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RESEARCH

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Risk factors of cognitive impairment post-ischemic stroke

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Abstract

Background Stroke is still remarked as one of the major ailments in Indonesia. Cognitive impairment occurs frequently after stroke events and its predictors are needed to identify patients with a high risk of cognitive impairment. However, the researches done in Indonesia still vary in results. This retrospective cohort study evaluated 236 ischemic stroke patients in Bethesda Hospital Yogyakarta from January–November 2020 through medical records. Cognitive impairment was measured by MMSE and CDT, defined as MMSE score ≤ 20 for patients with the educational attainment of 1–6 years; ≤ 24 for the educational attainment of > 6 years and/ or CDT < 4. All data were analyzed with univariate test and Chi-square test, followed by logistic regression.

Results Of 236 subjects, the frequency of cognitive impairment was 67.4% and the risk factors are age > 80 years old (RR: 1,545; CI 0.136–17.542; *p*: 0.026), educational attainment ≤ 6 years (RR: 20.016; CI 1.951–222.120; *p*: 0.012), temporal (RR: 4.238; CI 2.266–7.926; *p*: 0.007) or multiple site lesion location (RR: 7.522; CI: 3.522–17.532; *p*: 0.047) and multiple (> 1) lesions (RR: 1,819; CI 0.822–4.022; *p*: 0.040).

Conclusions The prevalence of post-stroke cognitive impairment is high, affecting up to 2 out of 3 people in this study. The risk factors of post-stroke cognitive impairment are age > 80 years, educational attainment ≤ 6 years, temporal or multiple site lesion, and > 1 lesion. Strict stroke prevention strategies are needed to halt the development of post-stroke cognitive impairment.

Keywords Cognitive impairment, Ischemic stroke, Risk factors

Background

Other than its high mortality rate, post-stroke disability remains the world's main problem. Post-stroke cognitive impairment (PSCI) is the most frequent disability [1], experienced by up to 30% of stroke survivors worldwide [2]. A later prospective study shows 62.6% [3] individuals affected by PSCI, and the rate was predicted to be increasing annually as the population ages. PSCI is manifested by impaired cognitive domain functions such as decreased memory function, especially short-term memory, language use, executive function, impaired attention, initiating activities, and planning and organizing [4], causing limitations in individual daily activities and dependence on others. Many factors significantly increase the risk of post-stroke cognitive impairment [5]. Identification of its predictive factors can be used as a preventive measure for worsening cognitive impairment in individuals, in which delaying the onset of PSCI for 5 years can reduce the overall incidence of PSCI by 50% [6]. Studies conducted in Indonesia to identify risk factors for post-stroke cognitive impairment showed variable results. The combination of MMSE and CDT as diagnostic tools for post-stroke cognitive disorders has never been done. This study was aimed at identifying risk factors for cognitive impairment in post-ischemic stroke patients.

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Methods

This study retrospectively analyzes medical records of ischemic stroke patients from the stroke registry at Bethesda Hospital Yogyakarta in the period January to November 2020 on 236 subjects. Any stroke patient above > 18 years old with complete medical records was included in this study and later screened for any exclusion criteria including any previous cognitive impairment, any disease which cognitively debilitating such as psychotic episodes of mental illnesses, and any disease which hinders communication such as aphasia of any types.

Cognitive impairment was measured 1 to 3 months after stroke onset using the Mini-Mental State Examination (MMSE) with a cut-off according to the Shanghai Mental Health Center and the Clock Drawing Test (CDT) using a 4-point scoring system. Cognitive impairment was defined as an MMSE with a score of 20 for a 1–6 year educational history; 24 for education history > 6 years and/or Clock Drawing Test score < 4. Any statistically significant variable will be further analyzed using multivariate logistic regression (Table 1).

Results

There were 236 subjects in this study with the highest number of subjects in the age group 50–60 years (33.5%), male gender (67.8%), with the majority of patients having education attainment more than 6 years old (89.8%), and without a history of previous stroke (83.5%). The most common risk factors for stroke were a history of dyslipidemia (59.3%), hypertension (53.4%), smoking habits (44.1%), and diabetes mellitus (25.8%). Most subjects had multiple lesion locations (47.9%) and lacunar lesions (49.6%). Details of the characteristics of the subject are in Table 2.

The results of cognitive impairment measurement using MMSE and CDT are provided in Table 3, showing

Table 1 Multivariate logistic regression test result

Variable	RR	CI (95%)	*p*
Age			
< 50 years	Ref		
50–60 years	0.320	0.033–4.630	0.055
61–70 years	0.892	0.030–3.375	0.043
71–80 years	0.925	0.083–9.622	0.125
> 80 years	1.545	0.136–17.542	0.026
Education			
≤ 6 years	20.016	1.951–222.120	0.012
> 6 years			
Lesion site			
No lesion	Ref		
Frontal	3.001	0.403–6.417	0.707
Parietal	5.637	2.504–7.269	0.591
Temporal	4.238	2.266–7.926	0.009
Multiple	7.522	3.522–17.532	0.047
Infra-tentorial	6.888	4.102–7.157	0.166
Lesion amount			
No infarct	Ref		
Lacunar infarct	0.401	0.023–7.010	0.531
Multiple infarcts	1.819	0.822–4.02	0.040

Table 2 Basic characteristics of subjects

Characteristic	Frequency (*n*)	Percentage (%)
Age (years)		
< 50	21	8.9
50–60	79	33.5
61–70	76	32.2
71–80	52	22
> 80	8	3.4
Gender		
Male	160	67.8
Female	76	32.2
Education		
≤ 6 years	24	10.2
> 6 years	212	89.8
Hypertension		
Yes	126	53.4
No	110	46.6
Diabetes mellitus		
Yes	61	25.8
No	175	74.2
Dyslipidemia		
Yes	140	59.3
No	96	40.7
Smoking		
Yes	104	44.1
No	132	55.9
Previous stroke		
Yes	39	16.5
No	197	83.5
Lesion location		
No lesion	52	22.0
Frontal	8	3.4
Parietal	58	24.6
Temporal	2	0.8
Multiple	113	47.9
Infra-tentorial	3	1.3
Lesion amount		
No lesion	48	20.3
Lacunar	117	49.6
Multiple	71	30.1

Table 3 Cognitive function test results

	Frequency (*n*)	**Percentage (%)**
Mini-Mental State Examination		
Cognitively impaired (MMSE score ≤ 20 for 1–6 years education attainment; MMSE score ≤ 24 for > 6 years education attainment)	95	40.2
Cognitively intact	141	59.7
Clock Drawing Test		
Cognitively impaired (score < 4)	146	61.8
Cognitively intact	90	38.1
Cognitive impairment		
Cognitively intact	77	32.6
Cognitively impaired (MMSE score ≤ 20 for 1–6 years education attainment; MMSE score ≤ 24 for > 6 years education attainment and/ or Clock Drawing Test score < 4)	159	67.4

67.4% of subjects are cognitively impaired, as defined by MMSE and CDT instrument cut-offs combined.

Based on the results of the bivariate test in Table 4, it was found that age, education attainment, lesion location, and the number of lesions ($p < 0.05$) had statistical significance and a significant relationship to the outcome of cognitive impairment in post-stroke patients.

Discussion

Residual events post-stroke attack is a concern to not only the patient, but also their caregiver and physicians. The incidence of post-stroke cognitive impairment is high, in which 67.4% of subjects of this study were proven to be cognitively impaired, higher than the previous study [7, 8]. Differences in the incidence are due to the demographic differences between the research subjects and the research instruments used by each researcher. The purpose of analyzing cognitive impairment in the subacute phase of stroke in this study is although most functional recovery occurred within the first 6 months [9], it is worth noting that the impairment would inhibit subsequent recovery of motor functions and daily activities independence thus interfering with the outcome of rehabilitation [10]. The incidence of cognitive impairment across different time horizons also varies between < 50% to 90% [11]. Adjustments of instruments cut-offs are used for equalization, avoiding bias and subject's perception misunderstanding regarding the questions on the assessment [12].

Demographic status and lesion characteristics on radiological imaging are associated with decreased cognitive function [13]. In this study, the highest incidence of cognitive impairment was shown in the > 80 years old age group, in accordance with previous studies [14]. Stroke increases the risk of cognitive impairment by 1.8 times compared to the elderly without stroke [15]. Cognitive function declines linearly with age due to changes in brain neurotransmitters, accumulation of oxidative stress, and changes in body biochemistry [16].

The length of education will increase the individual's cognitive reserve. Individuals with a high cognitive reserve can compensate for brain tissue damage more efficiently, thereby reducing the risk of cognitive impairment [17, 18]. Adherence to medication and lifestyle also affects the outcome of poor cognitive impairment in individuals with 6 years of education [19]. The results in this study are in accordance with the previous studies [8, 13].

Damage to brain tissue in certain locations determines the outcome of cognitive impairment [19]. The temporal location of the lesion increases the risk of post-stroke cognitive impairment related to the physiological function of that region [20], namely impaired episodic (long-term) memory function. The results of this study are in accordance with the previous studies [21]. Multiple lesions result in increasingly inadequate brain response to compensate for the progressive infarct damage [22]. The results of this study are the same as those of the previous studies [23].

Gender, history of the previous stroke, dyslipidemia, hypertension, diabetes mellitus, and smoking habits were not significant factors influencing the outcome of cognitive impairment as shown by previous studies [23]. Although controversial, the evaluation of smoking habits for cognitive impairment after stroke has a survival rate bias [24]. The relationship between gender and cognitive impairment after stroke has many biases including socioeconomic status, psychosocial status, sex hormones, and serum adiponectin [25–27], so that mentioned factors do not correlate significantly to the predictors of cognitive impairment after stroke.

This study is not without limitations. The results of this study could not analyze any progression of

Table 4 Chi-square test result

Variable	Cognitively impaired (*n*) %	Cognitively intact (*n*) %	RR	CI (95%)	*p*
Age (years)					
< 50 years	12 (57.1%)	9 (42.9%)	Ref	Ref	
50–60 years	42 (53.2%)	37 (46.8%)	2.804	0.230–34.232	
61–70 years	55 (72.4%)	21 (27.6%)	3.371	0.314–36.167	0.003
71–80 years	43 (82.7%)	9 (17.3%)	1.050	0.097–11.427	
> 80 years	7 (87.5%)	1 (12.5%)	0.664	0.058–7.638	
Sex					
Male	106 (66.3%)	54 (33.8%)	1.576	0.664–3.739	0.593
Female	53 (69.7%)	23 (30.3%)			
Education					
≤ 6 years	23 (95.8%)	1 (4.2%)	1.494	1.311–1.702	0.002
> 6 years	136 (64.2%)	76 (35.8%)			
History of HT					0.174
Yes	80 (63.5%)	46 (36.5%)	0.744	0.396–1.397	
No	79 (71.8%)	31 (28.2%)			
History of DM					
Yes	42 (68.9%)	19 (31.1%)	0.846	0.410–1.743	0.775
No	117 (66.9%)	58 (33.1%)			
History of dyslipidemia					
Yes	94 (67.1%)	46 (32.9%)	0.946	0.493–1.816	0.927
No	65 (67.7%)	31 (32.3%)			
Previous stroke					
Yes	28 (71.8%)	11 (28.2%)	0.803	0.392–1.644	0.519
No	131 (66.5%)	66 (33.5%)			
Cigarette smoking			0.867	0.407–1.847	0.765
Yes	69 (66.3%)	35 (33.7%)			
No	90 (68.2%)	42 (31.8%)			
Lesion site					0.010
No lesion	25 (48.1%)	27 (51.9%)	Ref		
Frontal	4 (50.0%)	4 (50.0%)	0.962	0.455–2.032	
Parietal	41 (70.7%)	17 (29.3%)	0.680	0.490–0.944	
Temporal	1 (50.0%)	1 (50.0%)	0.962	0.234–3.956	
Multiple	85 (75.2%)	28 (24.8%)	0.639	0.473–0.864	
Infra-tentorial	3 (100.0%)	0 (0.0%)	0.481	0.362–0.638	
Lesion amount					
No infarct	23 (47.9%)	25 (52.1%)	Ref		0.002
Lacunar infarct	80 (68.4%)	37 (31.6%)	0.351	0.018–7.013	
Multiple infarcts	56 (78.9%)	15 (21.1%)	1.768	0.790–3.954	

the cognitive impairment outside the study timeline (> 3 months). Moreover, the results cannot be used to predict the long-term prognosis of the disease. Due to this study design, the authors cannot guarantee error-free data collection as the data used are secondary data (medical records).

Conclusion

Stroke also poses many burden even after period of inpatient. Predictors of post-stroke cognitive impairment are age (> 80 years), education attainment (≤ 6 years), temporal or multiple lesion location, and multiple (> 1) brain lesions. Strict stroke prevention will be beneficial in reducing and preventing post-stroke cognitive impairment, especially in this aging population.

Abbreviations

CDT	Clock Drawing Test
DM	Diabetes mellitus
HT	Hypertension
MMSE	Mini-Mental State Examination
PSCI	Post-stroke cognitive impairment

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Not applicable.

Author contributions
RTP conceived the study. RTP, NPU participated in its design and coordination, and helped to draft the manuscript. RTP retrieved the data. NPU reviewed the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials
The datasets used in this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
This observational study was approved by the ethics committee of the Department of Neurosurgery, Faculty of Medicine Duta Wacana Christian University, and Bethesda Hospital Research Ethic Committee. The committee's reference number is 19/KEPK-RSB/II/21. All participants provided verbal informed consent to participate in the study.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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