

# The prevalence and determinant factors of post-stroke cognitive impairment

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## ABSTRACT

**Background:** Stroke is the main health problem in Indonesia. Cognitive impairment is one of the post-stroke problems. Research on cognitive impairment prevalence and the related risk factors in Indonesia is not yet satisfied.

**Objective:** This study aimed to measure the prevalence and determinant factors of cognitive impairment in post-stroke patients.

**Methods:** This study was a cross-sectional study. The subjects were post-ischemic stroke patients at Bethesda Hospital, Yogyakarta. Cognitive impairment was measured by Montreal Cognitive Assessment-Indonesian Version (MoCA-INA) instrument and clock drawing test (CDT). Cognitive impairment defined as MoCA-INA <26 dan CDT >1, whereas good cognitive function defined as MoCA-INA ≥26 dan CDT = 1. Other data were obtained from electronic stroke registry. All data were analyzed with univariate test, Chi-square test, and logistic regression test.

**Results:** There are 110 subjects consist of 72 (65.5%) male patients and 38 (34.5%) female patients. There were 75 (68.2%) patients with cognitive impairment and 35 (31.8%) patients with good cognitive function. Logistic regression test showed time to hospital (odds ratio [OR]: 52.723, 95% confidence interval [CI]: 3.982–698.07, *P*: 0.003), multiple lesions (OR: 9.878, 95% CI: 1.093–89.314, *P*: 0.041), and temporal lesion (OR: 26.102, 95% CI: 2.146–317.43, *P*: 0.010) was significant factors to cognitive impairment on post-ischemic stroke patients.

**Conclusion:** The prevalence of cognitive impairment on post-ischemic stroke patients is high. The determinant factors of post-stroke cognitive impairment are stroke onset, multiple lesions, and temporal lesion.

**Key words:** Clock drawing test, cognitive impairment, ischemic stroke, Montreal Cognitive Assessment-Indonesian Version

## INTRODUCTION

The WHO identified stroke as a major public health problem for both developed and developing countries. According to the WHO, stroke is associated with the fourth highest burden of disease worldwide.<sup>[1]</sup> Stroke leads to cell damage to cell death in brain and the result is disturbance in cognitive function.<sup>[2]</sup> About one-third of stroke survivors suffer from post-stroke cognitive impairment (PSCI).<sup>[3]</sup> Another statement by Al-Qazzaz *et al.* note that 20–50% of stroke patients suffer from memory intricacy that manifests during the period following a stroke diagnosis.<sup>[4]</sup>

PSCI includes all forms of cognitive decline that develops after stroke<sup>[5]</sup> includes executive function, memory, language, visuospatial ability, visuoconstructional ability, or global cognitive function.<sup>[6]</sup> PSCI may interfere with the quality of life in stroke survivor.<sup>[7]</sup> Cognitive impairment constitutes a substantial world health burden that is likely to increase with ageing populations and emphasize the critical need for effective treatments.<sup>[8]</sup>

The study in PSCI epidemiology and contributing factor(s) is limited in Indonesia. The combination of Montreal Cognitive Assessment-Indonesian Version (MoCA-INA) and clock drawing test (CDT) as the diagnostic tools for PSCI in Indonesia is not

yet performed. This study aimed to measure the prevalence and determinant factors of cognitive impairment in post-stroke patients.

## METHODS

### Research Design

This study was a cross-sectional study. This study conducted at Bethesda Hospital, Yogyakarta, from March to May 2017. Subjects' data were obtained from medical record and electronic stroke registry.

### Study Subjects and Sampling Calculation

The subjects were post-ischemic stroke patients. The inclusion criteria, i.e., (1) age >18 years, (2) suffered from ischemic stroke within 6 months, and (3) agreed to be a study subject. Ischemic stroke diagnosis was confirmed by neurologist supported by computed tomography (CT) scan examination. Every subject was given an informed consent before performed the tests. The exclusion criteria, i.e., (1) subjects with incomplete data, (2) subjects with a history of Alzheimer, Parkinson, dementia before time to hospital, epilepsy, head trauma, meningoencephalitis, delirium, motoric disorder on dominant side, visual impairment,

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auditory impairment, persistent decreased level of consciousness, and severe depression. The sampling technique was using consecutive sampling method. Every subjects meeting the inclusion criteria were selected. Total of the subjects were 110 subjects.

## Measurement

PSCI defined as any deficit on memory, language, problem-solving, and/or judgement caused by stroke. This study was using MoCA-INA instrument and CDT to measure the cognitive impairment. CDT was performed by asking the subjects to draw a circle and numbers that resemble a clock in a piece of paper. Then, the subjects were asked to draw hands of clock to show a specific time. The results were interpreted by score 1–6.<sup>[9]</sup> MoCA-INA is an instrument to detect any cognitive impairment by measure some aspects, i.e., (1) executive function, (2) visuospatial, (3) language, (4) delayed recall, by mention 5 words and repeat them after 5 min, (5) attention, (6) abstract thinking, (7) and orientation. The maximal score is 30.<sup>[2]</sup> MoCA-INA score <26 and/or CDT score >1 classified as cognitive impairment, whereas MoCA-INA score ≥26 and CDT score = 1 classified as normal cognitive function.

Variable assessed in this study, i.e., age, gender, education, time to hospital, stroke risk factors, stroke history, and brain lesion in CT scan. Age classified into 40–50, 51–60, 61–70, and >70 years. Time to hospital defined as duration from the beginning of stroke symptom(s) until patients come to the hospital. Time to hospital grouped into <3 h, 3–6 h, 6–12 h, 12–24 h, and >24 h. Education defined as a history of formal education in Indonesia, including elementary school, junior high school, senior high school, college, master degree, and doctoral degree. Education categorized into education ≤12 years and >12 years.

Stroke risk factors assessed in this study include smoking, Type 2 diabetes mellitus (DM2), dyslipidemia, and hypertension. Smoking differed into patients who smoking and patients who not smoking. DM2 defined as fasting plasma glucose ≥126 mg/dL, or 2 h plasma glucose ≥200 mg/dL during oral glucose tolerance test, or random plasma glucose ≥200 mg/dL with classic symptoms of hyperglycemia, or A1C ≥6.5%, or consuming antidiabetic drugs and/or insulin. Dyslipidemia defined as any increasing level of blood lipid: Low-density lipoprotein cholesterol level ≥140 mg/dL, high-density lipoprotein cholesterol <40 mg/dL, triglyceride level >200 mg/dL, total cholesterol level >200 mg/dL, and/or consuming lipid-lowering drug(s). Hypertension defined as systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg or consuming antihypertensive drug.

Brain lesion in CT scan classified based on number and location. Based on number, brain lesion differed into no lesion, single lesion, and multiple lesions. Based on location, brain lesion differed into the presence of cortical lesion and no cortical lesion. The presence of cortical lesion further differed into frontal lesion, occipital lesion, temporal lesion, and parietal lesion.

## Statistical Analysis

All of the variables were analyzed using SPSS program. Univariate analysis was performed to identify subject's characteristics. Chi-square test as bivariate analysis and logistic regression as multivariate analysis were performed to determine the

independent determinant factor(s) of cognitive impairment. Statistical significance was set at  $P < 0.05$ .

## Ethical Clearance

This study was verified by Faculty of Medicine Duta Wacana Christian University Ethical Research Committee. The number of ethical clearance was 309/C.16/FK/2017.

## RESULTS

Totally, there were 110 subjects who had stroke attack in the last 6 months before this study conducted. This study was dominated by male (65.5%), age >60 years, educated ≤12 years (60%), and suffered stroke for the 1<sup>st</sup> time (58.2%). The common stroke risk factors were dyslipidemia (50.9%) and hypertension (70%). As much as 40.1% subjects came to the hospital >24 h after the time to hospital. Most of the subjects had multiple lesions (36.4%) and the location was in brain cortex (67.3%), especially in parietal cortex (48.3%). The detail of subjects' characteristics showed in Table 1.

Table 2 summarizes the results of cognitive test measured using MoCA-INA instrument and CDT. Most of the subjects had cognitive impairment (68.2%). Further, the analysis was done to identify the determinant factor(s) of cognitive impairment.

Bivariate analysis showed age >70 years (odds ratio [OR]: 6.500, 95% confidence interval [CI]: 0.780–64.95,  $P = 0.007$ ), time to hospital, especially between 12 h and 24 h (OR: 31.43, 95% CI: 3.50–78.18,  $P < 0.001$ ), and stroke history (OR: 3.466, 95% CI: 0.116–0.716,  $P = 0.006$ ) was significant determinant factors to cognitive impairment. Number and location of brain lesion, especially multiple lesions (OR: 17.27, 95% CI: 3.990–86.18,  $P < 0.001$ ), located in parietal (OR: 4.100, 95% CI: 1.690–9.950,  $P < 0.001$ ), and temporal (OR: 16.00, 95% CI: 2.066–123.9,  $P < 0.001$ ), also significant interfere the cognitive function. The results of bivariate analysis showed in Table 3.

Logistic regression performed based on the results of bivariate analysis. Time to hospital, especially 12–24 h (OR: 52.723, 95% CI: 3.982–698.07,  $P = 0.003$ ), multiple lesions (OR: 9.878, 95% CI: 1.093–89.314,  $P = 0.041$ ), and temporal lesion (OR: 26.102, 95% CI: 2.146–317.43,  $P = 0.010$ ) were independent determinant factors of cognitive impairment in post-ischemic stroke patients [Table 4].

## DISCUSSION

The prevalence of PSCI in this study was high (68.2%). This result is higher than the previous study by Arciniegas *et al.* (2011) showed mild cognitive impairment was observed in 22.2% subjects and moderate or greater cognitive impairment was observed in 7.4% subjects.<sup>[10]</sup> Higher PSCI prevalence showed by two studies in Indonesia by Ningsih (2016)<sup>[11]</sup> and Wibowo (2015),<sup>[12]</sup> which is the prevalence are 100% and 97.1%, respectively.

There are a lot of differences in PSCI prevalence between various studies. It is because of differences between the countries, the races, and the diagnostic criteria.<sup>[13]</sup> This study was using MoCA-INA and CDT as the tools to measure PSCI, whereas another studies using MoCA-INA, mini-mental state examination (MMSE), trail making test (TMT)-A and B, or Addenbrooke's cognitive

examination-revised. Different tool to make PSCI diagnosis may lead to different results. A study by Paparang *et al.* (2013) showed different results using three types of instrument to diagnose PSCI. Impaired cognitive function showed in 56.86% subjects using CDT, 45.10% subjects using MMSE, 96.08% using TMT-A, and 84.31% using TMT-B.<sup>[14]</sup>

**Table 1: Subjects characteristics**

Subject characteristics	n=110 (%)
Age (years)	
40–50	12 (10.9)
51–60	36 (32.7)
61–70	34 (30.9)
>70	28 (25.5)
Gender	
Male	72 (65.5)
Female	38 (34.5)
Education (years)	
≤12	66 (60)
>12	44 (40)
Time to hospital (h)	
<3	27 (24.5)
3–6	7 (6.4)
6–12	19 (17.3)
12–24	12 (10.9)
>24	45 (40.1)
Smoking DM2	
Yes	48 (43.6)
No	62 (56.4)
Yes	45 (40.9)
No	65 (59.1)
Dyslipidemia	
Yes	56 (50.9)
No	54 (49.1)
Hypertension	
Yes	77 (70)
No	33 (30)
Stroke history	
First stroke	64 (58.2)
Recurrent stroke	46 (41.8)
Number of brain lesion	
No lesion	36 (32.7)
Single lesion	34 (30.9)
Multiple lesions	40 (36.4)
Location of brain lesion	
No cortical lesion	36 (32.7)
Presence of cortical lesion	74 (67.3)
Cortical lesion location	
Frontal	
Yes	28 (25.5)
No	82 (74.5)
Occipital	
Yes	8 (7.3)
No	102 (92.7)
Temporal	
Yes	25 (22.7)
No	85 (77.3)
Parietal	
Yes	53 (48.2)
No	57 (51.8)

DM2: Type 2 diabetes mellitus

Age is an important determinant of memory.<sup>[15]</sup> The prevalence of PSCI in this study was increasing gradually by age and peaked at age >70 years (34.7%). This result is parallel to previous studies. The prevalence of cognitive impairment was higher with increasing age (100% in the age group 80–89 years).<sup>[16]</sup> The cognitive impairment rate in stroke survivors was strongly associated with age at all-time points and it progressively increased after 5 years of stroke for patients aged 65–85 years old.<sup>[17]</sup> Another study by Cristy *et al.* (2012) mentioned age >70 years has a higher risk of cognitive impairment.<sup>[18]</sup>

As much as 68% of subjects in this study were male. Another study in India stated the same result; the prevalence is higher in men than in women.<sup>[19]</sup> Another research in Indonesia showed about 65.85% of subjects were male.<sup>[20]</sup>

Most of the subjects in this study were less educated (68.3%), it meant that most of the subjects did not complete their education until senior high school. The higher education level could increase the tolerance of the cognitive decline.<sup>[21]</sup> The patients' obedience in attending control appointments is also affected by their level of education.<sup>[22]</sup> Low education level is associated with decreased functional cognitive reserve and it also may have an impact on lifestyle and risk factor profile,<sup>[23]</sup> thus may also affect the quickness to seek for help when stroke symptom(s) appear. Our hypothesis is the level of education influence the time to hospital admission. Late onset to hospital admission is the risk factors for post stroke cognitive impairment. Cortical lesion is strongly associated with cognitive impairment compare with subcortical lesion. . It is supported by the result of this study. Most of the subjects were less educated and came to the hospital >24 h after onset (52%).

Some modifiable stroke risk factors identified in this study, i.e., smoking, DM2, dyslipidemia, and hypertension. The most common risk factor was hypertension (70.7%). This result is resembled to the previous study. Research on 4212 post-stroke subjects showed hypertension as the most common risk factors (69.5%), followed by smoking (28.6%), DM (22%), and hypercholesterolemia (16%).<sup>[17]</sup> The study by Arba *et al.* stated hypertension was also associated with cognitive impairment at 3 years.<sup>[24]</sup>

The percentage between first and recurrent stroke in this study was almost equal, 50.7% and 49.3%, respectively. In spite of that results, many previous studies showed recurrent stroke is associated with cognitive impairment.<sup>[25-27]</sup>

**Table 2. Results of cognitive tests**

Tests	n = 110 (%)
CDT	
1: No visuospatial disorganization	63 (57.3)
2: Minor visuospatial disorganization	8 (7.3)
3: Mild visuospatial disorganization	22 (20.0)
4: Moderate visuospatial disorganization	10 (9.1)
5: Severe visuospatial disorganization	7 (6.4)
MoCA-INA	
MoCA-INA < 26	75 (68.2)
MoCA-INA ≥ 26	35 (31.8)
Cognitive impairment	
MoCA-INA < 26 and/or CDT > 1	75 (68.2)
MoCA-INA ≥ 26 and/or CDT = 1	35 (31.8)

CDT: Clock drawing test, MoCA-INA: Montreal Cognitive Assessment-Indonesian Version

**Table 3: The results of Chi-square test**

Variable	Cognitive impairment (n=75)	No cognitive impairment n=35 (%)	OR	95% CI	P
Age (years)					
40–50	8 (10.7)	4 (11.4)	Reff		0.007
51–60	19 (25.3)	17 (48.6)	0.560	0.110–2.600	
61–70	22 (29.3)	12 (34.3)	0.920	0.180–4.430	
>70	26 (34.7)	2 (5.7)	6.500	0.780–64.95	
Gender					
Male	51 (68)	21 (60)	1.417	0.616–3.256	0.411
Female	24 (32)	14 (40)			
Education (years)					
≤12	46 (61.3)	20 (57.1)	1.190	0.527–2.688	0.676
>12	29 (38.7)	15 (42.9)			
Time to hospital (h)					
<3	7 (9.3)	20 (57.1)	Reff		<0.001
3–6	4 (5.3)	3 (8.6)	3.810	0.520–30.21	
6–12	14 (18.7)	5 (14.3)	8.000	1.780–39.03	
12–24	11 (14.7)	1 (2.6)	31.43	350–78.18	
>24	39 (52)	6 (17.1)	18.57	4.80–77.76	
Smoking					
Yes	33 (44)	15 (42.9)	1.048	0.466–2.355	0.910
No	42 (56)	20 (57.1)			
DM2					
Yes	33 (44)	12 (34.3)	1.506	0.654–3.466	0.334
No	42 (56)	23 (65.7)			
Dyslipidemia					
Yes	36 (48)	20 (57.1)	0.692	0.308–1.554	0.327
No	39 (52)	15 (42.9)			
Hypertension					
Yes	53 (70.7)	24 (68.6)	1.020	0.700–1.490	0.883
No	22 (29.3)	11 (31.4)			
Stroke history					
First stroke	38 (50.7)	8 (22.9)	3.466	0.116–0.716	0.006
Recurrent stroke	37 (49.3)	27 (77.1)			
Number of brain lesion (s)					
No lesion	15 (20)	21 (60)	Reff		<0.001
Single	23 (30.7)	11 (31.4)	2.930	0.990–8.800	
Multiple	37 (49.3)	3 (8.6)	17.27	3.990–86.18	
Location of brain lesion					
Frontal cortex	20 (18.3)	8 (19.5)	1.27	0.479–3.143	0.669
Occipital cortex	6 (5.5)	2 (4.9)	1.435	0.275–7.495	0.667
Temporal cortex	24 (22)	1 (2.4)	16.00	2.066–123.9	0.001
Parietal cortex	44 (40.4)	9 (22)	4.100	1.690–9.950	0.001
No cortical lesion	15 (13.8)	21 (51.2)	1.670	0.069–0.403	<0.001

DM2: Type 2 diabetes mellitus, OR: Odds ratio, CI: Confidence interval

Every subject in this study was underwent brain CT scan examination. Most of them had multiple lesions (49.3%), especially in parietal (40.4%). Damaged brain region is play a key role of the cognitive impairment.<sup>[28]</sup> Multiple lesions are the third factor contributing on cognitive impairment after wide and location.<sup>[29]</sup>

All of those variables were analyzed with Chi-square test. The results showed age >70 years, time to hospital, especially between 12 and 24 h, and time to hospital, number and location of brain lesion, especially multiple and temporal lesion were significant factors contributing PSCI. Logistic regression was performed based on the results of Chi-square test.

Time to hospital, especially 12–24 h (OR: 52.723, 95% CI: 3.982–698.07, P: 0.003), and was independent determinant factors

of cognitive impairment in post-ischemic stroke patients. The duration between stroke onset and time to hospital is important to cognitive impairment. There is a disturbance of blood flow in brain on ischemic stroke, leading to cell ischemic and apoptosis. If stroke patients do not get any treatment immediately, the ischemic area is getting bigger and the risk of cognitive impairment is getting higher.<sup>[30]</sup>

Multiple infarctions often cause progressive, step-like course of cognitive disorders, and undoubtedly increase the risk of PSCI.<sup>[31]</sup> Multiple lesions were increasing PSCI 9.878 times (95% CI: 1.093–89.314, P: 0.041). This result is higher compared to the previous study, which is multiple infarcts 2.5 times increasing PSCI.<sup>[32]</sup> Sundar and Adwani (2010) stated memory was significantly

**Table 4: Determinant factors of cognitive impairment**

Variable	OR	95% CI	P
Time to hospital (h)			
<3	Reff		0.002
3–6	1.377	0.135–14.088	0.788
6–12	8.064	1.223–53.190	0.030
12–24	52.723	3.982–698.07	0.003
>24	0.351	5.155–178.68	<0.005
Recurrent stroke	3.299	0.943–11.544	0.062
Number of brain lesion (s)			
No lesion	Reff		0.041
Single	0.865	0.137–5.463	0.877
Multiple	9.878	1.093–89.314	0.041
Location of brain lesion			
Parietal cortex	4.870	0.753–31.477	0.096
Temporal cortex	26.102	2.146–317.43	0.010

OR: Odds ratio, CI: Confidence interval

more commonly affected in multiinfarct strokes as compared to single infarcts.<sup>[33]</sup>

Cortical-subcortical and subcortical infarctions are more likely to lead to PSCI.<sup>[34]</sup> Temporal cortex lesion (OR: 26.102, 95% CI: 2.146–317.43, *P*: 0.010) was strongly associated with PSCI. Research on 132 post-stroke subjects showed subjects with subcortical cerebral infarctions may have even worse cognitive profiles than subjects with cortical infarctions.<sup>[35]</sup> A cohort study by Nys *et al.* stated cortical location of stroke was associated 3.6 times higher (95% CI: 1.3–9.9) having cognitive impairment.<sup>[36]</sup> Cognitive impairment in some patients with lacunar stroke is due to concurrent cortical hypoperfusion that might not have been apparent on imaging obtained acutely. Hypoperfusion of cortical regions was more strongly associated with impaired aphasia or neglect than was cortical infarction (*P* < 0.0001).<sup>[37]</sup> If there is reperfusion of the cortex, cognitive function may be restored improvement in cortical function depends not only on how much tissue is reperfused but also on the location of the cortex that is reperfused.<sup>[38]</sup>

Gender, education, recurrent stroke, smoking, dyslipidemia, DM2, and hypertension were not significant determinant factors of PSCI in this study. This result is parallel to previous studies. There was no substantial gender difference for the risk of PSCI (*P*: 0.792).<sup>[39]</sup> There was no significant difference of the rate of decline in cognitive function of the education level. The education level has no effect on the rate of the aggravation of the cognitive impairment.<sup>[13]</sup> The number of stroke attacks was not significantly associated with cognitive status even when the frequencies were higher in the cognitively impaired than in cognitively intact group.<sup>[40]</sup> Even though there were patients with multiple stroke risk factors, there was no certain association with the level of cognitive impairment because multiple risk factors were found among cognitively unimpaired patients too.<sup>[41]</sup>

## CONCLUSION

The prevalence of PSCI is high. More than half of the subjects have a cognitive impairment. The determinant factors of PSCI are stroke onset, multiple lesions, and temporal lesion.

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