



## Prevalence of Mild Cognitive Impairment in Chronic Obstructive Pulmonary Diseases (COPD) at Siriraj Hospital

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### Abstract

Chronic obstructive pulmonary disease (COPD) is systemic inflammation that is caused comorbidities such as metabolic syndrome (MetS), type 2 diabetes mellitus (type 2 DM), and cardiovascular disease. Mild cognitive impairment (MCI) has been reported as comorbidities in COPD. However, the prevalence of MCI and risk factors involved MCI in COPD, especially male, has been minimally reported. Almost all cases of the prevalence of COPD in Thailand have been found in the male. This paper aims to investigate the prevalence of MCI and the characteristics of MCI in male COPD. One hundred and sixty-nine males with COPD recruited into this study between 2017-2019. They were tested with cognitive impairment using the Thai version of the Montreal Cognitive Assessment (MoCA). The cut point for normal cognitive function when the score is  $\geq 25$  points. The prevalence of male with COPD was calculated. Also, the characteristics of MCI in male COPD were analyzed. The prevalence of MCI in males with COPD was 77.51%. A total score of MoCA of COPD with and without MCI was  $18.60 \pm 4.34$  and  $26.21 \pm 1.49$ , respectively ( $p=0.01$ ). Domains of memory, visuospatial/executive, attention, language, and abstract were decreased in COPD with MCI compared with non-MCI,  $p < 0.05$ . Risk factors of MCI in male COPD might be involved with age, education, smoking, and exacerbation. In conclusion, cognitive impairment was one comorbidity of male COPD, and the type of MCI in male COPD was the amnesic MCI multiple domains.

**Keywords:** COPD, mild cognitive impairment, Montreal Cognitive Assessment (MoCA), male, risk factors

### 1. Introduction

Chronic obstructive pulmonary disease (COPD) is frequently found in the aging population. The global prevalence of COPD between men and women is almost equal (GOLD, 2020), but the male is predominant in the Asia-Pacific region, including Thailand (Maranetra et al., 2002). Systemic inflammation associates with causing of chronic obstructive pulmonary disease (COPD) and its comorbidities (GOLD, 2020). The comorbidities related to COPD such as osteoporosis, chronic anemia, lung cancer, depression, atherosclerosis, type 2 diabetes mellitus (DM), cardiovascular diseases (CVD) (Barnes & Celli, 2009; Cavailles et al., 2013). Mild cognitive impairment (MCI) has been reported in COPD (GOLD, 2020). The MCI is the intermediate stage between the cognitive changes of normal aging and dementia. Several risk factors in COPD were associated with MCI, such as age, education, systemic inflammation, autonomic dysfunction, and the numbers of comorbidities, especially HT, type 2 DM, whereas CVD are more frequently found in COPD with MCI compared with non-MCI (Villeneuve et al., 2012). Frequent exacerbation has been reported in COPD with MCI compared non-MCI (Kirdsup, 2014). Cognitive impairment in patient with COPD might be disturbed their daily activity such as medication administration, recall memory, and communication with family.

The prevalence of MCI in COPD has been shown in 16.5%-36% (Villeneuve et al., 2012). Thirty-eight percent of prevalence MCI in Thai COPD has been reported, both male and female (Kirdsup, 2014). However, the prevalence of MCI and its characteristics in Thai COPD, especially male, has been lightly reported. Also, risk factors of MCI in male COPD were investigated in this study.



## 2. Objectives

1. To investigate the prevalence of MCI and type of MCI in male COPD
2. To investigate the risk factors of MCI in male with COPD

## 3. Materials and Methods

Siriraj Institutional Review Board approved the protocol of this study. One hundred and sixty-nine men with COPD were voluntarily participated in this study and recruited from the COPD clinic, Siriraj Hospital, Mahidol University. The inclusion criteria were; 1) male 2) COPD diagnosis with disease severity stage I-IV, 3) age  $\geq 40$  years, and 4) comprehend the conversation. Exclusion criteria were: 1) neurological disease that involved cognitive impairment such as stroke, Parkinson's disease, and Alzheimer's disease, 2) being unwilling for participation. Informed consent was obtained from all subjects before participating in this study. All participation was tested on the cognitive function by the Thai version MoCA questionnaire. The Thai version MoCA testing spent time about 10-15 minutes per time. The demographic data such as age, smoking, education, pulmonary functional test, exacerbation, and comorbidities were collected. Five milliliters (ml) of blood samples were collected in the morning after 12 hours of fasting by nurses at Siriraj hospital. The lipid profiles, hematological, and clinical laboratory chemistry values were tested by a certified laboratory at Siriraj hospital.

### Montreal Cognitive Assessment (MoCA)

It is a screening test for MCI in the elderly population, including COPD. In addition, MoCA is widely used in clinical and research because of its simplicity and time efficiency (10-15 minutes). Eight cognitive domains are covered: 1) visuospatial/executive function, 2) naming, 3) memory, 4) attention, 5) language, 6) abstraction, 7) delayed recall, and 8) orientation. The total score is 30 points and the cut point for normal cognitive function when the score is  $\geq 25$  points. Thai version of MoCA is available (The MoCA testing; online). Besides, its sensitivity and specificity have tested in COPD (81% and 72%, respectively) (Nasreddine et al., 2005).

### Statistical analysis

SPSS version 19.0 (SPSS Inc., Chicago, IL, USA) was used for data analysis. The statistically significant differences were  $p < 0.05$ . The demographic data were analyzed by descriptive statistics. The score of MoCA testing, the lipid profiles, hematological, and clinical laboratory chemistry values has been tested by an Independent t-test for comparison between COPD with MCI and non-MCI if these data were tested as a normal distribution. If they were not a normal distribution, the Mann-Whitney Test was analyzed.

## 4. Results and Discussion

The prevalence of MCI in male COPD was 77.51% ( $n=131$ ). Age and years of smoking in COPD with MCI were significantly higher than the non-MCI group ( $72.92 \pm 8.08$  vs.  $68.24 \pm 7.73$ ;  $39.66 \pm 14.56$  vs.  $32.58 \pm 13.13$ , respectively,  $p < 0.05$ ). Low education was significantly found in COPD with MCI compared non-MCI group ( $7.52 \pm 4.74$  vs.  $11.13 \pm 4.74$  yrs.). Furthermore, exacerbation rate was frequently found in COPD with MCI compared non-MCI group (28.91% vs. 16.67%,  $p=0.01$ ). These data have been shown in Table 1. However, the severity of COPD was not significantly different between COPD with MCI and without COPD. Although the number of comorbidities was similar between COPD with MCI and without COPD, patients COPD who were more two diseases of the cardiometabolic syndrome (CMS) highly trended in the MCI group compared with non-MCI. The total score of MoCA in COPD with MCI was  $18.60 \pm 4.34$  that indicated cognitive decline compared with COPD without MCI ( $26.21 \pm 1.49$ ). Their MCI type were the amnesic MCI multiple domains that were the impairments in memory domain with other domains such as visuospatial/executive, attention, language, abstract, and orientation domains, as shown in Table 2. The previous study has found 58.7% of prevalent MCI in COPD aged 82.7-year-old (Singh et al.,



2013). The prevalence of MCI in COPD in this study was higher than the previous study. This might be that education year in this study was lower than the study of Singh and coworkers (7.52±4.74 vs. 12.00 yrs.).

In addition, subtype of MCI in COPD and its risk factors in this study were similar with the study of Kirdsup and coworkers (Kirdsup, 2014). They found that patient with COPD mostly were amnesic MCI multiple domains. The risk factors of MCI in COPD were associated with age, low education ( $\leq 12$  yrs.), frequent exacerbation, and number of comorbidities in COPD. However, there were not significant of comorbidities between COPD with MCI and without MCI in this study. Dyslipidemia might be associated with prevalent MCI in COPD compared with non-MCI (109.5±58.73 vs. 90.00±33.69,  $p=0.016$ ) as shown in Table 3. This result was similar to the previous study (Villeneuve et al., 2012). Arteriosclerosis may affect hypo-perfusion of the brain and, consequently, hypoxemia. These may lead to neuron toxicity and glial cell dysfunction and hypoperfusion, resulting in impairment in many cerebral domains (Ortapamuk & Naldoken, 2006). The limitation of this study included an inflammatory marker is not collected. No patient with COPD could discontinue the taking medication, which may cause no significant difference in blood chemistry between COPD with MCI and non-MCI.

**Table 1** The demographic data of COPD with MCI and without MCI

Characteristics	MCI (n=131)	Non-MCI (n=38)	p-value
	mean±SD	mean±SD	
Age (yrs.)	72.92±8.08*	68.24±7.73	0.002
BMI (kg/m <sup>2</sup> )	22.15±3.93	22.70±3.68	
COPD diagnosis (yrs.)	5.91±4.44	6.39±3.59	
Education (yrs.)	7.52±4.74*	11.13±4.74	0.01
Education categorized, (%)			
lower high school	77.10*	52.63	0.04
higher high school	22.90	47.37	
Year of smoking (yrs.)	39.66±14.56*	32.58±13.13	0.005
Smoking history, (%)			
never	1.53 (2)	2.63 (1)	
ex-smoker	89.31(117)	92.11 (35)	
active smoker	9.16 (12)	5.26 (2)	
Pulmonary function test			
FEV <sub>1</sub> /FVC ratio	50.40±12.80	50.65±12.85	
predFEV <sub>1</sub>	65.39±25.34	64.97±23.55	
RV/TLC	51.91±9.78	49.47±9.13	
Disease severity (%)			
mild	29.01	28.95	
moderate	42.75	36.84	
severe	22.90	26.32	
very severe	5.34	7.89	
Exacerbation (%)			
none	71.09	83.33	
acute exacerbation	28.91*	16.67	0.01
CMS (%)			
DLP	54.96	40.54	
DM	17.56	16.22	
HT	64.12	64.86	
CAD	14.50	16.22	
≥ 2 diseases	53.44	37.84	

\* Significantly difference with COPD without MCI,  $p<0.05$ ; DLP=dyslipidemia; DM=diabetes Mellitus; HT=hypertension; CAD=coronary artery disease; CMS: cardiometabolic syndromes such as DM, DLP, HT, and CAD



MoCA score	MCI (n=131)	Non-MCI (n=38)	p-value
	mean±SD	mean±SD	
Visuospatial/executive (5 points)	2.50±1.42*	4.08±0.85	0.01
Naming (3 points)	2.85±0.50*	3.00±0.00	0.04
Attention (6 points)	4.44±1.39*	5.82±0.39	0.01
Language (3 points)	1.11±1.00*	2.08±0.91	0.01
Abstraction (2 points)	0.51±0.67*	1.42±0.76	0.01
Delayed recall (5 points)	1.11±1.46*	3.66±1.17	0.01
Orientation (6 points)	5.53±1.08*	5.97±0.16	0.01
Total score (30 points)	18.60±4.34*	26.21±1.49	0.01

**Table 2** Score of Thai version MoCA testing between COPD with and without MC

\* Significantly difference with COPD without MCI,  $p < 0.05$

**Table 3** Hematological and clinical laboratory chemistry values between COPD with and without MCI

Variables	MCI (n=119)	Non-MCI (n=34)	p-value
	mean±SD	mean±SD	
Hemoglobin (g/dL)	13.75±1.68	14.34±1.87	
Glucose (mg/dL)	100.33±21.43	103.94±24.22	
HbA1c (%)	6.43±5.29	5.97±0.85	
Insulin (μU/mL)	9.03±9.79	7.7±6.25	
HOMA index	2.45±3.44	2.05±1.91	
Triglyceride (mg/dL)	109.5±58.73*	90.00±33.69	0.016
HDL (mg/dL)	58.55±18.00	57.97±13.31	
LDL (mg/dL)	110.85±36.2	115.42±33.13	

\* Significantly difference with COPD without MCI,  $p < 0.05$

## 5. Conclusion

The prevalent MCI in male COPD at Siriraj hospital was 77.51%. A subtype of MCI in male COPD was the amnesic MCI multiple domains that impaired the memory domain and other domains. Age, low education, smoking, frequent exacerbation, and dyslipidemia may be associate with a decline in the cognitive in male COPD. Further study, inflammatory markers should be collected, and the number of blood chemistry sample sizes in COPD with non-MCI should increase to clearly investigate other MCI risk factors in male COPD such as hyperglycemia and insulin resistance.

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