

Positive Correlation between Left Hemisphere Lesion and Erectile Dysfunction in Post-Stroke Patients

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Abstract

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BACKGROUND: Stroke is a serious health condition and the leading cause of disability, including erectile dysfunction (ED). The mechanisms and factors that predict ED in stroke are not fully elucidated. Several studies have shown a relationship between the location of the lesion in stroke with the onset of ED. The left hemispheric lesion was believed to disrupt the parasympathetic nervous system which is responsible for the regulation of erection. Stroke attack in this region therefore can be the underlying reason for ED. However, there are still contradictory findings in this area, and very few studies attempted to look at this problem, particularly among Asian male.

AIM: We would like to evaluate the association between left hemisphere lesion after ischemic stroke and the subsequent risk of developing ED.

METHODS: The study was conducted in the neurology polyclinic of Sanglah and Wangaya Hospital from February to August 2013. Subjects are all post-stroke patients who visited the neurology polyclinic of Sanglah and Wangaya Hospital that met inclusion and exclusion criteria.

RESULTS: There is a significant positive correlation ($p < 0.05$) between left hemisphere lesions and ED in stroke patients with a correlation coefficient ($r = 0.361$) which means weak correlation and $p = 0.032$.

CONCLUSION: Left hemisphere lesions positively correlated with ED in stroke patients. Further longitudinal research is needed to see whether left hemisphere lesion in post-stroke patients is a risk factor for ED.

Introduction

Stroke is a serious health condition in which late and inadequate treatment leads to death in a short amount of time. Stroke is also one of the leading causes of permanent disability such as paralysis, speech difficulty, and facial drooping, and this gives a morbid perception of stroke in society.

According to the World Health Organization (WHO) Multinational Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA) Project in 1988, stroke is clinical syndrome with symptoms of focal or global disturbance of brain function, lasting 24 hours or longer, or resulting in death less than 24 hours, with no apparent cause other than of vascular origin [1]. Stroke is the third leading cause of death in the world with an incident of 5.5 million persons per year and is responsible for 50

million disability-adjusted life years (DALY) [2]. In the next 20 years, stroke is predicted to increase from its current position in the DALY table, from 7th to 4th [3].

Epidemiology studies in developed countries have shown that the number of deaths caused by stroke is proportional to the number of deaths caused by heart disease. A systematic review of literature published from 1980 to 2010 has shown the incidence of stroke in Southeast Asia varies from 123-145 per 100,000 persons with a prevalence of 45-471 per 100,000 [4]. Based on a community-based survey in 120 regions in Indonesia with a total of 4, 269, 629 samples, a prevalence of 1.7-2.2 per 100,000 [5].

Stroke increasingly causes more deaths and disability in Indonesia. From sporadic data collected from hospitals, there was a trend of increase in morbidity rate from stroke as the life expectancy increased and the lifestyle changed. According to the Indonesia Health Department in 2007, stroke is the

number one cause of death and disability in Indonesia.

Post-stroke disability frequently involves physical problem such as walking and speech difficulty but also causes a no-physical problem such as depression. This will eventually affect overall daily activities, including sexual activity. There is still very little resources that explored this issue [6], [7], regardless of frequent complaints of sexual problems in patients with chronic diseases such as cerebrovascular accident [8], [9]. Several literature reviews and studies have shown that sexual function is frequently disturbed after a stroke attack [6], [8], [10], [11], [12] This will affect the quality of life [7]. In one systematic review, sexual dysfunction was mentioned as one of five social consequences from stroke aside from work life, family relationship, financial issue, and social activity [13].

In Indonesia, there are very little reports regarding sexual dysfunction following a stroke attack. There are several possibilities as to the reason behind this: doctor's attention is mostly focused on life-saving procedures, treating the risk factors, and toward the physical disability resulting from the stroke attack. Stroke patients are mostly above 50 years old and are usually not paying much attention to their sexual life at this period. Patients mostly feel ashamed and self-conscious to bring up their sexual problem to their doctors as they may think that such a problem is a minor issue compared to the more life-threatening symptoms of stroke. The partners also usually take sexual dysfunction as "normal" after such a major attack such as stroke, so they don't feel the need to bring it up. Thus, post-stroke sexual dysfunction is rarely reported in Indonesia. In men, erectile dysfunction (ED) is the most common sexual problem found in post-stroke patients.

Although the relationship between stroke and ED has been widely studied, however, the mechanisms and factors that predict ED in stroke are few known. Several studies have shown a relationship between the locations of the lesion in stroke with the onset of ED. The regulation of erectile function is more influenced by the parasympathetic than the sympathetic nervous system [14]. Some studies have shown consistent results that the left hemisphere is predominantly regulating parasympathetic modulation, while the right hemisphere is dominant for sympathetic modulation [15], [16], [17]. Several studies have suggested that ED is more commonly obtained in stroke with right hemispheric lesions [18], [19]. Other studies have shown opposite results, namely in the left hemispheric lesions [6], [20] Jung et al., [10] stated lesions in the left basal ganglia and right cerebellum are associated with decreased sexual desire and ejaculation disorders. Sikiru et al., [20] wrote that DE is often found in stroke patients with right hemiplegia. However other study stated there is no significant relationship between the location of the lesion and the occurrence of ED in patients after

stroke [21], [22], [23]. These contradictory results are what interested us in making a study in this field.

Also, comorbid factors that are thought to have important roles in the occurrence of ED in stroke patients are hypertension, diabetes mellitus (DM), and hypercholesterolemia [6], [11], [24], [25], [26], [27]. The risk factors are age, smoking and obesity [8], [22], [28]. Besides these physical factors, psychic factors also have a role in the occurrence of ED [6], [8], [10], [12], [29], [30], [31]. Post-stroke depression is the most common emotional disorder in post-stroke patients, and sexual dysfunction is also commonly found in patients who experience post-stroke depression [7], [32]. Left hemisphere stroke lesions are associated with depression [33], although other systematic reviews concluded that post-stroke depression was not significantly associated with the hemisphere location of the lesions [34].

This study aimed to evaluate the association between left hemisphere lesion after ischemic stroke and the subsequent risk of developing ED.

Methods

This research is an analytic observational study with a cross-sectional design. In the study subjects (post-stroke patients) analysis will be conducted to determine the relationship between the location of the lesion and the occurrence of ED. The study was conducted in the neurology polyclinic of Sanglah and Wangaya Hospital from February to August 2013. Subjects are all post-stroke patients who visited the neurology polyclinic of Sanglah and Wangaya Hospital that met inclusion and exclusion criteria.

Inclusion criteria include the following: Post-stroke patients minimum 6 months after stroke, men aged 40-59 years, married and living with his wife at the time of the study, Modified Rankin Scale (mRS) < 3. Exclusion criteria include the following: neurological disorders other than stroke, confirmed to have been diagnosed with ED before the stroke. Samples were taken by consecutive sampling.

Instruments used to collect data included data collection form and questionnaire. The data collection form was used to record basic characteristics such as age, type of stroke, location of lesion, hypertension, diabetes mellitus, smoking, obesity, and hypercholesterolemia, the result of the international index of erectile dysfunction-5 item (IIEF-5) questionnaire, modified Rankin scale (mRS), and Hamilton depression rating scale. IIEF-5 is a simple, reliable, and well-validated questionnaire to diagnose ED [35]. A score between 22-25 indicates no ED, 17-21 indicates mild ED, 12-16 indicates mild-to-

moderate ED, 8-11 indicates moderate ED, and 5-7 indicates severe ED [36]. The data was then analyzed with the SPSS version 20 for Mac. The correlation was analysed using a Lambda correlation test.

Results

In this study, a total of 74 post-stroke patients visited the Neurology Polyclinic of Sanglah and Wangaya during the period from February to August 2013. This study was an observational study with a cross-sectional design which aimed to determine the correlation between left hemisphere lesions with ED in stroke patients.

Characteristics of Subjects

There were 74 stroke patients who met the inclusion and exclusion criteria as a sample in this study. The mean age of stroke patients sampled in this study was 52.19 ± 4.37 with the youngest age of 42 years and the oldest 59 years. Characteristics of subjects including age group, type of stroke, the location of lesion, hypertension, diabetes, smoking, obesity, hypercholesterolemia, depression, erectile dysfunction, and degree of severity of ED are presented in Table 1.

Table 1: The characteristic of subjects

Characteristic	Frequency (n)	Percentage (%)
Age group		
40-49 years old	23	31.1
50-59 years old	51	68.9
Stroke type		
Hemorrhagic	20	27.0
Ischemic	54	73.0
Location of lesion		
Left hemisphere	35	47.3
Right hemisphere	39	52.7
Hypertension		
Yes	45	60.8
No	29	39.2
DM		
Yes	19	25.7
No	55	74.3
Smoking		
Yes	40	54.1
No	34	45.9
Obesity		
Yes	27	36.5
No	47	63.5
Hypercholesterolemia		
Yes	22	29.7
No	52	70.3
Depression		
Yes	39	52.7
No	35	47.3
Erectile Dysfunction*		
Yes	38	51.4
No	36	48.6
The degree of severity of ED		
Severe	9	12.2
Moderate	11	14.9
Mild-Moderate	8	10.8
Mild	10	13.5
Normal	36	48.6

*According to IIEF-5 score.

The table found the highest age group in the 50-59 years group (n = 51; 68.9%). Based on the type of stroke, most of the samples experienced ischemic

stroke with as many as 54 subjects (73.0%), while those with hemorrhagic stroke were 20 subjects (27.0%).

Based on the location of the lesion, more samples experienced lesions in the right hemisphere, with as many as 39 subjects (52.7%), compared to lesions in the left hemisphere (47.3%). Most of the samples experienced hypertension (n = 45; 60.8%). Only 19 subjects (25.7%) had diabetes. There were 40 subjects (54.1%) who smoked. Most of the samples were not obese (63.5%), and 52 subjects (70.3%) were not hypercholesterolemic. There were also 39 subjects (52.7%) who were depressed. Mean \pm SD IIEF-5 score was 17.82 ± 6.56 . From the sample, 38 subjects (51.4%) had erectile dysfunction, with the most being moderate (14.9%), followed by mild degrees (13.5%), severe (12.2%) and mild-moderate (10.8%).

Correlation between Left Hemisphere Lesions and ED in Post-stroke Patients

In stroke patients with lesions in the left hemisphere, 25 subjects (33.8%) had ED, and 10 subjects (13.5%) did not develop ED, whereas in stroke patients with lesions in the right hemisphere, 13 subjects (17.6%) had ED, and 26 subjects (35.1%) did not. The correlation between left hemisphere lesions and ED in stroke patients was analysed using the Lambda correlation test. The results of the significance analysis are presented in Table 2.

Table 2 shows that there is a significant positive correlation ($p < 0.05$) between left hemisphere lesions and ED in stroke patients with a correlation coefficient (r) = 0.361 which means weak correlation and $p = 0.032$.

Table 2: Correlation between left hemisphere lesion and erectile dysfunction (ED) in post-stroke patients

	ED		Total N (%)	r	p
	Yes N (%)	No N (%)			
Location of lesion					
Left Hemisphere	25 (33.8)	10 (13.5)	35 (47.3)	0.361	0.032*
Right Hemisphere	13 (17.6)	26 (35.1)	39 (52.7)		
Total	38 (51.4)	36 (48.6)	74 (100)		

*, significant ($p < 0.05$).

Discussion

Stroke is the third most common cause of death in the world, and one of the main causes of disability [8]. The relationship between stroke and ED has been widely studied, but the mechanisms and factors that predict ED in stroke have not been widely known. This study looked at the correlation between left hemisphere lesions and other variables with ED in

post-stroke patients.

In this study, 74 stroke patients who fulfilled the inclusion and exclusion criteria were sampled. The average age of post-stroke patients sampled was 52.19 ± 4.37 years with the youngest age of 42 years and the oldest 59 years. This study grouped the age into two: the 40-49 years age group and 50-59 years age group. This age grouping was done to reduce bias due to the hormonal status which was influenced by age. Derouet et al., [37] in their study stated that there were significant differences between free testosterone levels in men aged 40 years and over and 40 years and under. The incidence of ED increases after the age of 50 years [26]. The risk of ED also increases with age; it is reported that the risk increases up to 6 times in the age group 60-69 compared to the age group 40-49 [38].

Toglia et al., [39] reported that in 67 stroke patients, 40.3% came with left hemisphere lesions and 59.7% with right hemisphere lesions. This finding is slightly different what was reported by Sikiru et al., [20] wherein out of 105 stroke patients, 55 people (52.4%) had lesions in the left hemisphere, and 50 people (47.6%) had lesions in the right hemisphere. It was reported that the difference in the distribution of hemispheric lesions was not significant [40]. Also, the accuracy of determining the location of lesions is also determined by the availability of diagnostic tools such as CT-scan or MRI.

In this study, as many as 45 subjects (60.8%) had hypertension. In men with hypertension, impaired erectile function is not due to increased blood pressure itself, but because of arterial stenosis. Vascular failure to close during erection (venous-occlusion dysfunction) can cause ED [29]. Post-stroke patients suffering from DM in this study were 19 people (25.7%). These results are not much different from those reported by Icks et al., [41], who found 25.6% of male stroke patients aged 45-64 years with DM. The research used data taken from insurance in Germany between 2005 and 2007. DM has been well known as a risk factor for ED. Phé and Rouprêt [42] stated that increasing HbA1c levels and hyperglycemia in men with DM type 2 could reduce NO activity and reduce endothelial relaxation factors, resulting in increased risk for ED. A HbA1c level above 8.1% increases the incidence of ED threefold. Smoking is also closely related to the incidence of ED. Austoni et al., [43] reported an association between ED and smoking, defined by a smoking history of 10 cigarettes or more per day. Smoking can induce vasoconstriction and penile venous leak due to contractile effects on the cavernous smooth muscle.

The relationship between obesity, hypercholesterolemia, and stroke has been widely investigated about primary prevention [44], [45]. In this study 27 subjects (36.5%) were obese, and 22 subjects (29.7%) had hypercholesterolemia. Bener et al. [8] obtained the prevalence of obesity in stroke and

ED patients by 42.1% compared to non-ED patients at 28.4% ($p = 0.0005$). High-Density lipoprotein (HDL) cholesterol and the ratio of total/HDL cholesterol were found to be significant predictors of ED. Furthermore, post-stroke depression is common. In this study, 39 subjects (52.7%) were depressed. This statement is by Bhogal et al., [33] who reported the prevalence of post-stroke depression by 20-50%. Gaete and Bogousslavsky [32] also reported the prevalence of depression in the first four weeks after a stroke at 17-52%. The relationship between ED and depression has been investigated and shown significant results [6], [8], [10], [12], [29], [30], [31]. Post-stroke depression is the most common emotional disorder found in post-stroke patients [7], [32].

This study found a weak correlation between left hemisphere lesions and ED in post-stroke patients. However it was statistically significant (Table 2). The correlation is positive which means the post-stroke patient who has left hemisphere lesions are more likely to develop ED. These results are supported by the research of various studies. Kimura et al., [6] reported from 67 male samples in his research, the proportion of the sexual function disorder occurred higher in post-stroke patients with left hemisphere lesions versus right (40.3% vs 19.4%; $p = 0.013$). Sikiru et al., [20] studied the correlation of hemiplegia and ED in stroke patients. There were 105 stroke patients with left hemiplegia and 55 stroke patients with right hemiplegia, then assessed with the IIEF-5 questionnaire. Erectile function was found to decrease significantly in both patients with left and right hemiplegia. The mechanism for the relationship of left hemisphere lesions to ED is not known with certainty. But some studies that try to link hemispheres with the autonomic nervous system can indirectly support this statement. Regulation of erectile function is more influenced by the parasympathetic nervous system than by the sympathetic [14]. Avnon et al., [17] stated that brain function about the autonomic nervous system is asymmetrical, where the dominant left hemisphere regulates parasympathetic modulation, whereas the right hemisphere brain is dominant for sympathy. This statement is also by other studies [15], [16]. Braun et al., [46] revealed patients with left hemisphere lesions (especially in the temporal lobe) tend to experience hyposexual activity, whereas patients with right hemisphere lesions tend to experience hypersexual drive.

Of note, Winder et al., [47] had performed lesion mapping using voxel-wise analysis and found that ischemic stroke was related to erectile dysfunction if the lesion was found in the right occipital-parietal cortex and thalamus which are responsible for visual and somatosensory input integration, as well as lesions in the left insular and parietal-temporal region, areas responsible for generating and mapping visceral arousal state. A lesion affecting insula due to another insult (i.e., multiple sclerosis) was also associated with ED [48].

Different results were reported by other researchers, where ED was more frequently found in post-stroke patients with right hemisphere lesions [19], [49]. This difference can occur because of this study excluded depression from the study sample, whereas the number of depression in stroke patients was almost one third and Bhogal et al., [33] reported about 70% of stroke patients with depression had lesions in the left hemisphere. So, when the studies excluded depression, a direct proportion of stroke patients with left hemisphere lesions consequently would decrease and could, therefore, affect the results of the study. In this study, the proportion of ED patients who suffered from depression was 35.1%. When connected between depressed patients and location of lesions, this study obtained the proportion of stroke patients who experienced lesions in the left hemisphere and suffered from ED as 33.8% compared to 18.9% of those who experienced lesions in the right hemisphere. This shows the tendency for stroke patients with lesions in the left hemisphere to experience depression.

Furthermore, the same study also confirmed a relationship between left hemisphere lesions and the occurrence of depression in post-stroke patients. One of the inclusion criteria in this study was using a sample of right-handed patients, but not differentiated further whether the right-handedness was absolute or not. Absolute certainty was known from the history where the patient always used his right hand and leg, and there was no history of left-handedness in his family. The dominant hemisphere in absolute left-handed people is the left hemisphere. The relative right-handed person was defined by the history of a left-handed person in the family. The right-handed group did not have a cerebral ambivalence. Likewise, in the left-handed group, the patient could use both of his left and right hand and legs, even though usually better with the left side.

In conjunction with erectile function, the role of the autonomic nervous system is not solely determined by the hemispheric sympathetic and parasympathetic activity of the brain, but it also involves the somatomotor, endocrine, and autonomic system itself. These systems are represented by overlapping areas of the brain. Three important components of the central autonomic control pathway include the solitary nucleus who receive visceral sensory information, the hypothalamus which is the centre neural control most important for controlling endocrine and visceral functions, and the nucleus ventrolateral rostral reticular (nRVL) which is the motor nucleus that regulates the autonomic nervous system. The hypothalamus is part of the limbic system which has two-way connections between the cortical and subcortical areas complexes. Assessing depression is of more value in this study than in the research done by Jung et al., [10], although this study also has a weakness because it does not check hormonal levels in post-stroke patients.

In conclusion, based on the results of the research above, the conclusion can be drawn as following: left hemisphere lesions positively correlated with ED in stroke patients. Further longitudinal research is needed to see whether left hemisphere lesion in post-stroke patients is a risk factor for ED.

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