

# Dementia Among Patients with Ischemic Stroke in Maharaj Nakorn Chiang Mai Hospital: Prevalence and Its Associating Factors

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**Phadungtham Thiengburanathum, MD\*, Kanokwan Watcharasaksilp, MD\***

*\*Division of Neurology, Department of Internal Medicine, Maharaj Nakorn Chiang Mai Hospital, Chiang Mai University, Chiang Mai 50200 Thailand*

## **Abstract**

**Objective:** To study the prevalence of dementia and related cognitive disorders in patients with stroke followed up at internal medicine and neurology outpatient clinics and to study its associating factors.

**Materials and Methods:** The retrospective cross sectional cohort study was conducted in 98 patients with ischemic stroke, which has undergone cognitive assessments via Mini-mental status examination: Thai version (MMSE – Thai 2002) and Montreal cognitive assessment (MoCA). The diagnosis of cognitive disorders was based on these neuropsychological scores.

**Results:** In 98 patients with ischemic stroke studied, the overall prevalence of vascular dementia (VAD) was 30.61%. Dementia was significant was associated with older patients (OR=1.06; 95%CI, 1.02–1.11; P<0.01) and hypertension (OR=3.55; 95%CI, 1.11–11.36; P=0.03). In the multivariate analysis, hypertension was not statistically significant (adjusted for age) (OR=2.64; 95%CI, 0.78–8.88; P=0.12).

**Conclusion:** The prevalence of dementia in internal medicine and neurology outpatient clinic was about one-third. There is no statistically significant difference in clinical and neuroimaging characteristics between stroke patients with and without dementia, which should be further studied.

**Keywords:** Cognitive impairment, dementia, stroke, vascular dementia, neuropsychological assessment (J Thai Stroke Soc. 2018;17(3):21–30)

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*Corresponding author: Phadungtham Thiengburanathum, MD (E-mail: alef.thieng@gmail.com)*

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## Introduction

Stroke is the second most important cause of disability and death worldwide.<sup>1</sup> In addition to disability caused by motor, perception and sensory deficits, stroke also leads to the impairment of cognitive functions. The cognitive impairment can occur in various degree of severity and in variable domains of cognitive functions. The impairment ranges from single domain to multiple domains and from mild cognitive impairment to dementia.<sup>2-4</sup>

Vascular cognitive impairment can be the result of all types of brain infarctions. Ischemic stroke can occur in many forms such as small vessel infarction, large vessel infarction, non-infarct ischemic change and atrophy.<sup>5</sup> Cognitive impairment may occur slowly and/or sub-clinically in case of the silent brain infarction.

In elderly patients, vascular cognitive impairment usually accompany by aging brain change and neurodegenerative brain disease such as Alzheimer disease<sup>6</sup> which cause the cognitive impairment more severe.<sup>7</sup>

Prevalence of cognitive impairment at 3 months after stroke onset was reported in prior studies varied from 13.6% – 92%.<sup>8-15</sup> The cognitive impairment that commonly occurred after stroke were calculation, mental speed and executive function.<sup>16,17</sup>

Prevalence of mild cognitive impairment varied by timing from the onset of stroke. The prevalence of cognitive impairment after onset of stroke was 71.1% at the first month, 61.3% at 6<sup>th</sup> month, and 51.5% at 12<sup>th</sup> month. Cognitive impairment after stroke usually improved over 12 – 18 months.<sup>10</sup> The prior longterm follow up study reported the prevalence of dementia after the onset of stroke was 7% at first year, 10% at 3<sup>rd</sup> year, 15% at 5<sup>th</sup> year, 23% at 10<sup>th</sup> year, and 48%

at 25<sup>th</sup> year<sup>18</sup>. Cognitive domains which usually improved after cerebral infarction were visual perception/ construction (83%) and visual memory (78%).<sup>19</sup>

The factors that associated with improvement of cognitive impairment were age, language skill, frontal lobe lesion, temporal lobe lesion, occipital lobe lesion, size of lesion, diabetes, hypertension and smoking.<sup>11,20</sup>

Mini-mental status examination: Thai version (MMSE – Thai 2002)<sup>21</sup> and Montreal cognitive assessment (MoCA)<sup>22</sup> are neuropsychological test that were widely used. Both MMSE – Thai 2002 and MoCA tests were recommended by the dementia association of Thailand to be used for evaluate patients with cognitive impairment.

MMSE – Thai 2002 have cut off value for diagnose severe cognitive impairment compatible with dementia.<sup>21</sup> The cut-off was different by level of education. For population educated more than 6 years (primary school), the cut-off of 22 or less has been used. The sensitivity and specifictiy were 92.0% and 92.6%, respectively. For population that educated in level of primary school, the cut-off of 17 or less has been used. The sensitivity and specifictiy were 56.6% and 93.8%, respectively. For population that was unschooled, the cut-off of 14 or less has been used. The sensitivity and specifictiy were 35.4% and 76.8%, respectively.

Montreal cognitive assessment (MoCA)<sup>22</sup> are used together with MMSE – Thai 2002 to evaluate and quantify degree of mild cognitive impairment (MCI).<sup>23</sup> The cut-off of 25 or more had been used to document the level of cognitive function comparable to normal population.

This study aims to study prevalence of dementia and related cognitive disorders in

patients with stroke and study its associating factors such as neuroimaging finding and clinical risk factors.

### ***Theoretical/Operational Definition of Terms***

The following terms are defined for the purpose of this study.

Dementia refers to the diagnosis of dementia, based on DSM 4 criteria. Cognitive deficits was graded by Mini-Mental State Examination: Thai version (MMSE-Thai 2002) documented in Thai clinical practice guideline for dementia in 2003.<sup>21</sup> The significant impairment in social or occupational functioning was evaluated by ADL and instrumental ADL (ADL and IADL)<sup>24</sup> and/or clinical note in medical record signified loss of social or occupational functioning.

Mild cognitive impairment (MCI) refers to the diagnosis of MCI, based on the cognitive impairment evaluated using Montreal Cognitive Assessment (MoCA), published in 2012 by Budson et al.<sup>22</sup>

Neuroimaging lesion was reviewed in diagnosis of vascular dementia using the operational definitions of the imaging guidelines of the NINDS-AIREN criteria.<sup>25</sup>

### ***Materials and Methods***

#### **Population and sample**

The population in this study was patient who had ischemic stroke for more than 1 month that was defined by clinical and/or imaging, aged more than 20 years. Stroke can be either first-ever stroke or recurrent stroke and followed up at the internal medicine and neurology outpatient clinics, Maharaj Nakorn Chiang Mai hospital. Patient with ischemic stroke who had

these following conditions were excluded, including 1) diagnosed with dementia before having stroke, 2) language barrier, and 3) severe pre-exist condition that can contribute to dementia such as psychiatric illness, post cardiac arrest. Data were collected between August and November 2015. Ninety eight subjects were included in the study.

#### **Research instruments**

A questionnaire was used to elicit data from electronic medical records (EMR), including patient's demographic data, characteristics of stroke, Mini-Mental State Examination: Thai version (MMSE-Thai 2002), Montreal Cognitive Assessment (MoCA), activities of daily living and instrumental activities of daily living (ADL and IADL) and neuroimaging data.

#### **Protection of the Rights of Human Subjects**

This study was conducted with the approval of the Institutional Review Board (IRB) of the Faculty of Medicine, Chiang Mai University to assure the protection of human subjects. Confidentiality of all information was maintained. All data were analyzed and reported as group data.

#### **Data Analysis**

Data entry and analysis were performed using SAS software, version 9.3. All data were double entry and compared for any errors. Descriptive statistical analysis was used for demographic data and clinical data such as risk factors and/or co-morbidities and neuroimaging findings. Logistic regression analyses were deployed to determine the relationship between dementia and a set of its associating factors, including risk factors and comorbidity (i.e., smoking, dyslipidemia, hypertension, diabetes, impaired fasting glucose, atrial fibrillation,

coronary artery disease, migraine headache, epilepsy), and type, neuroimaging finding subtype of ischemic stroke (i.e., small vessel).

### Study design

The retrospective cross sectional cohort study was used to describe the prevalence of dementia and related cognitive disorders in patients with ischemic stroke who followed up at either the internal medicine or the neurology outpatient clinics and to explore its associating factors, including risk factors and comorbidity (i.e., smoking dyslipidemia, hypertension, diabetes, impaired fasting glucose, atrial fibrillation, coronary artery disease, migraine headache, epilepsy), and type, neuroimaging finding subtype of ischemic stroke (i.e., small vessel).

### Results

There were 98 patients with ischemic stroke, ranging in age from 32 to 98 years (mean = 69.73, SD = 13.33 years). Fifty-two percent was male. Approximately 57 percent earned at least secondary school. More than 90 percent had risk factors and/or co-morbidity beside ischemic stroke. The top three risk factors and/or co-morbidity that subjects had were hypertension, dyslipidemia, and diabetes with the percent of 71.4, 62.2, and 27.6, respectively. Duration after the onset of ischemic stroke ranged between 2 and 160 months (mean = 35.45, SD = 33.50 months). According to neuroimaging subtypes of ischemic stroke, 70.3 percent of patients had only small vessel stroke. The majority of patients with ischemic stroke were able to perform activities of daily living by themselves. Characteristics of patients with ischemic stroke are presented in Table 1.

**Table 1.** Characteristics of Patients with Ischemic Stroke (N=98)

Characteristics	N=98
Age (year), mean $\pm$ SD	69.73 $\pm$ 13.33
Male, N (%)	52 (53.06)
Level of education†	
No formal education, N (%)	9 (9.38)
Primary school, N (%)	32 (33.33)
At least secondary school, N (%)	55 (57.29)
Risk factors/ co-morbidity	
No	9 (8.16)
Smoking, N (%)	16 (17.98)
Dyslipidemia, N (%)	61 (62.24)
Hypertension, N (%)	70 (71.43)
Diabetes, N (%)	27 (27.55)
Impaired fasting glucose, N (%)	7 (7.14)
Atrial fibrillation, N (%)	5 (5.10)

Characteristics	N=98
Coronary artery disease, N (%)	3 (3.06)
Migraine headache, N (%)	7 (7.14)
Epilepsy, N (%)	3 (3.06)
Impaired activities of daily living	36 (36.73)
Duration after stroke onset <sup>†</sup> (months), mean $\pm$ SD	35.45 (33.50)
Neuroimaging subtypes of ischemic stroke <sup>†</sup>	
Small vessel, N (%)	64 (70.33%)
Large vessel, N (%)	15 (16.48%)
Mixed, N (%)	12 (13.19%)

<sup>†</sup>The number was calculated by using non missing cases

### ***Cognitive Functions in Patients with Ischemic Stroke***

MMSE – Thai 2002 was employed as the initial method to assess cognitive functions in all 98 patients. The MMSE–Thai 2002 scores, ranged between 6 and 30 (mean = 22.98, SD = 5.53). More than half of the patients had MMSE–Thai 2002 scores between 23 and 30. MMSE–Thai 2002 scores were compared against scores for each education level, 68 patients (69.4%) had

normal MMSE scores. MoCA was then deployed for additional assess cognitive functions among those with normal MMSE score. However, out of 68 patients, only in 53 patients were tested with MoCA. The MoCA scores, ranged from 10 to 30 with mean score of 21.64 and standard deviation of 5.17. Of those 53 patients, 35 patients (66.04 %) had abnormal MoCA test. Cognitive functions in patients with ischemic stroke is shown in Table 2.

**Table 2.** Cognitive Functions in Patients with Ischemic Stroke (N=98)

Tools	N=98
MMSE – Thai 2002	
Raw score: 0-1	7 (7.1)
15-17	8 (8.2)
18-22	28 (28.6)
23-30	55 (56.1)
Classification based on education level	
- Normal MMSE	68 (69.4)
- Impaired MMSE	30 (30.6)
MoCA <sup>†</sup>	
- Normal MoCA (score = 25-30)	18 (33.96)
- Abnormal MoCA (score $\leq$ 24)	35 (66.04)

MMSE–Thai 2002 = Mini Mental State Examination – Thai version; MoCA = Montreal Cognitive Assessment.

<sup>†</sup>The number was calculated by using non missing cases

When cognitive domains were assessed by MoCA, delayed recall test and abstract thinking were most common problems in patients with MCI with the frequency of 100% and 82.9%,

respectively. While problem with orientation was rarely found among all patients. The details of each domains evaluated by MoCA test were show in Table 3.

**Table 3.** Cognitive domains evaluated by MoCA (N=53)

Domains	All patients (N=53)	Cognitive intact (N=18)	MCI (n=35)
Executive and visuospatial			
Modified trail making	22 (41.5)	2 (11.1)	20 (57.1)
Copy of cube	23 (43.4)	2 (11.1)	21 (60.0)
Clock drawing test	24 (45.3)	5 (27.8)	19 (54.3)
Naming	10 (18.9)	4 (22.2)	6 (17.1)
Attention			
Digit spans	14 (26.4)	2 (11.1)	12 (34.3)
Digit tapping test	12 (22.6)	2 (11.1)	10 (28.6)
Serial 7 subtraction	30 (56.6)	6 (33.3)	24 (68.6)
Language			
Sentence repetition	20 (37.7)	2 (11.1)	18 (51.4)
Letter fluency	31 (58.5)	5 (27.8)	26 (74.3)
Abstract thinking	32 (60.4)	3 (16.7)	29 (82.9)
Delayed recall	45 (84.9)	10 (55.6)	35 (100)
Orientation	2 (3.8)	0	2 (5.6)

### ***Prevalence of Dementia and Mild Cognitive Impairment Among Patients with Ischemic Stroke***

Of those 98 patients with ischemic stroke, less than 20 percent of sample had cognitive intact. Approximately 30 percent of sample met

the diagnosis criteria for dementia while the majority of sample fit with the criteria for mild cognitive impairment. A schematic diagram indicating the cognitive disorder classification showed in Figure 1.

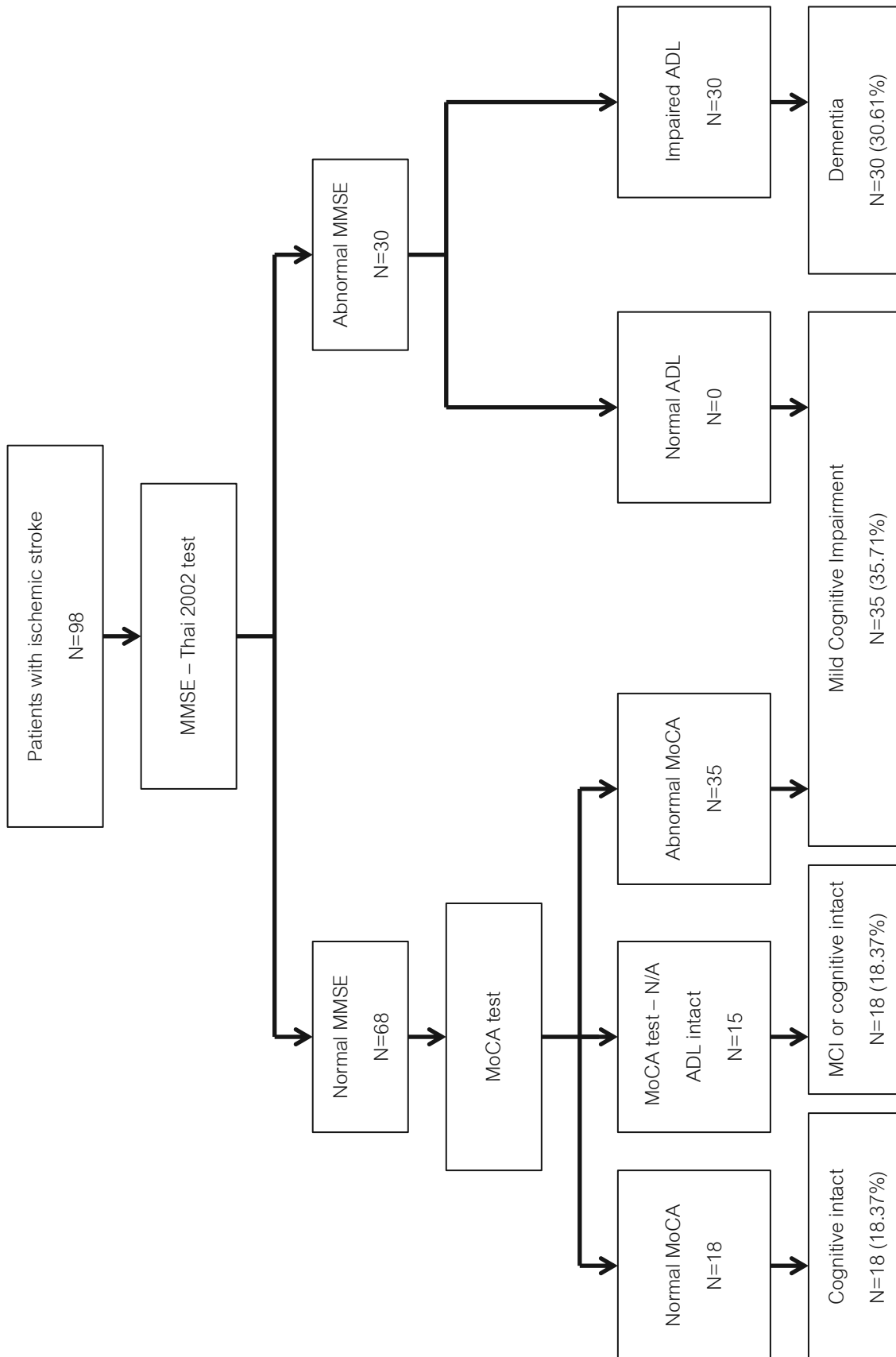


Figure 1: Simplified scheme of neuropsychological test used to evaluate patients

## Dementia and associating factors

The association between dementia and its associating factors, including risk factors and comorbidities (i.e. smoking, dyslipidemia, hypertension, diabetes, impaired fasting glucose, atrial fibrillation, coronary artery disease, migraine headache, epilepsy), and neuroimaging finding type of ischemic stroke (i.e., small vessel)

were tested by using univariate logistic regression analyses. There is statistically significant difference in ages and hypertension between groups. In multivariate analysis adjusted for age, hypertension was not associated with dementia (OR=2.64; 95%CI, 0.78–8.88; P=0.12). The detail was showed in Table 4.

**Table 4 : Odds Ratio for Associating Factors of Dementia in Patient with Ischemic Stroke (N=98)**

Variable	Dementia		Odds ratio (95% CI)	P-value
	No (N=68)	Yes (N=30)		
Age (years)	66.93 ± 12.56	76.10 ± 13.03	1.06 (1.02-1.11)	< 0.01
Male	37	15	0.84 (0.35-1.98)	0.69
Education (years)†	9.69±/-5.83	7.23±/-5.47	0.92 (0.85-1.00)	0.05
Risk factors/ comorbidity				
Smoking†	10	6	1.40 (0.45-4.30)	0.57
Dyslipidemia	43	18	0.87 (0.36-2.10)	0.76
Hypertension	44	26	3.55 (1.11-11.36)	0.03
Diabetes	16	11	1.88 (0.74-4.78)	0.18
Impaired fasting glucose	7	0	< 0.01 (<0.01->999.99)	0.97
Atrial fibrillation	4	1	0.55 (0.06-5.16)	0.60
Coronary artery disease	2	1	1.14 (0.10-13.05)	0.92
Migraine headache	6	2	0.36 (0.04-3.10)	0.35
Epilepsy	3	0	<0.01 (<0.01->999.99)	0.98
Duration after stroke onset (months)†	32.95 ± 31.81	40.38 ± 36.67	1.01 (0.99-1.02)	0.33
Neuroimaging finding†			1.95 (0.50-7.68)	0.34
Large vessel	12	3		
Small vessel	43	21		

†The number was calculated by using non missing cases



## **Discussion**

At internal medicine and neurology outpatient clinics at Maharaj Nakorn Chiang Mai hospital, the prevalence of dementia was about 30 percent.<sup>18</sup> Comparison with a prior study, the prevalence of dementia varied by timing after onset of stroke range from 7 percent to 48 percent. The prevalence in each was varied in studies because of difference in characteristics of populations, burden load of brain infarction, severity of individual stroke, and neuropsychological assessment.

In prior studies, various conditions (i.e. increasing age, age, language skill, hypertension and smoking)<sup>11,19,20</sup> were associated with vascular cognitive decline. However, our study found only age and hypertension have association with dementia.

There are some limitations in this study. First, the design of study was retrospective study, which led to the limitation on data availability. Second, population in this study was the patients who were follow up at internal medicine and neurology clinic. This may limit the application to general population. Third, the small number of populations affects the power to determine the association of risk factors and comorbidities.

## **Conclusion**

The prevalence of dementia in internal medicine and neurology outpatient clinic was about 30 percent. Hypertension showed trend to predicted dementia in our preliminary study, but was not statistically significant in a multivariate analysis. However, further studies are needed to explore the relationship between hypertension and dementia.

## **Originality and Body of Knowledge**

1. About two-third of patients survived from stroke that is still followed up at outpatient clinic suffered from cognitive impairment ranged from mild cognitive impairment to dementia.
2. Cognitive impairment in stroke can affect multiple cognitive domains in variable degree. Testing for delayed recall memory and abstract thinking are two of most sensitive tests (sensitivity 100%, 82.9% respectively) that might be used to develop a screening tool for cognitive impairment among these patients.

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