Section: Miscellaneous

Original Research Article

ASSESSMENT OF COGNITIVE FUNCTIONS IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE – A CROSS-SECTIONAL STUDY

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ABSTRACT

Background: Chronic Obstructive Pulmonary Disease (COPD) is defined as a disease state characterised by airflow limitation that is not fully reversible. It is the fourth major cause of mortality in the world. COPD, apart from pulmonary effects also leads to many extrapulmonary effects that result in significant comorbid conditions. One of them is cognitive dysfunction. Deteriorating cognition and intellectual disability indirectly plays role in poor compliance of patient when treatment is given. This study aims to assess the cognitive function of the COPD patients.

Materials and Methods: Male patients with clinical features suggestive of COPD were recruited and their pulmonary functions were assessed using computerised spirometer. Their cognition was assessed using 3 different scales, namely, Addenbrooke Cognitive Scale (ACE III), Montreal Cognitive Assessment (MoCA) and Trail Making Test Part A & B (TMT – A, B). Normal subjects were recruited as controls and their cognition was also assessed. Cognition scores and time taken to complete TMT were compared using independent 't' test. Correlation of cognitive scores with the Forced Expiratory Volume at 1st second (FEV_1) & FEV1/FVC (Forced Vital Capacity) was done using Pearson correlation.

Result: The ACE III scores was significantly lower in COPD group (76.99 ± 8.58) than the control group (94.31 ± 2.19). MoCA score was also lower in cases group (22.51 ± 2.76) when compared to the control group (27.65 ± 0.98). The mean time taken to complete TMT-A & TMT-B in cases group was 64.2 s & 154.75 s respectively, which was significantly more than the mean time taken in control group (37.5 s & 70.91 s respectively).

Conclusion: COPD is marked by chronic hypoxemia as a result of cerebral hypoperfusion. Systemic inflammation and oxidative stress also contribute to neuronal damage. These changes predominantly occur in the frontal lobe, which is concerned with cognitive functions. Our study pointed towards cognitive decline in COPD patients due to chronic hypoxia thereby stressing the importance of earlier screening in patients and addressal to the issue, thereby indirectly helping them in being compliant with the treatment and lead a better life.

Keywords: Cognition, COPD, Hypoxia, Addenbrooke Cognition Test III, Montreal Cognitive Assessment, Trail Making Test.

INTRODUCTION

Chronic Obstructive Pulmonary Disease is defined as a disease state characterised by airflow limitation that is not fully reversible. It is the fourth major cause of mortality in the world.[1] Cigarette smoking is the major risk factor for COPD. It has a variable natural history. However, it is generally a progressive disease if the exposure to noxious agents continues. Apart from pulmonary effects, COPD leads to many

extrapulmonary effects that results in significant comorbid conditions.[2]

Weight loss, nutritional abnormalities and skeletal muscle dysfunction are well recognised extrapulmonary effects of COPD and patients are at an increased risk for myocardial infarction, angina, osteoporosis, bone fractures, depression, diabetes, sleep disorders.[3] Apart from the above conditions, brain is also known to be affected as the severity of the disease increases leading to cognitive impairment and dementia. This is attributed to the chronic hypoxemia the patient suffers.[3]

The cognitive dysfunction is noticed only in the later stages of the disease as the main focus lies on pulmonary rehabilitation. The reason behind giving importance to assess the cognitive function is that deteriorating cognition and intellectual ability indirectly plays role in poor compliance of patient when treatment is given, as the patient becomes forgetful and is unable to follow the instructions given.

Not many studies have been done in Indian set up in this regard. The aim of this study is to assess the cognitive function in COPD patients in a tertiary care centre. Cognitive function was assessed by 3 different scales namely, Addenbrooke Cognitive Scale (ACE III), Montreal Cognitive Assessment (MoCA) and Trail Making Test part A & B (TMT – A, B).

MATERIALS AND METHODS

The study was planned as a cross-sectional study. The assessment was done in the thoracic medicine outpatient department at a tertiary care centre. Recruitment of the cases and controls was done as per the following criteria.

Inclusion criteria – Cases

Male patients of age between 40 – 60 years with complaints of cough and sputum production with auscultatory finding of wheeze were selected. A thorough and meticulous history was taken regarding smoking habits, duration of illness, occupational exposure. Patient records were reviewed and those who had been diagnosed previously based on spirometry as Chronic Obstructive Lung Diseases were recruited for the study after following the exclusion criteria.

Exclusion Criteria – Cases

History and physical examination suggestive of tuberculosis, neurological disorders, psychiatric illnesses, diabetes, hypertension, thyroid disorders. Those who are on chronic steroid therapy. Associated interstitial lung diseases as ruled out by doing PFT and chest radiograph. Acutely ill patients. Illiterate patients.

Controls were normal persons of similar age group without any morbidities as mentioned above.

Calculation of sample size was done by Open-epi software. Prevalence of cognitive impairment was 51.71 % in cases group and 36.66 % in control group in this study done by Fekri et al.[4] 120 male subjects were recruited as cases and same numbers of age and gender matched normal individuals were controls.

After obtaining ethical committee clearance and informed and written consent, the subjects were instructed and were subjected to Pulmonary Function Testing using a computerised spirometer available in the department. If the parameters were suggestive of obstruction, they were recruited as cases in the study. (PHOTO 2)

The subjects were administered the ACE III test. It is a cognitive assessment tool developed by Glasgow University. The test was administered in local language (in this case Tamil). The translated version was available in the University of Sydney. This tool assesses 5 domains of cognition namely attention, memory, verbal fluency, language and visuospatial ability. Scores out of 100 were noted. (PHOTO 1).

After ACE III, MoCA was administered. Scores out of 30 were noted. This tool also assesses similar domains. Following MoCA, TMT A & B was administered. This test was administered after a trial. The time taken to complete each part of the test was noted.

Independent variables like age, body mass index, literacy level were expressed as frequency. Total scores of ACE III, MoCA was compared between the two groups by independent 't' test. Time taken to complete TMT A & B were also compared between the groups by using independent 't' test. Correlation of cognitive scores with FEV1 & FEV1/FVC was done using Pearson correlation.

RESULTS

The results were analysed using SPSS software version 26. The mean age in the cases group was 50.56 ± 5.397. The mean age in the control group was 50.04 ± 4.623. Among the cases, 37% had COPD for duration of 1 – 5 years, 33% suffered from the same for past 5 – 10 years. 16% and 14% of the people had 10 years.

The mean scores of both ACE III and MoCA were compared between the two groups (Table 1). The mean scores were significantly low ('p' value < 0.001) in the cases group as assessed by both the tests. [Table 1]

Table 1: Comparison of cognition scores between cases and control groups

	CASES (Mean ± SD)	CONTROLS (Mean ± SD)	INDEPENDENT 't' TEST VALUE	'p' VALUE
ACE III SCORE	76.99 ± 8.58	94.31 ± 2.191	21.46	<0.001
MOCA SCORE	22.51 ± 2.76	27.65 ± 0.98	10.87	<0.001

The individual domains of ACE III were compared among both the groups (Table 2). All the domains were significantly affected in the COPD group.

Table 2: Comparison of individual cognition domain between cases and control groups

COGNITIVE DOMAIN	MAXIMUM SCORE	CASES MEAN ± SD	CONTROLS MEAN ± SD	INDEPENDENT 'T' TEST VALUE	P VALUE
ATTENTION	18	15.57 ± 2.10	17.37 ± 0.79	8.728	<0.001
MEMORY	26	16.67 ± 4.36	23.27 ± .96	14.71	<0.001
FLUENCY	14	9.92 ± 1.81	13.23± .87	12.41	<0.001
LANGUAGE	26	22.90 ± 1.916	25.41± .85	13.10	<0.001
VSA	16	12.82 ± 2.01	15.04± .99	10.87	<0.001

VSA – Visuospatial ability

Subjects belonging to GOLD category 4 were amongst the most affected as suggested by the lowest scores when assessed by both ACE III and MoCA. [Table 3]

Table 3: Distribution of ace iii score

COPD GRADE	ACE III SCORE	
	N	MEAN ± SD
GRADE 1	25	81.92 ± 5.656
GRADE 2	28	78.64 ± 9.72
GRADE 3	33	78.21 ± 6.83
GRADE 4	34	74.85 ± 9.25

The MoCA scores were correlated with the GOLD category and in our study, though there was no linear correlation, our findings suggests that MoCA score was lowest in category 4. Cognition is most impaired in severely affected COPE patients. [Table 4]

Table 4: Distribution of MoCA Score

COPD GRADE	MoCA SCORE	
	N	MEAN ± SD
GRADE 1	25	22.96 ± 1.684
GRADE 2	28	22.29 ± 2.891
GRADE 3	33	23.03 ± 2.984
GRADE 4	34	21.85 ± 3.016

The cut off time to complete the TMT part A & B are 40 seconds and 91 seconds respectively in a normal person. From figure 1, we can conclude that the time taken to complete the tests were significantly prolonged in both the tests for the COPD subjects.

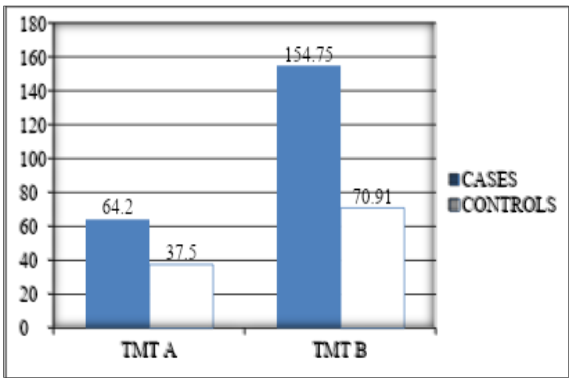

Figure 1: Comparison of TMT a & b of cases & controls

We correlated the domains of cognition with the ACE III scores. (Table 5). Individual domains scores were lowest in category 4 of COPD patients. The scores of attention and memory showed a linear relation with increasing severity of the disease.

The Forced Expiratory Volume at 1st second (FEV1) was correlated with ACE III scores and showed moderate correlation of 0.333 (r=0.333) and was statistically significant. [Figure 2]

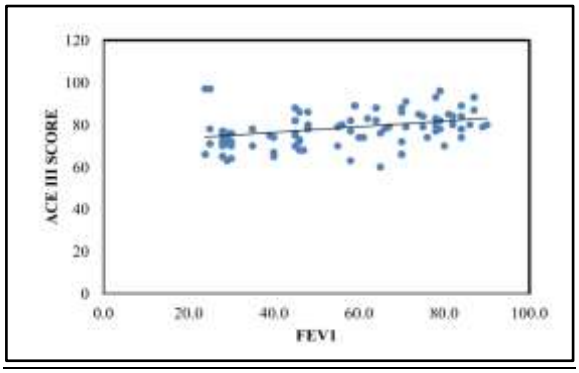

Figure 2: Correlation of FEV 1 values with ace III score

Similarly, the FEV1 / FVC ratio showed a statistically significant (p <0.001) moderate positive correlation (r=0.360) with the ACE III scores.

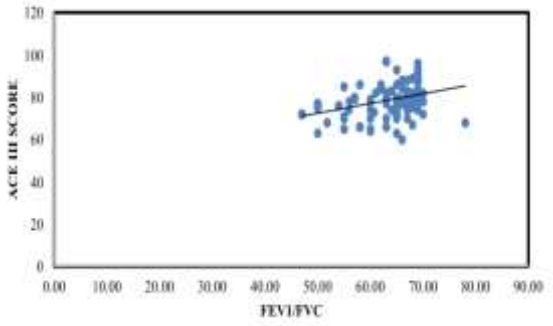

Figure 3: Correlation of ACE III score with FEV1 / FVC

Correlation of FEV1 with MoCA score however showed poor correlation of 0.138 (r = 0.138) and was found to be statistically insignificant (p = 0.073).

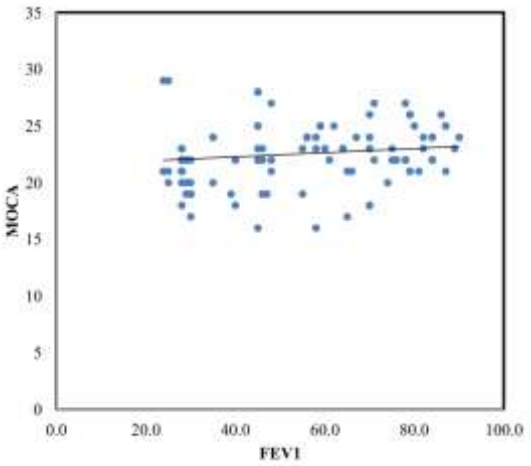

Figure 4: Correlation of FEV1 values with MoCA Score

DISCUSSION

Our study aimed at importance of detecting and addressing to one of the extrapulmonary effects of COPD – cognitive decline. In our study, it was proven that cognitive functions declined in COPD patients which was statistically significant. Similar finding was found in a study by Fekri et al., in Iran, where prevalence of cognitive impairment was 51.71% in case group compared to 36.66% in control group.[4]

Few studies have pointed that the quality of life is affected in COPD patients who have cognitive dysfunction. This is in particular to treatment adherence. In a review study by Restrepo et al., they had concluded that only 40 – 60% of patients with COPD adhered to prescribed regimen. Also only 1 out of 10 patients performed all the steps of using metered dose inhaler correctly. Forgetting or refusing to take a prescribed dose is the most common cause of non-adherence.[5]

The reason attributed being lack of concentration and poor memory.[6]

The reason most commonly stated behind the cognitive decline in COPD patients is cerebral hypoperfusion. Ortapamuk et al., study showed that the perfusion indices on frontal Region of Interests (ROI) in non hypoxemic COPD patients and frontal and parietal ROIs in hypoxemic COPD patients were significantly reduced.[7]

A study by Shim et al., was conducted in which the cerebral metabolic abnormalities in COPD patients was detected by using proton magnetic resonance spectroscopy. There was a positive correlation between choline levels in the spectra obtained from parietal white matter and the general memory quotient of Wechsler Memory Scale-revised.[8]

The domains tested in neuropsychological assessments are memory, attention, language, executive functions and visuo spatial skills. In our study, all these domains were significantly affected compared to controls. Executive function as tested by time taken to complete TMT tests were also prolonged in COPD patients.

This is in correlation with the review study by Dodd et al., which had reviewed many studies of cognition in COPD. According to them attention, memory, motor and executive functions were found to be most affected among other domains.[9] Similar finding was given in the Ortapamuk et al., study. There was a decrease in the verbal memory, recent memory and attention.[7]

In our study, there was dysfunction in visuo spatial domain and fluency. This goes in accordance with the study by Antonelli – Incalzi et al., study. They had concluded that spatial thinking, verbal fluency and recent verbal and visual memory were more affected than other domains.[10]

The time taken by participants from COPD group to complete both parts of TMT was delayed in our study compared to that of healthy volunteers. This is in accordance with the study by Negro et al. In this study, visual processing, cognitive flexibility and shifting capacity as assessed by TMT-A & B parts, were more significantly affected than memory and attention as assessed by MMSE and CDT.[11]

The area concerned with attention, working memory is the prefrontal cortex. Visuo spatial skills and verbal tasks are carried out here. Frontal lobe is involved in decision making, problem solving and planning. Temporal lobe is involved in speech and language. Basal ganglia and cerebellum are involved in executive functions by being responsible for co-ordination, repetition, modulation and bring out habitual responses. Hippocampus is the centre for consolidation of long term memory.[12]

The main mechanism behind cognitive dysfunction in COPD is brain hypoperfusion and hypoxia. Studies have shown that there is a frontal dominant perfusion decline in frontal regions than in other regions. This is due to greater sensitivity of frontal region to hypoxia.

The above finding is seen in study by Antonelli Incalzi et al. In this study they used Single Photon Emission Computed Tomography (SPECT) and correlated them with neuropsychological scores. They had concluded that perfusion of anterior cortical and subcortical regions of the dominant hemisphere correlated positively with the number of tests performed correctly on neuropsychologic tests.[13]

In another study by Jing Li et al., they divided COPD patients into mild to moderate and severe forms and compared them with control groups. MRI 81 revealed reduced hippocampal volume in COPD patients and it positively correlated with MMSE scores, oxygen saturation levels and arterial blood gas analysis. This is the mechanism behind impairment in memory domain in cognitive testing.[14] With increasing severity of COPD other areas are also affected leading to global cognitive dysfunction and finally dementia. Apart from hypoxemia, systemic

inflammation and oxidative stress are also hypothesized as possible mechanisms behind cognitive impairment.[9,6] Nicotine induced oxidative stress by generation of free radical which leads to neuronal cell damage has been postulated as a cause of cognitive decline in non hypoxemic COPD.[15]

In our study there was an inverse relationship between ACE III scores and severity of COPD based on GOLD criteria. Grade 4 COPD patients had the lowest scores. This happens as a result of increased hypoxemia leading to further neuron damage and hence reduced scores on cognitive assessment. This correlates with the study by Fekri et al, where there was an inverse relationship between severity of COPD and MMSE scores.[16]

FEV1 / FVC values showed a positive significant correlation with ACE-III scores. Fekri et al., study also demonstrated a positive correlation of FEV1% with MMSE scores.[16] Study by Kirkil et al,[17] and Li et al,[18] have found significant correlations with FEV1 and FEV1 / FVC parameters with cognition scores. Another study by Chyou et al., also found a significant correlation of cognition score with FEV1.[19]

We preferred using Addenbrooke Cognitive Examination version III and Montreal Cognitive Assessment scale. The scales we used are free to access for health professionals. Morris et al., study had used ACE-III scale to assess cognitive dysfunction in COPD and AD group. They had shown significant decrease in scores in COPD group when compared with controls.[20] The research findings that ACE-III is more sensitive than MMSE in early stages of dementia makes it a more reliable tool.[21] ACE-III has more questions than MoCA and MMSE and hence has an advantage of a more comprehensive assessment of individual domains of cognition. This may be the possible reason for significant correlation of PFT parameter with ACE-III score in our study.

Earlier detection of mild cognitive impairment in COPD has an advantage in treatment and outcome in such patients. Studies have shown that use of supplemental oxygen therapy can improve the cognitive functions in COPD patients. Thakur et al., study has demonstrated decreased risk for cognitive impairment with regular use of supplemental oxygen therapy.[22]

Limitations

Possibilities of undiagnosed diabetes, hypertension and other neurological or psychiatric illness might affect the study results.

Cognitive assessment is only a screening test. Correlation with CT / MRI could be more significant. Considering the cost and invasiveness of the test, arterial blood gas levels was not estimated. Hence severity could not be assessed on PaO2 levels.

Future perspectives

This was a cross sectional study. This study can be expanded by following the patients over time after giving oxygen therapy and converting it to a cohort study. ¬

Correlation with inflammatory markers can add more value to the study. ¬

Along with cognitive screening tests we can do P300 event related potential study and correlate them.

CONCLUSION

From the current study we can conclude that there is a definite cognitive impairment in patients who suffer from Chronic Obstructive Pulmonary Disease. Since normal cognition is required for effective day to day activities, it being affected can lead to a variety of other issues starting from depression to being a burden to family. Moreover compliance with the treatment which includes correct schedule and dose of drugs and inhalers, remembering appointments etc, is also affected significantly thereby creating a vicious cycle and worsening of both respiratory and psychological symptoms. Recent researches are being done more on the extrapulmonary effects of COPD, thereby referring it to be more of a systemic illness rather than being only a pulmonary disease. Although correcting the primary cause may reverse some of the effects, the importance of concurrent screening for other co-morbidities is not to be undervalued. Cognitive dysfunction holds an important aspect considering the above fact. Earlier screening for cognitive dysfunction is bound to help the patients more in adhering to the current treatment. Awareness of the same among young and adolescent smokers can be a motivation for them to quit smoking. Initiation of cognitive training and oxygen therapy at the earliest after diagnosis will go a long way in reducing this co-morbidity and provide them a better quality of life.

REFERENCES

1. Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, Aboyans V, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet. 2012 Dec 15;380(9859):2095–128.
2. Chronic obstructive pulmonary disease (COPD) [Internet]. [cited 2025 Aug 18]. Available from: https://www.who.int/news-room/fact-sheets/detail/chronic-obstructive-pulmonary-disease-(copd)
3. Page not found | Institute for Health Metrics and Evaluation [Internet]. [cited 2025 Aug 18]. Available from: https://www.healthdata.org/policy-report/india-health-nation%E2%80%99s-states
4. Fekri MS, Hashemi-Bajgani SM, Naghibzadeh-Tahami A, Arabnejad F. Cognitive Impairment among Patients with Chronic Obstructive Pulmonary Disease Compared to Normal Individuals. Tanaffos [Internet]. 2017 [cited 2025 Nov 4];16(1):34. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC5473380/
5. Coutts JAP, Gibson NA, Paton JY. Measuring compliance with inhaled medication in asthma. Arch Dis Child. 1992 Mar;67(3):332–3.
6. Archana D, Mann R, Malay S, Padam A. Cognitive decline in patients of chronic obstructive pulmonary disease. Indian Journal of Basic and Applied Medical Research. 2014;(June):142–51.

7. Ortapamuk H, Naldoken S, Article O. Brain perfusion abnormalities in chronic obstructive pulmonary disease : INTRODUCTION. Ann Nucl Med. 2006 Feb;20(2):99–106.
8. Shim TS, Lee JH, Kim SY, Lim TH, Kim SJ, Kim DS, et al. Cerebral metabolic abnormalities in COPD patients detected by localized proton magnetic resonance spectroscopy. Chest. 2001 Nov;120(5):1506–13.
9. Dodd JW, Getov S V., Jones PW. Cognitive function in COPD. European Respiratory Journal. 2010 Apr 1;35(4):913–22.
10. Antonelli-Incalzi R, Corsonello A, Pedone C, Trojano L, Acanfora D, Spada A, et al. Drawing impairment predicts mortality in severe COPD. Chest [Internet]. 2006 Dec [cited 2019 Jul 27];130(6):1687–94. Available from: http://www.ncbi.nlm.nih.gov/pubmed/17166983
11. Dal Negro RW, Bonadiman L, Bricolo FP, Tognella S, Turco P. Cognitive dysfunction in severe chronic obstructive pulmonary disease (COPD) with or without Long-Term Oxygen Therapy (LTOT). Multidiscip Respir Med. 2015;
12. Khurana I. Textbook of Medical Physiology. 2nd ed. Elsevier; 2015. 1114–1130 p.
13. Antonelli Incalzi R, Marra C, Giordano A, Calcagni ML, Cappa A, Basso S, et al. Cognitive impairment in chronic obstructive pulmonary disease--a neuropsychological and spect study. J Neurol. 2003 Mar;250(3):325–32.
14. Li J, Fei GH. The unique alterations of hippocampus and cognitive impairment in chronic obstructive pulmonary disease. Respir Res. 2013;14(1).
15. Areza-Fegyveres R, Kairalla RA, Carvalho CRR, Nitrini R. Cognition and chronic hypoxia in pulmonary diseases. Dementia e Neuropsychologia. 2010;4(1):14–22.
16. Samareh Fekri M, Hashemi-Bajgani SMM, Naghibzadeh-Tahami A, Arabnejad F, Fekri MS, Hashemi-Bajgani SMM, et al. Cognitive impairment among patients with chronic obstructive pulmonary disease compared to normal individuals. Tanaffos [Internet]. 2017 [cited 2019 Jul 27];16(1):34–9. Available from: http://www.ncbi.nlm.nih.gov/pubmed/28638422
17. Kirkil G, Tug T, Ozel E, Bulut S, Tekatas A, Muz MH. The evaluation of cognitive functions with P300 test for chronic obstructive pulmonary disease patients in attack and stable period. Clin Neurol Neurosurg. 2007 Sep;109(7):553–60.
18. Li J, Huang Y, Fei GH. The evaluation of cognitive impairment and relevant factors in patients with chronic obstructive pulmonary disease. Respiration. 2013;85(2):98–105.
19. Chyou PH, White LR, Yano K, Sharp DS, Burchfiel CM, Chen R, et al. Pulmonary function measures as predictors and correlates of cognitive functioning in later life. Am J Epidemiol. 1996;143(8):750–6.
20. Morris C, Mitchell JW, Moorey H, Younan HC, Tadros G, Turner AM. Memory, attention and fluency deficits in COPD may be a specific form of cognitive impairment. ERJ Open Res. 2019;
21. Wang BR, Ou Z, Gu XH, Wei CS, Xu J, Shi JQ. Validation of the Chinese version of Addenbrooke's Cognitive Examination III for diagnosing dementia. Int J Geriatr Psychiatry. 2017;
22. Thakur N, Blanc PD, Julian LJ, Yelin EH, Katz PP, Sidney S, et al. COPD and cognitive impairment: the role of hypoxemia and oxygen therapy. Int J Chron Obstruct Pulmon Dis. 2010;5:263.