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Preliminary study of assessing cognitive impairment in older patients with chronic obstructive pulmonary disease by using a cognitive functional assessment tool *via* a touchscreen personal computer

Masahiro Ogawa,[1*] Ayame Uchiumi,[1§] Susumu Sato,[2,3] Yoko Hamakawa,[4] Mizuki Kobashi,[1^] Tomoki Aoyama,[1] Hitoshi Tanimukai[1,5]

[1]Department of Human Health Sciences, Graduate School of Medicine, Kyoto University, Kyoto
[2]Department of Respiratory Care and Sleep Control Medicine, Graduate School of Medicine, Kyoto University, Kyoto
[3]Department of Respiratory Medicine, Graduate School of Medicine, Kyoto University, Kyoto
[4]Department of Respiratory Medicine, Kitano Hospital, Osaka
[5]Department of Palliative Medicine, Kyoto University Hospital, Kyoto, Japan

**Present address: Faculty of Rehabilitation, Kobe Gakuin University, Kobe*
§Present address: Procurement Department, Hitachi High-Tech Corporation, Hitachinaka
^Present address: Department of Rehabilitation, Kyoto Hakuaikai Hospital, Kyoto, Japan

ABSTRACT

Background: Unique cognitive impairments related to chronic obstructive pulmonary diseases (COPD) have been increasingly reported. Considering the dementia risk and medication management, older patients with COPD should be evaluated for cognitive impairment. This study aimed to examine whether specific cognitive impairments related to COPD could be detected by an assessment tool using a touchscreen personal computer (PC) in older patients with COPD.

Methods: This study included 28 older male patients with COPD and 30 healthy older male individuals. A touchscreen PC-based cognitive assessment application called CogEvo was used to assess and compare the cognitive function according to five domains: spatial cognition, orientation, working memory, executive function, and attention.

Results: Analysis of variance showed an interaction effect on the indices of cognitive function based on five domains between the two groups, indicating differences in the characteristics of cognitive function in such groups. Between-group comparisons as a subtest showed that attention, executive function, and working memory were significantly lower in the COPD group than in the healthy group.

Conclusions: CogEvo can detect specific cognitive impairments associated with COPD, suggesting that it can be potentially used as a screening tool for cognitive impairment in older patients with COPD.

Key words: COPD; cognitive impairment; elderly; assessment; computer; touchscreen.

Correspondence: Masahiro Ogawa, 518 Arese, Ikawadani-cho, Nishi-ku, Kobe 651-2180, Japan. Tel. +81.78.974-2043.
E-mail: mogawa@reha.kobegakuin.ac.jp

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Introduction

Chronic obstructive pulmonary disease (COPD) is a chronic respiratory condition affecting the physical function as well as the cognitive function. Cognitive impairment related to COPD could be attributed to hypoxemia, depression, and hypoactivity resulting from breathlessness [1,2]. Patients with COPD have a higher risk for cognitive impairment by up to threefold than healthy individuals [2-4]. The prevalence of mild cognitive impairment in COPD ranges from 6% to 63%, with wide-ranging rates [5] One of the possible reasons for this wide range is the absence of both clear definitions and standard assessment methods of COPD-related cognitive impairment.

Different characteristics of common cognitive impairments related to age also contribute to the difficulties of assessing COPD-related cognitive impairment. The first characteristic is that COPD-related cognitive impairment is a nonamnestic cognitive impairment, which includes decreased attention and information processing ability [6-8]. Conversely, aging-related cognitive impairment is commonly considered as an amnestic cognitive impairment, which includes memory impairment and disorientation; this characteristic differs from COPD-related cognitive impairment. Second, COPD-related cognitive impairment can be relatively mild. Therefore, Mini-mental State Examination (MMSE), which is the most globally known screening assessment tool for cognitive function, seems to be unsuitable for COPD-related cognitive impairment [2,6]. Tools for assessing the characteristics of mild nonamnestic cognitive impairment have not yet been established for clinical practice.

Cognitive impairment related to COPD affects inhaler mismanipulation [3,9], lowers the competence of pharmacotherapy and exercise therapy [10], restricts patients' activities of daily living [3,11-13], and can lead to COPD exacerbation, and mortality [1,7,14]. Therefore, COPD management must include early and continuous assessment of particular cognitive impairments associated with COPD to make counterplans in advance. Furthermore, cognitive impairment can interfere in the diagnosis and treatment of COPD by hampering patients' ability to perform respiratory function tests reliably. In addition to these problems, with manpower shortage in clinical practice, the assessment can hardly be implemented. Therefore, cognitive function assessment that requires less manpower can be beneficial.

In recent years, cognitive function assessment using a computer has been reported to offer various alternatives to conventional neuropsychological tests [8]. Considering that COPD is common in older people, a simpler method that does not depend on one's computer operation ability is preferred. Using a touchscreen PC could be easier to manipulate and could be performed by the patients themselves. Therefore, CogEvo (Total Brain Care, Kobe, Japan) has been developed recently to measure cognitive function by using a touchscreen PC [15-17]. Hence, this cognitive function assessment tool may be used to detect cognitive impairment in patients with COPD.

This study aimed to examine the characteristics of cognitive function in older patients with COPD by using CogEvo to preliminarily verify the potential clinical use of this device. To achieve this aim of the study, two comparisons were performed: i) the characteristics of cognitive function between patients with COPD and healthy older individuals were compared; iii) three cognitive assessments - CogEvo, MMSE, and Japanese version of the Montreal Cognitive Assessment (MoCA-J) - for patients with COPD were compared.

Methods

Subjects

This study included 28 older male patients with COPD. All patients with COPD were outpatients in Kyoto University Hospital and aged 70 years or older. They were in the stable phase of COPD, with no exacerbation of respiratory symptoms 4 weeks prior. COPD diagnosis was confirmed by a postbronchodilator forced expiratory volume in 1 second (FEV_1)/forced vital capacity (FVC) ratio <70%, and patients with COPD were classified into stages I-IV according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) [18]. To compare the characteristics of cognitive function between patients with COPD and healthy older individuals, 30 healthy, older male individuals were also recruited from a regional health-measurement event in Kyoto Prefecture. These subjects had no history of respiratory and psychiatric disorders affecting cognitive function, such as dementia, depression, and schizophrenia. Age of the healthy, older subjects was matched with that of patients with COPD.

Before sampling, we calculated the study's sample size by estimating an effect size from a previous study in which cognitive function assessments were conducted on a PC for patients with COPD [8], using the effect size as d=0.67, with a power of 80% and a significance level of 5%. The calculated sample size was 29 in each group.

Before the start of the study, we obtained consent from all subjects after they were informed about the purpose, method, freedom of participation, withdrawal of consent for research cooperation, and protection of privacy. All data were anonymized for subject confidentiality. This study was approved by the Ethics Committee of the Kyoto University, Graduate School of Medicine (Approval number: R1660-2, R2419) and was performed according to the provisions of the Declaration of Helsinki.

Measurements

Cognitive function tests

CogEvo was used as a cognitive screening tool for both the COPD and healthy groups, whereas MMSE and MoCA-J were conducted only for those with COPD. The patients with COPD were assessed at scheduled outpatient visits. Meanwhile, the healthy older subjects were measured at a health-measurement event in a local area. CogEvo was the only parameter measured in the healthy older subjects.

The MMSE and MoCA-J are the most commonly used tests for screening cognitive function worldwide and are also commonly used to assess cognitive impairment in patients with COPD. To compare the relationships with CogEvo, the MMSE and MoCA-J were used as tools to assess cognitive function in this study, although this study only included patients with COPD. All the cognitive assessments were performed in a quiet room by raters who were familiar with cognitive function.

CogEvo

CogEvo measures cognitive function with the use of a touchscreen PC. CogEvo has 12 types of tasks to measure several aspects of cognitive functions; however, a shorter version of CogEvo is used to measure the five domains of cognitive function, namely, spatial cognition, orientation, working memory, executive function, and attention [17]. Hence, this tool seemed to be suitable for assessing the cognitive function of a patient with COPD which showed the lowering of the frontal lobe function such as attention, executive function, or information processing ability. CogEvo can be self-performed according to voice guidance; therefore, the raters were tasked only to offer advice or help as necessary: for example, how to use the touch panel PC and how to locate the next button on CogEvo, *etc*. Because the patients never had used a touch panel PC or CogEvo, raters helped them.

The index of each task (referring to the domain) was approximately calculated as the sum of two scores: the correct answer score (the number of correct answers) and time score (duration of answering). For the task of "working memory" only, a prescribed score was calculated for each correct answer, and the shorter the answer time, the higher the score. The index of each task was standardized for each age by referring to the accumulated database and was calculated by collecting it for each generation. The mean of the index was calculated at 100, and the standard deviation (1 SD) was 25. The indices of each task were used for comparison in this study. The characteristics of the five tasks - spatial cognition, orientation, working memory, executive function, and attention - with the definitions of these cognitive functions are briefly summarized subsequently.

i. Spatial cognition is a cognitive ability to quickly and accurately visually recognize a state and relationships of the objects presented. In the spatial cognition task of CogEvo, the subjects should choose the same shape presented on the center of the screen from other six shapes surrounding the center shape. The center shape and the answer shape are irregularly rotated to make the identification of the answer shape difficult. Four questions are randomly provided from 34 figure sets.
ii. Orientation is a cognitive ability to recognize basic situations surrounding a subject, such as the date, hour, and the current place that the subject is in. In the orientation task of CogEvo is composed of three questions regarding the hour, date, and day of the week; each question has 14 choices on the screen, and only one answer is correct.
iii. Working memory is an amount of information that can be temporarily stored and processed in the brain when a person performs a task. In the working memory task of CogEvo, the subjects memorize an order of four randomly flashed lights (*i.e.*, red, blue, green, and yellow lights) and touch the lights in the same order. Each light flashes for 1 s. The task starts with two lights flashing, and then, the number of lights is increased when a correct answer is provided.
iv. Executive function is an ability to analyze and predict situations and devise and execute optimal plans. In the executive function task of CogEvo, the subjects trace square panels from "start" to "goal" with the following randomly displayed numbers sequentially in a matrix diagram. The numbers are from 1 to 10. Three tasks are provided: 16 (4 × 4), 36 (6 × 6), and 64 (8 × 8) square panels.
v. Attention is a cognitive ability to be aware of necessary information, concentrate and sustain consciousness, and distribute consciousness to multiple things simultaneously. In the attention task of CogEvo, the subjects select digit numbers and HIRAGANA characters (one of Japanese characters) in order. These numbers and characters are randomly scattered on the screen. The order of choosing numbers and hiragana is alternating. For example, a subject should choose 1, A, 2, B, 3, C, *etc.* in order. A subject has three kinds of questions. Each question consisted of the following 6 (in other words, three numbers and three characters), 12, and 16 digits.

MMSE and MoCA-J

MMSE [19] and MoCA-J [20] are widely used as screening tests for cognitive function. Both of these assessments score 0-30 points and consist of multifaceted subtests, including orientation, memory, computation, verbal abilities, executive function, working memory, and visuospatial cognition. Mild cognitive impairment (MCI) was considered if the total score of MMSE was 27 points or less [21] and the total score of MoCA-J was 25 points or less [22]. In addition, a total score of 23 points or less in MMSE was classified as dementia [21].

Pulmonary function tests

Only the COPD group underwent pulmonary function tests. After the subjects inhaled bronchodilators (400 µg of salbutamol and 80 µg of ipratropium), spirometry measurements were performed. Lung volume subdivisions and single-breath diffusion capacity were measured using Chestac-8900 (Chest MI, Inc., Tokyo, Japan). All the baseline samples of arterial blood gas analysis were collected after the subjects had been sitting for 15 min. Partial pressure of arterial oxygen (PaO_2) and partial pressure of carbon dioxide ($PaCO_2$) were measured using RAPIDlab 1265 Blood Gas Analyzer (Siemens Healthcare Diagnostics Inc., Malvern, PA, USA). Alveolar-to-arterial difference for oxygen (A-aDO_2) was calculated from the PaO_2 and the $PaCO_2$ ($A\text{-}aDO_2 = 150 - PaCO_2/0.8 - PaO_2$).

Statistical analysis

To investigate the differences in the characteristics of cognitive function between the COPD and healthy groups, we used the two-way analysis of variance (ANOVA) to compare the index of five tasks of CogEvo between the two groups. When a main effect was observed between these groups, the Tukey-Kramer method was used as a subtest.

Moreover, differences in cognitive function by COPD severity based on GOLD were compared by Kruskal-Wallis test. The correlation between the cognitive assessments and blood gas tests (PaO_2, $PaCO_2$, and A-aDO_2) was also investigated by Spearman's rank correlation coefficient. We also used Spearman's rank correlation coefficient to determine the relationship between the cognitive function assessments by analyzing the association between the index of each test of CogEvo, MoCA, and MMSE in the COPD group. All statistical data were analyzed using the software IBM SPSS (version 25.0), and the significance level was set at 5%.

Results

The mean age and SD of the COPD group (n=28) was 76.8±5.6 years, whereas that of the healthy group (n=30) was 75.9±4.8 years, showing no significant differences (p=0.522). Table 1 shows the respiratory function, MMSE, and MoCA-J results of the COPD group. According to GOLD staging, 7, 15, 4, and 2 subjects were at stages I, II, III, and IV, respectively. The mean and SD of PaO_2 (n=21) and $PaCO_2$ (n=21) was 81.5±11.7 and 40.0±4.5 Torr, respectively. Two subjects were hypoxemic (PaO_2 <60 Torr), and one subject had hypercapnia ($PaCO_2$ >45 Torr). Seven patients refused to undergo arterial blood sampling for blood gas measurement as it is a painful procedure. The mean and SD of MMSE total score in the COPD group was 27.0±2.1 points. From the results of the MMSE total score, 15 (53.5%) and 2 subjects (7.1%) had MCI and dementia, respectively. In addition, the mean and SD of MoCA-J total score was 22.9 ± 2.2 points, and 27 subjects (96.4%) were found to have MCI.

The means and standard deviations of the five CogEvo indices for the COPD and healthy individual groups are listed in Table 2. The mean indices for spatial cognition were 102.2±31.4 and 101.5±15.8, respectively; for orientation, 122.2±25.8 and 105.7±17.4, respectively; for working memory, 84.5±18.0 and 102.6±16.9, respectively; for executive function, 86.8±22.8 and

101.4±17.3, respectively; and for attention, 96.5±14.8 and 110.4±17.4, respectively. The indices of CogEvo were according to the results of two-way ANOVA for cognitive function; the indices of the five tasks of CogEvo demonstrated an interaction effect in each group ($F[1, 56] = 20.140$; $p<0.001$; $\eta^2 = 0.265$). Between the two groups, the main effect was found in the five-item index of CogEvo ($F[1, 56] = 6.199$; $p=0.016$; $\eta^2 = 0.100$), and the subtests revealed that significant differences were found in orientation ($p=0.006$), working memory ($p<0.001$), executive function ($p=0.008$), and attention ($p=0.002$). The result of the two-way comparison was a disordinal interaction. A disordinal interaction, also called a "crossover interaction," refers to a result of a two-way ANOVA in which two lines on a line graph intersect. Specifically, according to this result, the indices of working memory, executive function, and attention were lower in the COPD group than in the healthy group, whereas orientation was higher in the COPD group.

By COPD severity, no significant difference was noted among the groups of stages I, II, III and IV for all cognitive function assessments. In the analysis of the relationship between blood gas tests and cognitive function assessments, significant moderate correlation was only found between $PaCO_2$ and MoCA-J total score ($\rho = -0.444$, $p=0.044$); no significant correlation was found for other variables, including PaO_2 and $A\text{-}aDO_2$.

Between the five tasks of CogEvo and the sum scores of MMSE and MoCA-J, significant moderate correlation ($\rho=0.402$, $p=0.042$) was only found between CogEvo's working memory and MoCA-J (Table 3). Between the subtests of MMSE and MoCA-J, and each task of CogEvo, significant moderate correlation ($\rho=0.466$, $p=0.012$) was only observed between CogEvo's attention and MoCA-J's delayed words replay.

Table 1. Respiratory function and MMSE and MoCA-J of older patients with COPD (n=28).

Mean and standard deviation of each assessment	
Assessment items	**Mean ± SD**
FVC (L)	3.13±0.61
FEV_1 (L)	1.68±0.56
FEV_1/FVC (%)	53.5±12.9
%FEV_1 (%)	65.1±20.0
PaO_2 (Torr) (n= 21)	80.1±11.7
$PaCO_2$ (Torr) (n21)	39.7±4.5
$A\text{-}aDO_2$ (Torr) (n=21)	20.2 ±13.1
MMSE (points)	27.0±2.1
MoCA-J (points)	22.9±2.2
Number of subjects identified by the assessments	
Assessment items	**n of subjects**
GOLD stage	
Stage I	7
Stage	15
Stage	4
Stage	2
PaO_2 < 60 Torr	2
$PaCO_2$ > 45Torr	1
MMSE (below the cutoff)*	15
MoCA-J (below the cutoff)°	27

*MMSE cutoff for mild cognitive impairment was ≤ 27 points; °MoCA-J cutoff for mild cognitive impairment was ≤25 points; FVC, forced vital capacity; FEV_1, forced expiratory volume in 1 second; PaO_2, partial pressure of arterial oxygen; $PaCO_2$, partial pressure of arterial carbon dioxide; $A\text{-}aDO_2$, alveolar-to-arterial difference for oxygen; MMSE, Mini-mental State Examination; MoCA-J, Japanese version of Montreal Cognitive Assessment.

Discussion

An important finding of this study was that CogEvo could be used to assess cognitive impairment in patients with COPD. The following discussion addressed the possible clinical uses of CogEvo, considering the results of this study, the relationship between cognitive decline and aging, and the relationship between cognitive function and blood gas.

Clinical utilities of CogEvo

This study revealed that the attention, working memory, and executive function were significantly decreased in subjects with COPD, indicating a tendency of cognitive impairment compared with the healthy older subjects. These findings suggest that CogEvo can detect impaired frontal lobe functions, such as attention, working memory, and executive function, in older subjects with COPD. Moreover, executive function and attention ability, which were decreased in CogEvo, did not significantly correlate with MMSE and MoCA-J. Thus, CogEvo could possibly identify a cognitive impairment that is difficult to detect by MMSE and MoCA-J. CogEvo have several strong points as a cognitive assessment tool [23]. For example, it can be self-performed even at home, owing to its computer-based speech guidance, and the data can be stored digitally in computers. Moreover, variation caused by different examiners can be reduced. The examination time is approximately 10 min per person [23], thereby not time consuming. Therefore, CogEvo may be a practical tool to continuously capture changes in cognitive function in clinical practice.

Table 2. Comparison of the 5-task index of CogEvo between the COPD group and the healthy older group (mean ± SD).

Cognitive function items	COPD (n=28)	Healthy (n=30)	p
Spatial cognition	102.2±31.4	101.5±15.8	0.917
Orientation	122.2±25.8	105.7±17.4	0.006**
Working memory	84.5±18.0	102.6±16.9	<0.001**
Executive function	86.8±22.8	101.4±17.3	0.008**
Attention	96.5±14.4	110.4±17.4	0.002*

The results of the analysis of variance confirmed an interaction ($p<0.001$) and a main effect between two groups ($p<0.001$). The p in the table indicate comparisons between two groups with the Tukey-Kramer method as a subtest; *p<0.05; **p<0.01.

Table 3. Correlations between the five tasks of CogEvo, and MMSE and MoCA-J of older patients with COPD (n=28).

	MMSE		MoCA-J	
	ρ	p	ρ	p
Spatial cognition	0.325	0.105	0.261	0.198
Orientation	0.067	0.745	0.217	0.286
Working memory	0.236	0.246	0.402	0.042*
Executive function	0.255	0.208	0.22	0.281
Attention	-0.120	0.558	0.083	0.685

*p<0.05.

Patients with cognitive impairment experience learning difficulties and misuse of inhaler devices [24,25]. Cognitive function decline caused by COPD suggests the need for simplifying medication teaching methods and devices in the future. Moreover, we found a significant correlation between the delayed words replay task of MoCA-J and the attention task of CogEvo, indicating cognitive function decline in subjects with COPD. This result suggests a decrease in attentional capacity and distributivity. In other words, these patients might not understand and remember complex verbal instructions, suggesting the need for cognitive function assessment before they are instructed on how to use inhaler devices and take their medications.

Thus, a tool that can evaluate cognitive function, mainly the frontal lobe function, using a touchscreen PC, such as CogEvo, should be introduced in clinical practice. As a result of the increasing evaluation of cognitive function in clinical practice, disease-specific cognitive functions may be conveniently and continuously assessed. By screening cognitive function in patients with COPD at an early stage, exercise therapy [26,27], pharmacotherapy [28] and oxygen therapy [29,30] may be further emphasized to prevent cognitive impairment and to adapt to their activities of daily living while compensating for cognitive impairment.

Relationship between cognitive decline and aging

This study involved relatively older patients. Additionally, one of the characteristics of CogEvo is that the index scores are calculated by age generation. Therefore, the cognitive function evaluation using CogEvo in this study was unaffected by cognitive decline. Cognitive function is mostly affected by aging. Therefore, this study clarified a characteristic that could only be considered in older patients with COPD. Aging is one of the crucial factors that affect cognitive function, and investigating younger patients who were excluded in this study and verifying the effectiveness of CogEvo as an evaluation tool for assessing younger individuals are necessary.

Relationship between cognitive function and blood gas

Furthermore, we could not find any association between PaO_2, A-aDO_2, COPD severity, and the cognitive assessment tools (CogEvo, MMSE, and MoCA-J), except for a weak negative significant correlation between $PaCO_2$ and MoCA-J. This result indicated that compensatory hyperventilation was associated with cognitive impairment in patients with COPD. However, CogEvo indices were not associated with arterial hemodynamics, and the factors contributing to cognitive impairment and domains of impaired cognitive function might be different. Further research is definitely needed, especially that the sample size is small.

Limitations of this study and future prospects

This study found that older subjects with COPD had significantly higher orientation than healthy older subjects, probably because subjects with COPD who were outpatients in this study had an appointment to visit the hospital in advance. For the orientation task on CogEvo, subjects were asked for the time, date, and day of the week. The outpatient appointments were always scheduled on the same day of the week, and patients were scheduled to come in time for their consultations. Therefore, outpatients were able to recall days and times more easily, accurately and quickly than inpatients. Otherwise, they could not attend their scheduled clinical visit. This observation could be a sampling bias of the present study. In future studies, assessing cognitive impairment with COPD without such sampling bias is recommended.

Various factors that probably caused cognitive impairment were not examined in this study. For example, according to one literature review, cognitive impairment in COPD could be attributed to smoking history, depression, and sleep status [1]. Furthermore, educational history, which is a basis of cognitive function, was not addressed in this study. Hence, it would be crucial to consider these factors that affect cognitive function in investigating the characteristics of cognitive function in COPD.

This study has a cross-sectional study design. Here, only cognitive function at one time could be assessed; how cognitive function at the time of measurement had changed from its original cognitive function could not be determined. Therefore, cognitive function needs to be continuously and longitudinally assessed to better define the impacts of COPD on cognitive function. Other limitations of this study include the small sample size, older patients and the exclusion of females. As described in the methods section, the required sample size was calculated to be ~29 to find significant differences between subjects with COPD and normal subjects. Therefore, the sample size could be enough to lead the present conclusion and this result would apply to older patients with COPD only. Another limitation is that although CogEvo could be an excellent tool, no cutoff has been set to judge cognitive impairment, unlike MMSE and MoCA-J. For enhancing the clinical application of CogEvo in the future, further studies are needed to establish the cutoff value of each CogEvo task to be considered as a cognitive impairment.

Conclusion

This study detected that the attention, working memory, and executive function were significantly decreased in patients with COPD according to a new assessment method using a touchscreen personal computer. This result indicates the possibility that touchscreen personal computer applications, such as CogEvo, could be used as screening tools to assess cognitive impairment in older patients with COPD. Further research is needed for the clinical application of this tool.

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