***Original Research Article***

# Study of cognitive function in patients with chronic obstructive pulmonary diseases


## Abstract

***Backgrounds:*** Cognitive impairment is a frequent feature of COPD, so Cognitive function study should be a part of the initial respiratory assessment in COPD patients especially for those patients presenting with evident or self-reporting symptoms of cognitive deficit.

***Objectives:*** The aim of our work was to study the cognitive function among COPD patients by using specific cognitive function tests and to assess the validity of these tests in detecting this impairment among COPD population.

***Subjects and Methods:*** A cross sectional observational study was carried out on 100 patients with COPD diagnosed according to Global initiative for Chronic Obstructive Lung Disease. [(1)] Subjects of the study were selected from Chest Department Outpatients Tanta University Hospitals and Mansoura Chest Hospital Outpatients between March 2019 and November 2020. They were divided into three groups; group I including 34 grade II COPD patients, group II including 32 grade III COPD patients and group III including 34 grade IV COPD patients.

***Results:*** Half of group III patients had severe cognitive impairment compared to 34.4% among group II patients and 26.5% among group I patients with a statistically significant differences in the MMSE between the three studied groups. ($\chi 2$ =9.699, p=0.015). Group III patients had 29.4% with severe impairment, while group II had 34.4% and group I had 17.6% with severe impairment with a statistically significant difference in digit symbol test distribution between different studied groups. As regards to Trail A and B tests, group III had high percent impaired test results, compared to group I and II with a statistically significant differences in its distribution between the different studied groups. As regards to Digit Span Tests A and B, there was no statistically significant difference in its distribution between different studied groups.

***Conclusions***: The Mini Mental State Examination Test may be used as a part of the initial respiratory assessment to give an idea about the cognitive state of the patient and if the patient needs more care for his cognitive status or not.


***Key Words*:** COPD, Trail making test; cognitive function; digit symbol test.


## Introduction

Chronic Obstructive Pulmonary disease (COPD) is a major health problem. It's a common preventable and treatable disease, characterized by enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases. [(2)]

Over the past few decades, COPD was considered a disease of the lungs. Nowadays, it is regarded as a systemic disease. Extrapulmonary features including; decrease muscle mass, cardiovascular diseases, psychological and cognitive function impairment are associated with the disease. [(3)]

Cognitive functions are those mental processes that lead to the acquisition of knowledge and allow us to carry out our daily tasks. They allow the subject to have an active role in the processes of receiving, choosing, transforming, storing, processing and retrieval of information. [(4)]

Patients with COPD may have cognitive impairment, either globally or in single cognitive domains, such as information processing, attention, memory, problem solving, decision making, executive functions, language and social cognition. [5]
Medical care for COPD has focused mainly on the lung pathology itself. But little attention was paid to management of any cognitive impairment. This negatively affects the evolution of the respiratory disease and the patient's quality of life; it also increases healthcare and social costs. [6]
They are both independently associated with increased mortality and morbidity. [7]
There is a need for using a cognitive screening tool that can be used in routine practice for screening of any cognitive function impairment among COPD patients.

## Subjects and Methods

A cross sectional observational study was carried out on 100 patients with COPD diagnosed according to Global initiative for Chronic Obstructive Lung Disease. Subjects of the study were selected from Chest Department Outpatients Tanta University Hospitals and Mansoura Chest Hospital Outpatients. They were divided into three groups; group Ⅰ including 34 grade II COPD patients, group II including 32 grade Ⅲ COPD patients and group Ⅲ including 34 grade Ⅳ COPD patients.

**Inclusion criteria:** COPD patients diagnosed by spirometry and classified by GOLD 2020 Stage II, III, IV. Clinically stable patients (no exacerbations in the last 3 months) with optimized stable pharmacological therapy (inhalation therapy with long-acting anticholinergic and/or β2-agonists, inhaled corticosteroids when needed)

**Exclusion criteria:** Stage Ⅰ COPD patients, acute exacerbation of COPD or acute respiratory failure, history of exacerbation in last 3 months, severe medical conditions that did not enable evaluation such as severe chronic inflammatory diseases, chronic heart failure and neoplastic diseases, other underlying chest diseases such as ILD, Bronchiectasis, other underlying heart diseases such as congenital heart diseases, patient refusal, history of head trauma, epilepsy, dementia and organic brain diseases, intellectual disabilities, illiterate patients and patients more than 70 years old.

**As approved by the ethical committee**; an informed consent was taken from all subjects to participate in this work which included aim of the research and details of the tests. All data in our study are confidential and used in research only. There was code number for each patient in a special folder and the results of the research were used in scientific publishing only. Each patient had the right to agree to complete the research or reject and participation was voluntary. No unexpected risks appeared during the course of the research.

**The followings were done to each subject: Full history taking:** to take information about demographic data, occupational status and special habits. **Complete physical examination:** including general and local chest examination to confirm the disease and exclude other concomitant conditions. **Spirometric confirmation of COPD diagnosis:** FEV1/FVC<0.70 after patient is given a bronchodilator such as an inhaled beta agonist as salbutamol 200 μg.
**These tests included: Mini-mental state examination (MMSE):** The **Folstein** Mini-Mental State Examination (MMSE) [8] is a 30-question assessment of cognitive function that evaluates attention, orientation, memory, registration, recall, calculation, language and ability to draw a complex polygon. **Trail making test (TMT):** [9] It is a brief tool that it is widely used to measure motor speed, visual attention, and cognitive flexibility. TMT is a suitable measure of the overall integrity of the brain. It has two parts (Parts A & B). **Digit Symbol test (DSY):** [10] It is a part of the Wechsler Adult Intelligence Test (WAIS), a well-known test that measures an individual's intelligence quotient (IQ). It measures visual scanning, motor speed, attention and mental flexibility. **Digit Span Test (DS):** [10] It is a part of Wechsler's Intelligence Scale, which was

designed to measure a person's intelligence quotient (IQ). Forward span captures attention efficiency and capacity. Backward span is an executive task particularly dependent on working memory.

**Results**

The mean values of the ages of the patients in the studied groups were 58.9±14.9, 53.5±9.7, and 56.9±6.6 in group I, II and Ⅲ respectively. No statistically significant difference was present regarding the age or the gender between different studied groups. (p=0.138, 0.183 respectively) Table (1)

**Table (1):** Socio demographic characteristics of the studied groups

| Sociodemographic | The studied groups | | | sig. test | P |
|---|---|---|---|---|---|
| | Group I (n=34) | Group II (n=32) | Group III (n=34) | | |
| **Age** | | | | **F** | |
| **Range** | 29.0 - 80.0 | 29.0 - 69.0 | 45.0 - 69.0 | **2.024** | |
| **Mean ± s.d** | 58.9 ± 14.9 | 53.5 ± 9.7 | 56.9 ± 6.6 | | **0.138** |
| **Gender** | | | | **χ 2** | |
| **Male** | 29 85.3% | 30 93.8% | 33 97.1% | **3.393** | **0.183** |
| **Female** | 5 14.7% | 2 6.2% | 1 2.9% | | |

More than half of the patients in group I can only read and write (55.9%) with no statistically significant difference regarding the educational level between the three studied groups. (p=0.625) No statistically significant difference was noticed regarding either the marital status or the occupation between the three studied groups. (p=0.168, 0.128 respectively) Table (2)

**Table (2):** Marital status, occupation and education of the three studied groups.

| Sociodemographic | The studied groups | | | χ 2 | P |
|---|---|---|---|---|---|
| | Group I (n=34) | Group II (n=32) | Group III (n=34) | | |
| **Marital status** | | | | | |
| **Married** | 19 55.9% | 18 56.3% | 20 58.8% | | |
| **Divorced** | 3 8.8% | 5 15.6% | 4 11.8% | **9.110** | **0.168** |
| **Not Married** | 8 23.5% | 1 3.1% | 2 5.9% | | |
| **Widow** | 4 11.8% | 8 25.0% | 8 23.5% | | |
| **Occupation** | | | | | |
| **Not working** | 6 17.6% | 7 21.9% | 14 41.2% | | |
| **Manual worker** | 14 41.2% | 12 37.5% | 8 23.5% | **9. 920** | **0.128** |
| **Employee** | 6 17.6% | 9 28.1% | 8 23.5% | | |
| **Retired** | 8 23.5% | 4 12.5% | 4 11.8% | | |
| **Education** | | | | | |
| **Read& write** | 19 55.9% | 15 46.9% | 15 44.1% | | |
| **Technical education** | 12 35.3% | 11 34.4% | 12 35.3% | **2.613** | **0.625** |
| **University education** | 3 8.8% | 6 18.8% | 7 20.6% | | |

A statistically significant difference was present regarding the FVC% of predicted, FEV1% of predicted and FEV1/FVC ratio between different studied groups (p=0.001 for all of them). FVC% of predicted had the least value among group Ⅲ patients. Table (3)

**Table (3):** FVC% of predicted, FEV1% of predicted and FEV1/FVC% characteristics of the studied groups

| Pulmonary function tests | The studied groups | | | F | P |
|---|---|---|---|---|---|
| | Group I (n=34) | Group II (n=32) | Group III (n=34) | | |
| **FVC% of predicted** | | | | | |
| **Range** | 54.2 - 94.1 | 35.0 - 78.0 | 23.0 - 59.1 | **151.199** | **0.001*** |
| **Mean ± s.d** | 72.1 ± 12.0 | 50.2 ± 10.7 | 29.7 ± 6.7 | | |
| **Groups comparison Post hoc Sheffe test** | $P^4$ 0.001* | $P^5$ 0.001* | $P^6$ 0.001* | | |
| **FEV1 % of predicted** | | | | | |
| **Range** | 50.0 - 72.2 | 30.0 - 49.5 | 18.0 - 28.0 | **278.886** | **0.001*** |
| **Mean ± s.d** | 58.5 ± 8.5 | 38.7 ± 7.0 | 22.2 ± 2.7 | | |
| **Groups comparison Post hoc Sheffe test** | $P^4$ 0.001* | $P^5$ 0.001* | $P^6$ 0.001* | | |
| **FEV1/FVC%** | | | | | |
| **Range** | 65.6 - 69.2 | 61.1 - 65.4 | 31.7 - 60.0 | **3.830** | **0.001*** |
| **Mean ± s.d** | 67.5 ± 1.1 | 63.2 ± 1.3 | 55.0 ± 6.8 | | |
| **Groups comparison Post hoc Sheffe test** | $P^4$ 0.140 | $P^5$ 0.034* | $P^6$ 0.843 | | |

**As regards to Mini Mental State Examination,** half of group Ⅲ patients had severe cognitive impairment, compared to 34.4% among group II patients and 26.5% among group I patients with a statistically significant differences between the three studied groups. Table (4)

**Table (4):** Mini Mental State Examination Test of the studied groups

| Mini Mental State Examination | The studied groups | | |
|---|---|---|---|
| | Normal Cognitive Function | Moderate Cognitive Impairment | Severe Cognitive Impairment |
| **Group I (n=34)** | 14 41.2% | 11 32.4% | 9 26.5% |
| **Group II (n=32)** | 8 25.00% | 13 40.6% | 11 34.40% |
| **Group III (n=34)** | 3 8.80% | 14 41.20% | 17 50.0% |
| **Comparison of each Cognitive Function category** | $\chi^2$ (9.490) | $\chi^2$ (0.699) | $\chi^2$ (9.699) |
| | P (0.009) * | P (0.705) | P (0.015) * |

**As regards to Trail A and B tests,** group III had high percent impaired test results, compared to group I and II with a statistically significant differences in its distribution between the different studied groups. Table (5)

**Table (5):** Trail making test of the three studied groups

| Trail making test | The studied groups | | | |
|---|---|---|---|---|
| | Average | | Impaired | |
| **Trail A** | | | | |
| **Group I (n=34)** | 19 | 55.90% | 15 | 44.10% |
| **Group II (n=32)** | 11 | 34.40% | 21 | 65.60% |
| **Group III (n=34)** | 6 | 17.60% | 28 | 82.40% |
| **Comparison of Trail making test category** | $\chi^2$ (10.841) | | $\chi^2$ (9.940) | |
| | P (0.004) * | | P (0.009) * | |
| **Trail B** | | | | |
| **Group I (n=34)** | 21 | 61.8% | 13 | 38.2% |
| **Group II (n=32)** | 10 | 31.3% | 22 | 68.8% |
| **Group III (n=34)** | 7 | 20.6% | 27 | 79.4% |
| **Comparison of Trail making test category** | $\chi^2$ (13.144) | | $\chi^2$ (11.329) | |
| | P (0.001) * | | P (0.001) * | |

**As regards to Digit Symbol Test,** group III patients had 29.4% with severe impairment, while group II had 34.4% and group I had 17.6% with severe impairment with a statistically significant difference in its distribution between different studied groups. Table (6)

**Table (6):** Digit symbol test of the three studied groups

| Digit Symbol Test | The studied groups | | |
|---|---|---|---|
| | **Normal Cognitive function** | **Mild to moderate CI** | **Severe Impairment** |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Group I (n=34)** | 24 | 70.6% | 4 | 11.8% | 6 | 17.6% |
| **Group II (n=32)** | 11 | 34.4% | 10 | 31.2% | 11 | 34.4% |
| **Group III (n=34)** | 4 | 11.8% | 20 | 58.8% | 10 | 29.4% |
| **Comparison of Digit Symbol Test category** | $\chi^2$ (25.149) | | $\chi^2$ (16.935) | | $\chi^2$ (6.492) | |
| | P (0.001) * | | P (0.001) * | | P (0.028) * | |

**As regards to Digit Span Tests A and B,** there was no statistically significant difference in its distribution between different studied groups. Table (7)

**Table (7):** Digit span test of the three studied groups

| **Digit Span Test** | **The studied groups** | | | | | |
|---|---|---|---|---|---|---|
| | **Normal Cognitive function** | | **Mild to moderate CI** | | **Severe Impairment** | |
| **Digit Span Test A** | | | | | | |
| **Group I (n=34)** | 2 | 5.9% | 30 | 88.2% | 2 | 5.9% |
| **Group II (n=32)** | 5 | 15.6% | 23 | 71.9% | 4 | 12.5% |
| **Group III (n=34)** | 5 | 14.7% | 20 | 58.8% | 9 | 26.5% |
| **Comparison of each Digit Span Test A** | $\chi^2$ (1.839) | | $\chi^2$ (0.491) | | $\chi^2$ (0.882) | |
| | P (0.399) | | P (0.724) | | P (0.844) | |
| **Digit Span Test B** | | | | | | |
| **Group I (n=34)** | 1 | 2.9% | 15 | 44.1% | 18 | 52.9% |
| **Group II (n=32)** | 2 | 6.3% | 11 | 34.4% | 19 | 59.4% |
| **Group III (n=34)** | 1 | 2.9% | 13 | 38.2% | 20 | 58.8% |

| | | | |
|---|---|---|---|
| **Comparison of each Digit Span Test B** | $\chi^2$ (0.620) | $\chi^2$ (0.670) | $\chi^2$ (0.348) |
| | P (0.733) | P (0.615) | P (0.840) |

## Discussion

Cognitive impairment is a frequent feature of COPD. However, the proportion of the cognitive impairment in COPD is still unknown, and no screening test has been validated to date for detecting this impairment in that population. [(11)]

The present study was carried out on a total number of 100 patients with chronic obstructive pulmonary diseases. They were selected from Chest Department Outpatients Tanta University Hospitals and Mansoura Chest Hospital Outpatients and divided into three groups.

The goal of this current study was to determine the frequency and subtypes of the cognitive impairment in patients with COPD and to assess the validity of cognitive screening tests in detecting this impairment in that population.

The current study demonstrated that the mean values of the ages of the patients in the studied groups were 58.9±14.9, 53.5±9.7, and 56.9±6.6 in group I, II and III respectively. No statistically significant difference was noticed regarding the age in the three studied groups. (F=2.024, p=0.138).

Similarly, **Bhatt et al,** 2016 found that no statistically significant difference was present regarding the age between different stages. Stage II patients had a mean age of 63.3 (8.4) years old, compared to 64.1 (7.9) among stage III and 62.8 (7.6) among stage IV patients. [(12)]

Also, in the present study, higher level of male patients was observed. Group I had 85.3% males compared to 93.8% and 97.1% among group II, III respectively. No statistically significant difference was present regarding the gender between the three studied groups ($x^2$=3.393, p=0.183).

Similarly, **Pierobon and his colleagues,** 2018 examined sixty-five stable COPD inpatients, mainly stage III and IV GOLD. Higher level of male patients was observed (72.3%). [(13)]

The present study demonstrated that higher level of married patients was present. Group I had 55.9 % married patients compared to 56.3% and 58.8% among group II and III respectively with no statistically significant difference regarding the marital status between the three studied groups. ($\chi^2$=9.110, p=0.168).

Similarly, **Castelino F. and his colleagues,** 2017 studied 140 COPD patients regarding their sociodemographic characteristics including the marital status and found that all patients were married n=140(100%) including (n=120 ,85.7% living with a partner), (n=4, 2.9% separated) and (n=16,11.4% widow). [(14)]

The present study demonstrated that regarding occupation, group I had 41.2 % patients with manual working compared to 37.5 % and 23.5% among group II and III respectively with no statistically significant differences between the three studied groups. ($\chi^2$=9. 920, p=0.128).

Similarly, in **Amora O. et al.,** 2014 study to assess knowledge, practice and self-efficacy for COPD patients, they found that more than half of the studied subjects (54%) were working. This may be in order to cover high cost of medications. [(15)]

In contrast to our results, **Pierobon and his colleagues,** 2018 examined sixty-five stable COPD inpatients, mainly stage III and IV GOLD and found that according to occupation 93.8 % of patients were retired. [(13)]

The current study demonstrated that the mean values of FVC % of predicted in the three studied groups were 72.1±12.0, 50.2±10.7 and 29.7±6.7 in group I, II and III respectively. There was a statistically significant difference regarding the FVC% of predicted between the three studied groups. (F=151.199, p=0.001)

Similarly, **Bhatt et al,** 2016 found that For GOLD 0 participants, mean FVC% predicted was 96.2 (11.3) ml/yr. Those with GOLD grade I had 108.5 (11.2), with increasing GOLD grades: 87.4

(13.4), 72.4 (12.8), and 59.1 (11.6) for GOLD grades II, Ⅲ, and IV respectively. (Trend test for grades 1–4; $P < 0.001$) [12]

The mean values of FEV1% of predicted in the three studied groups were 58.5±8.5, 38.7.5±7.0 and 22.2±2.7 in group I, II and III respectively. There was a statistically significant difference regarding the FEV1% of predicted between the three studied groups. (F=278.886, p=0.001)

Similarly, **Bhatt et al,** 2016 found that for GOLD Grade 0 participants, mean rate of FEV1 decline was 41.8 (47.7) ml/yr. Those with GOLD grade I had the most rapid rate of decline of 53.8 (57.1) ml/yr, with progressively slower rates of decline with increasing GOLD grades: 45.6 (61.1), 31.6 (43.6), and 5.1 (35.8) for GOLD grades II, Ⅲ and Ⅳ respectively (trend test for grades 1–4; $P < 0.001$) [12]

The present study demonstrated that half of group Ⅲ patients had severe cognitive impairment, compared to 34.4% among group II patients and 26.5% among group I patients with statistically significant differences between the three studied groups.

Similarly, **Pierobon and his colleagues,** [13] examined sixty-five stable COPD patients mainly stage III and IV, underwent Mini-Mental State Examination (MMSE) and found different percentages of mild cognitive impairment (MCI) prevalence in the COPD sample depending on the type of neuropsychological test used 6.2% by (MMSE).

In accordance to our findings, in **Gupta et al.,** study [16], eighty male subjects were included: 40 stable COPD patients (smoking history >20 pack years) and 40 healthy volunteers. MMSE scores were evaluated in these groups. 27/40 COPD patients (67.5%) had significantly reduced MMSE scores ($p<0.001$).

In contrast, a cohort study by **Thakur et al.,** 2010 of adults with COPD (n = 1202) and referent subjects matched by age, sex, and race (n = 302) to study the potential risk factors for cognitive impairment among subjects with COPD. Cognitive impairment was defined as a Mini-Mental State Exam score of <24 points. The risk of cognitive impairment was not associated with COPD severity as defined by either the COPD severity score or BODE score. [17]

In the present study, as regards to Trail A and B tests, group Ⅲ patients had high percent impaired test results, compared to group I and II with a statistically significant differences in its distribution between the three studied groups.

In the same way, in **Fumagalli et al.,** 2020 study, series consisted of 68 stable COPD outpatients followed-up every 6 months for $52.6 \pm 27.6$ months. Enrolled patients underwent a baseline comprehensive neuropsychological assessment, including TMT-A, -B and -B-A. Defective TMT was more prevalent among patients, who died, but such a difference was statistically significant only for TMT-B, TMT-B was significantly associated with mortality. No significant association was found between exacerbation and either TMT-A ($p = 0.275$), TMT-B ($p = 0.813$) or TMT-BA ($p = 0.823$). [18]

In the present study, as regards to the digit symbol test, group Ⅲ patients had 29.4% with severe impairment, while group II had 34.4% and group I had 17.6% with severe impairment with a statistically significant difference in its distribution between the different studied groups.

Similarly, **Sarawag and Bhaskar,** [19] reported that COPD patients in the stage III and IV performed worse on all the cognitive tests. There is highly significant difference in MMSE total score, DSST total time and TMT-B total time. There is significant difference in DSST error and TMT-B errors (p=0.001).

As regards to Digit Span Tests A and B, there was no statistically significant difference in its distribution between different studied groups.

In accordance to our findings, **Lv Z et al.,** study [20] demonstrated that there was no significant difference observed between the COPD group and the healthy control group with respect to short-term memory assessed by digit span test ($P > 0.05$).

In contrast to our study, **Lu et al.,** [21] study, a total of 28 COPD patients and 26 healthy controls were enrolled in this study. For all the subjects, structural and functional MRI data, spirometry tests performance and neuropsychological assessments of different cognitive domains were collected. COPD patients performed worse in the Digit Span Test (reverse) than controls.

## Conclusion

Cognitive function study should be a part of the initial respiratory assessment in COPD patients especially for those patients presenting with evident or self-reported symptoms of cognitive deficit. The Mini Mental State Examination Test is recommended to be used as a part of the initial respiratory assessment to give an idea about the cognitive state of the patient and if the patient needs more care for his cognitive status or not.

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