http://mnj.ub.ac.id/
DOI: 10.21776/ub.mnj.2022.008.01.7
eISSN: 2442-5001 **pISSN:** 2407-6724
Accredited by DIKTI Decree No: 21/E/KPT/2018

MALANG NEUROLOGY JOURNAL MNJ

RESEARCH ARTICLE OPEN ACCESS

COMPARISON OF COGNITIVE FUNCTION BETWEEN FIRST ISCHEMIC STROKE AND RECURRENT ISCHEMIC STROKE PATIENTS

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Article History:
Received: October 12, 2021
Accepted: December 8, 2021
Published: January 1, 2022

Cite this as:
Rizkia FI, Calista C, Gunadharma S, Hermawan AN, Amalia L, Ong PA. Comparison of cognitive function between first ischemic stroke and recurrent ischemic stroke patients. Malang Neurology Journal; 2022.8:30-34. DOI: http://dx.doi.org/10.21776/ub.mnj.2022.008.01.7

ABSTRACT

Background: Cognitive impairment is a common condition that may affect up to 50% of stroke patients. Post stroke cognitive impairment is associated with reduced quality of life, which may increase the number of dependency. Recurrent stroke may happen in approximately 25% patients and they have higher rates of cognitive impairment.
Objective: The aim of this study is to examine the comparison of cognitive function between first ischemic stroke and recurrent ischemic stroke patients in Hasan Sadikin Hospital, Bandung.
Methods: This study is a retrospective, cross-sectional study using the data recruited between the year 2012 - 2016 at the Department of Neurology at the Hasan Sadikin Hospital Bandung. The data collected in this study were demographic data, including age, level of education, and residence, and the clinical data as well. Cognitive function was assessed using Mini-Mental State Examination (MMSE). The comparison between the cognitive function between both groups were analyzed using the Mann-Whitney U test.
Results: There were 428 subjects eligible for this study, with 207 subjects categorized as first ischemic stroke group and 221 subjects categorized as recurrent ischemic stroke group. There was a statistically significant difference in MMSE scores between the first ischemic stroke patients (24.90 ± 4.64) and recurrent ischemic stroke patients (22.85 ± 4.64) with a *p* value of 0.002.
Conclusion: Recurrent ischemic stroke patients had lower MMSE scores than the first ischemic stroke patients. Clinicians should be more aware in detecting early cognitive impairment in stroke patients and in preventing the incidence of recurrent stroke.

Keywords: Cognitive function, first ischemic stroke, recurrent ischemic stroke

Introduction

Stroke is the second leading cause of death globally and the third leading cause of disability.[1] The occurrence of stroke may cause disability, which decrease the capacity to do daily activities and cognitive function.[2] Twenty-six percent of patients report limitations in functional activities and 51% report limitations with higher level activities of daily living (ADL) at 3 years post stroke.[3] Cognitive impairment is a common post-stroke condition that may limit functional outcomes, affecting 50% patients. Post-stroke cognitive impairment are associated with reduced quality of life, poorer functional outcome, more recurrent strokes, higher mortality[3], and even as a factor for long-term disability.[4]

Cognitive impairment is related to memory and attention deficits or executive dysfunction, which may reduce patient's ability to perform self-care tasks or to plan and organize.[3] The impairment may vary depending for each patient's stroke characteristics, such as type, location, severity and number of occurrence.[5] Cognitive impairment after stroke is frequently neglected compared to other neurological deficits such as sensory or motor impairment.[5,6] Risk of recurrent stroke is approximately 25% on 5-year cumulative. Recurrent stroke patients have higher rates of long-term disability with more severe physical and cognitive impairments compared to first strokes.[7] Mini-Mental State Examination (MMSE) is a screening instrument for cognitive impairment that has been used extensively, even though it seems to be unsuitable to identify subtle or specific cognitive deficits.[4]

The aim of this study was to examine the comparison between cognitive function of first ischemic stroke patients and recurrent ischemic stroke patients. Therefore, clinicians would be more attentive on detecting cognitive impairment in stroke patients and do possible measures to prevent the recurrence of the stroke event.

Methods

This was a retrospective, cross-sectional study conducted in Hasan Sadikin Hospital, Bandung, which is a top referral hospital in East Java. Data was retrieved from the neurology department from January 2012 until December

2016. There were 1567 ischemic stroke inpatients who were fulfilling the diagnostic criteria for stroke by the World Health Organization included in this study. Patients with Glasgow Coma Scale score less than 15, history of head trauma, inadequate education background, visual or auditory impairment, incomplete medical resume and who were deceased were excluded from the study.

From all the patients recruited, 1139 subjects were excluded from the data, with 506 patients had no MMSE score, 251 had not done the MMSE scoring because of aphasia, dysphasia, dysarthria, 208 patients were deceased, 142 patients had decreased consciousness and 32 patients were not educationally capable for cognitive function testing. A total 428 medical resumes were included and eligible for further study analysis. There was no statistically significant difference of gender and age among the excluded and included groups. But there was a statistically significant difference (*p* 0.027) on the mean of education years, which was higher among the excluded group (8.37 years ± 3.05).

The study was approved by the Commission of Ethics Faculty of Medicine Padjadjaran University number 770/UN6.KEP/EC/2020. Data analysis was done by comparing the medical records between the patients with first ischemic stroke and recurrent ischemic stroke. The analysis was conducted using IBM® SPSS 25th version. Cognitive functions were assessed using the Mini-Mental State Examination (MMSE). Data were tested for normality using the Kolmogorov-Smirnov test for normality test. Student independent t-test were conducted if the data were normally distributed, otherwise, the Mann-Whitney test was used for the non-normally distributed data. The chi-square test was used to analyze the categorical data. Analysis was performed by comparing the MMSE score between the first and recurrent ischemic stroke patients. This study was performed according to the Declaration of Helsinki on guidelines for biomedical research involving human subjects.

Results

Of all 428 patients, 207 patients had first ischemic stroke and 221 others had recurrent ischemic stroke. Table 1 showed demographic characteristics and risk factors by first and recurrent ischemic stroke. Among these patients, 216 (50.5%) were male and 212 (49.5%) patients were female. The mean age was 57.81 (SD 11.54) years, ranging between 24 and 96 years old and patients with first ischemic stroke (55.63 ± 11.63) were more likely to be younger recurrent ischemic stroke group (59.52 ± 10.08). Both groups had nearly the same average of education years (8.26 years, SD 3.00), with the majority had only finished elementary school. More than half of the patients lived in urban areas. Other factors, including employment status, residency, hypertension and dyslipidemia were also found statistically significant differences among both groups.

Mann-Whitney analysis showed a statistically significant difference between first ischemic stroke and recurrent ischemic stroke patients. The average MMSE score (Table 2) among recurrent ischemic stroke patients were found lower (22.85 ± 4.64) than the first ischemic stroke patients (24.90 ± 4.64).

Table 1. Demographic and Clinical Characteristics of the Study Subjects

Characteristics	Total (n = 428)	First Ischemic Stroke (n = 207)	Recurrent Ischemic Stroke (n = 221)	*P* value
Gender				
Male, no. (%)	216	98 (47.3)	118 (53.4)	0.211
Female, no. (%)	212	109 (52.7)	103 (46.6)	
Age Group				
< 40, no. (%)	20	17 (8.2)	3 (1.4)	
40 – 49, no. (%)	73	46 (22.2)	27 (12.2)	
50 – 59, no. (%)	164	77 (37.2)	87 (39.4)	0.0001*
60 – 69, no. (%)	107	41 (19.8)	66 (29.8)	
>= 70, no. (%)	64	26 (12.6)	38 (17.2)	
Age, mean ± SD	57.64 ± 11.04	55.63 ± 11.63	59.52 ± 10.08	0.0001*
Education level				
Elementary, no. (%)	258	123 (59.4)	135 (61.1)	
Junior high, no. (%)	70	36 (17.4)	34 (15.4)	0.685
High school, no. (%)	81	41 (19.8)	40 (18.1)	
University, no. (%)	19	7 (3.4)	12 (5.4)	
School years, mean ± SD	8.07 ± 2.91	8.05 ± 2.81	8.09 ± 2.99	0.890
Residence				
Urban, no. (%)	284	146 (70.5)	138 (62.5)	
Rural, no. (%)	125	50 (24.2)	75 (33.9)	0.036*
Unknown, no. (%)	19	11 (5.3)	8 (3.6)	
Etiology				
Cardioembolism, no. (%)	50	31 (15.0)	19 (8.6)	
Thromboembolism, no. (%)	39	21 (10.1)	18 (8.1)	
Atherothrombosis, no. (%)	276	123 (59.4)	153 (69.2)	0.135
Lacunar (SAO), no. (%)	18	11 (5.3)	7 (3.2)	
Undetermined, no. (%)	45	21 (10.1)	24 (10.9)	
Vascular risk factor				
Hypertension, no. (%)	375	174 (84.1)	201 (90.9)	0.031*
Dyslipidemia, no. (%)	233	123 (59.4)	110 (49.8)	0.045*
Diabetes Mellitus, no. (%)	93	40 (19.3)	53 (24.0)	0.243
Atrial Fibrillation, no. (%)	22	10 (4.8)	12 (5.4)	0.779
Ischemic heart disease, no. (%)	32	13 (6.3)	19 (8.6)	0.362
Stroke location				
Right hemisphere, no. (%)	208	98 (47.3)	110 (49.8)	
Left hemisphere, no. (%)	165	85 (41.0)	80 (36.2)	0.528
Vertebrobasilar, no. (%)	55	24 (11.6)	31 (14.0)	

*statistically significant difference ($p < 0.05$)

Table 2. Comparison of MMSE Score among First Ischemic Stroke Subjects and Recurrent Ischemic Stroke Subjects

	First Ischemic Stroke (n = 207)	Recurrent Ischemic Stroke (n = 221)	*P* value
Mean ± SD	24.90 ± 4.64	22.85 ± 4.64	0.002*
Median	26	25	

*statistically significant difference ($p < 0.05$)

Discussion

Sample description

In this study, the first ischemic stroke group had more women patients than the recurrent stroke group. But**,** there was no statistically significant difference among the gender. Recurrent group consisted of more male patients**.** This was consistent with the study[8] that mentioned that male sex was a non-predictive factor of recurrent stroke because male was associated with risk factors such as hypertension and tobacco smoking. Based on a retrospective hospital-based study conducted at Sayad Shirazi Hospital in Gorgan[9], ischemic stroke patients had high prevalence in age >=70 years with mean age of 62.93 years (SD ± 15.68), which was higher than this study, with mean age of 57.64 years (SD ± 11.04). In this study, ischemic stroke had the highest prevalence in the age group of 50 – 59 years old. In another study conducted in Indonesia[10], it was found that ischemic stroke patients had the highest prevalence between the age of 45-54 years among 722,320 patients enrolled in the study.

There was no statistically significant difference found between both groups in this study based on educational years, with an average of 8.07 years (SD ± 2.91). This background was higher than a study conducted by Lei Zhao et al.[11] which the average educational background years was 5.9 (SD ± 4.7) years. Similar to this study, a study conducted in Indonesia[10] showed the majority of the patients had only finished elementary school.

This study dominated with patients who lived in urban areas, similar with a study conducted in Iran[9], either first ischemic stroke patients or recurrent stroke patients had higher prevalence to live in urban areas. Urban population were more prone to several risk factors such as diabetes mellitus, hypertension, tobacco smoking, obesity, and dyslipidemia, which may cause higher rates of ischemic stroke incidence.[12] In this study, atherothrombotic patients were found higher in number in both groups (>50% in both groups). Similar to this study, a study conducted in Korea[13] showed the majority of the patients had atherothrombotic ischemic stroke subtype, accounting for more than 30%.

This study showed that the highest risk factor found between both groups was hypertension (>80%). A study conducted by Patrick H. Kitzman among Appalachian Stroke Registry[14] identified that the highest prevalence in the study population were hypertension (84%), dyslipidemia (69%), and diabetes (44%). Another study conducted by Frans Kauw et al.[8] also mentioned that diabetes mellitus (HR 1.2) and atrial fibrillation (HR 1.6) were the predictive factors of recurrent ischemic stroke. In a study conducted in Sweden[15], it was also found more atrial fibrillation (29.4% vs 27.1%), diabetes mellitus (22.5% vs 20.2%), and hypertension (57.3% and 52.8%) in patients with recurrent stroke than first ischemic stroke.

Study conducted based in Pakistan showed a higher rate of left hemisphere ischemic stroke patients than right.[16] Different from our study, most of the patients had strokes on their right hemispheres (47.2%). In a former study, it was found that left middle cerebral artery stroke patients may be more prone to greater degree of cognitive impairment than right MCA.[16]

Primary outcome measures

This study found a statistically significant difference in cognitive impairment among first and recurrent ischemic stroke patients based on MMSE score. The recurrent stroke group had a lower mean of MMSE score (22.85 SD ± 4.64) in comparison to the first stroke group (24.90 SD ± 4.64). A recent study conducted in the United Kingdom[17] suggested that 10% of patients developed cognitive impairment after the first stroke and over one-third of patients developed cognitive impairment after recurrent stroke.

A study with 1240 patients which were divided to three tertiles (highest tertile with MMSE score 28-30, middle tertile with score of 24-27, and lowest tertile with 0-23 score)[18], the analysis showed that the lowest tertile was significantly associated with recurrent ischemic stroke. In a systematic-review and meta-analysis study[8], recurrent stroke patients had multiple lesions, multiple stage lesions, multiple territory lesions, chronic infarcts, and isolated cortical lesions, based on MRI findings. Cognitive impairment could be severely affected when the infarcts were located on strategic areas, such as basal ganglia, internal capsule, thalamus, corpus callosum, angular gyrus, cingulate cortex, and frontal subcortical regions.[11]

In this study, the recurrent ischemic stroke patients were older than the first ischemic stroke patients, with the average age of 59.52 vs 55.63 years, respectively. Prior study[19] mentioned that older patients were severely impaired in cognition due to the nature of stroke that accelerates cognitive decline. There was no statistically significant difference in study years among both groups. Longer education years were less likely to be affected in their cognitive functioning because they have larger brain reserve capacity which can compensate for the brain damage.[19] A study conducted by Herpan Syafii Harahap et al mentioned that the level of education had a significant relationship with the impairment of post-ischemic stroke cognitive status among hospital-based ischemic stroke survivors.[20]

Other factors that may affect the cognitive impairment were vascular risk factors. Based on a study conducted by Agnes Jacquina et al. in France[21], stroke patients who had hypertension (OR 2.36), diabetes mellitus (OR 3.57), atrial fibrillation (OR 2.68) were more likely to develop post-stroke cognitive impairment. Our study demonstrated that there was a statistically significant difference in hypertension and dyslipidemia among both groups, whereas diabetes mellitus, atrial fibrillation, and ischemic heart disease showed no significant difference. History of hypertension may reduce brain volume and also cause white matter lesions, which impaired the cognitive functioning.[19] In a study conducted by Natasha Tipnis et al, hypertension in population > 60 years showed statistical significance with cognitive declines, specifically in cognitive domain such as orientation to time, registration, recall, and 3 step demands.[22] The association between hypercholesterolemia and cognitive impairment was still controversial. But, lipid metabolism might be associated with the pathogenesis of vascular dementia, although further studies were needed.[23] Besides, hypertension and dyslipidemia were major risks factor for the recurrence of ischemic stroke.[2]

Patient's place of residence was also found to have a statistically significant difference in this study (p <0.05), with urban populations dominated in both groups. Based on a study conducted among Chinese rural and urban populations[24], the prevalence of cognitive impairment was higher in rural populations than urban populations. The possibilities that rural populations were more vulnerable to cognitive dysfunction were because of low socioeconomic status, distant health service access, and lower educational level than people in urban areas. Dissimilar with the rural populations, urban populations were associated with diabetes mellitus and lack of physical activity which might also cause cognitive impairment.[24]

It is very important to acknowledge how to maintain blood pressure, blood glucose level, and blood cholesterol level to reduce the possibility of recurrent stroke. Other measures such as tobacco abstinence and regular physical activity also reduce the stroke risk.[2] By keeping these risk factors at bay, it is expected to prevent the recurrent strokes and deterioration of cognitive function in patients.

Limitations of this study were that it involved relatively small samples from the exclusion criteria, although there was no statistically significant difference among age and gender groups. This study was cross-sectional in nature, so it could not represent the progressiveness of the cognitive impairment. As a top referral in East Java, most patients admitted from urban populations, so this study might not represent the rural population. Other limitations, there was no adequate information about the preceding risk factors that may contribute to the progressiveness of the cognitive impairment, which may bias the result of this study. The amount of recurrence of the stroke, cognitive domains affected, and specific location of brain infarct were not available, so it could not be analyzed any further. More recent, robust, and directly comparable data will be needed to confirm and strengthen any conclusions made on this study and for further study.

Conclusion

In conclusion, this study indicated that there was a statistically significant difference of cognitive function between first ischemic stroke patients and recurrent ischemic stroke patients (p = 0.002). The MMSE score among recurrent stroke patients was lower than the first ischemic stroke patients. Thus, it is important to modify the modifiable risk factors of recurrent stroke to prevent more severe impairment in cognitive function.

Conflict of Interest

The authors declare there is no conflict of interest.

Acknowledgement

We would like to express our gratitude to all the staff and management of Neurology Department of Dr. Hasan Sadikin General Hospital, Bandung, Indonesia for the support throughout this study.

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