (20%) or widowed (28%). A study in India by Srivastava et al.[8] was closer to the demographic profile in this study where marital status was more prevalent in patients suffering from post-stroke depression even though it was not statistically significant. Some other studies also showed that the length of study > 8 years was not significantly related to post-stroke depression [9], [4]. Therefore, it can be concluded that socio demographic profiles such as sex, age, ethnicity, marital status, and education level can be removed as confounding factors in this study.

According to Robinson et al. study [2], major depression in the post-stroke period showed a significant association with characteristics of localization and dexamethasone suppression tests. A preliminary PET scan study showed an increase in sensitivity of cortical serotonin receptors among patients who had a stroke in the right hemisphere compared with the left so that there was a suspected lateral link with post-stroke depression. In this study, patients with lesions in the left hemisphere tended to get three times more severe depression compared to the right (60% vs 20%). This is likely because the left hemisphere is the dominant hemisphere responsible for emotional and language centers, and deficit in the left hemisphere is more serious in stroke patients according to radiology studies. Furthermore, it is said that the pathophysiology of major depressive disorder involves the limbic-cortical-striatal-pallidal-thalamic circuit (LCSPT). Terroni et al. [10] reported that among patients with ischemic stroke, larger lesions in the left cortical region of the LCSPT circuit were associated with a higher incidence of major depressive episodes.

Until now, there is still debate about the relationship between lesion location and post-stroke depression. Berg et al. [11] in 2003 who studied about stroke lesions in the left hemisphere and brainstem found the severity of stroke was related to depression. Choi-Kwon S, et al. [12] in 2012 state that the location of the lesion is associated with emotional changes in acute and sub-acute stroke patients. Wu RH, et al. [13] in 2014 further found that micro hemorrhage in the left hemisphere and basal ganglia was an independent risk factor for slow onset depression. Even in a meta-analysis study by Shi Y, et al. [14] and also supported by Vataja et al. [15] and Rajashekar et al. [16], showed that damage in the left hemisphere has a strong association with depression post stroke in the acute and subacute stages.

In addition to studies comparing the two hemispheres, other studies have also tried to look at the relationship between affected lobes and post-stroke depression. Several studies have shown the presence of lesions in the frontal lobe, basal ganglia and temporal lobes associated with post-stroke depression. Glodzik-Sobanska L, et al. [17] and Shi Y Z, et al. [14] suggest that lesions in the frontal lobe are associated with persistent or recurrent post-stroke depression. It is suspected that there is a relationship between depression and the subcortical frontal pathway where this pathway is responsible for emotional and behavioral control. Wu RH, et al. [13] also found that lacunar infarction in the basal ganglia is associated with a higher risk for depression. Metoki et al. [9] state that infarction in the frontal and temporal lobes is an independent risk factor for early depressive symptoms in the acute stroke stage. In this study, most subjects were affected in the basal ganglia, but there was no significant relationship between affected lobes and post-stroke depression. This may be due to uneven proportion of samples between specific anatomic lesions.

This study has several limitations. Researchers only assessed the location of the infarction lesions seen on the head CT-scan investigations, whereas many stroke sufferers had lacunar infarction which was sometimes not seen on head CT scan. The size of the infarction lesion and the duration of stroke were not assessed in this study.

### Conclusion

Left hemisphere lesions can be a predictive factor in the occurrence of more severe post-stroke depression compared with right hemisphere lesions in ischemic stroke patients. This study reaffirms previous research



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which states that there is a biological causal relationship in addition to psychological causal (psychosocial factors of patients) to the occurrence of post-stroke depression. Nearly one third of cases of ischemic stroke that have passed the acute phase can develop into post-stroke depression. Patients with ischemic stroke regarding lesions in the left hemisphere and multiple lesions are more at risk for depression so early screening needs to be done especially if the patient shows changes in mood, loss of interest, and other symptoms of depression in follow up. Delay in handling post-stroke depression will cause a decrease in quality of life and slow down the rehabilitation process.

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