**ORIGINAL ARTICLE**

# The Cognitive Impairment in Patients with Chronic Obstructive Pulmonary Disease

OLEG MICHAILOVICH URYASEV[1], ANTON VALEREVICH SHAKHANOV[2], IRINA VIKTOROVNA SIDOROVA[3]
*[1]Therapy Department, Ryazan State Medical University, Vysokovoltnaya str., 9, Ryazan, Russian Federation.*
*[2,3] Student of Faculty of Medicine, Ryazan State Medical University, Vysokovoltnaya str., 9, Ryazan, Russian Federation.*
*Correspondence to Dr. Anton Valerevich Shakhanov, Email:: shakhanovav@gmail.com, +7-910-635-95-75, Vysokovoltnaya*

## ABSTRACT

**Background:** Actuality: the cognitive impairment have important role among extrapulmonary manifestations in chronic obstructive pulmonary disease (COPD). At the moment there is no clear understanding of the role of chronic obstructive pulmonary disease in their formation.
**Aim:** To study the role of chronic obstructive pulmonary disease in cognitive impairment formation and their features at various stages of COPD.
**Methods:** Study included 55 men divided into two groups: 28 patients with chronic obstructive pulmonary disease and 27 healthy volunteers in the control group. Were performed general clinical examination, spirometry, pulse oximetry, a CAT assessment and cognitive assessment using the MoCA test.
**Results:** In patients with COPD, the cognitive function decreased according to the MoCA test (24 points against 27 points in the control group, p=0.003). The greatest contribution to the cognitive functions reduction in patients with COPD has motor disorders (p = 0.032), memory changes (p = 0.016), coordination disorders (p = 0.010), and sleep disturbances (p <0.001). It was found that in COPD patients the total score of the MoCA test correlated with the scores of the CAT test score (r = -0.580, p = 0.001) and saturation (r = 0.420, p = 0.026).
**Conclusion**: In patients with COPD, there is cognitive function decreasing. An increase in bronchial obstruction severity and amount of symptoms combines with progressive decrease in cognitive functions. In patients with chronic obstructive pulmonary disease, sleep and memory disorders are more frequent, speech and the ability to abstract, and visuospatial and executive skills suffer.
**Keywords:** chronic obstructive pulmonary disease, MoCA test, cognitive impairment.

## INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a common, preventable and treatable disease that characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases, as defined by the Global Strategy for Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease (GOLD). Recently, COPD has been seen as a systemic disease, with many extrapulmonary manifestations.[1,2] An important role among them belongs to cognitive impairments, which in turn are associated with a deterioration in the quality of life.[3] There is evidence that COPD is an independent predictor of cognitive decline, but this problem requires more study. The prevalence of COPD increases with age, while the aging of the body is accompanied by a progressive decline in cognitive functions associated with degenerative processes in the brain.[1] Chronic hypoxia, hypercapnia, hyperventilation, and disorders of the arterial and venous cerebral circulation are distinguished from the mechanisms of possible participation of COPD in cognitive impairment formation and damage to neuronal structures.[4] In this regard, it seems relevant to study the role of COPD in cognitive impairment formation and their features at various stages of chronic obstructive pulmonary disease, which was the purpose of this study.

---
Received on 03-04-2018
Accepted on 04-09-2018

## METHODS

The study was conducted in 2017 at the Department of Intermediate Therapy of Ryazan State Medical University in accordance with the requirements of Good Clinical Practice and the WMA Declaration of Helsinki – Ethical principles for medical research involving human subjects. The study recruited 55 men aged 50 to 80 years, which were distributed into 2 groups. The main group included 28 patients with chronic obstructive pulmonary disease aged 50 to 79 years (median 65 [60; 68] years). The control group included 27 healthy volunteers aged from 51 to 80 years (median 58 [55; 68] years). The studied groups were comparable in terms of age and comorbidities. The study included patients who meet the following inclusion criteria: signed voluntary informed consent to participate in the study; the ability to understand research procedures, and ability to cooperate adequately with the researcher; age over 50 years; a diagnosis of Chronic Obstructive Pulmonary Disease, verified according to the GOLD guidelines. The study did not include patients with a history of the presence of organic brain damage and mental disorders, including dependence on psychoactive substances or alcohol. All patients underwent general clinical examination, spirometry to determine the severity of airflow rate limitations and pulse oxymetry. To assess the severity of the clinical manifestations of COPD, COPD Assessment Test (CAT) was used. For assessing cognitive functions, the Montreal scale of cognitive functions (MoCA test) was used, which includes an assessment of several cognitive spheres, including taking into account visuospatial skills, memory, attention, speech skills, ability

to abstraction and orientation.[5] The largest amount of points according to the results of the MoCA test is 30, and a value of less than 26 points indicates a decrease in cognitive functions.

Statistical processing of the obtained results was performed using Microsoft Excel 2010, StatSoft Statistica 10 and DoctorStat 1.9. The evaluation of the distribution of traits was carried out using the Shapiro-Wilk criterion; with the calculated value of P>0.05, the distribution was recognized as normal. The description of the quantitative traits is given in the form Me [Q25; Q75], where Me is the median, and Q25 and Q75 are the values of the lower and upper quartile, respectively. For comparison of groups by quantitative trait, Kruskal-Wallis and Mann-Whitney criteria were used. Comparison of relative indicators of qualitative features (frequencies and fractions) was performed using Fisher's exact test. An estimate of the relationship of features between each other is given using the Spearman's r-correlation coefficient. Differences were considered statistically significant at P<0.05.

## RESULTS

Among the patients of the main group 54% has second degree of airflow limitation by GOLD (FEV1 50-80%), 39% has third degree (FEV1 30-50%) and 7% has fourth degree (FEV 1 <30%). According to the current classification of COPD, 46% of the patients studied were in group C (high risk, few symptoms), 54% were in group D (high risk, many symptoms). The results are presented in table 1. Compared with the control group, patients with COPD significantly differed in smoking status, having a higher pack-year index. In addition, patients with COPD had higher CAT scores (25 points versus 3 in the control group), which is obviously due to the presence of symptoms of the disease. Saturation in the main group was slightly lower than in the control group (96% vs. 97%).

Analyzing the distribution of symptoms of cognitive impairment, it was found that patients with COPD with the same frequency as in the control group had motor and coordinator disorders, headaches, memory changes, decreased performance, tinnitus and emotional instability (Table 1). It pays the attention that patients of the main group have three times more common complaints of dizziness, possibly caused by systemic hypoxia, and more than twice as high frequency of sleep disorders. That may be associated not with impaired cognitive function, but with the influence of the disease on the sleep of patients due to severe shortness of breath and hyperproduction of sputum at night. However, these results were not statistically significant and need more studies (Table 1).

It became clear that patients with COPD compared with the control group had a significant decrease in cognitive functions, in particular due to visuospatial and executive skills, as well as speech disorders and ability to abstraction (Table 1). When studying the effect of the symptoms of cognitive impairment in the total score of MoCA-test found that the manifestations of motor and coordinated impairments, memory changes and sleep disorders play a role in the overall decrease in cognitive functions in patients with chronic obstructive pulmonary disease (Table 2).

Analyzing the relationship of the studied parameters among themselves, it was found that the total score for the MoCA test, which characterizes the decrease in cognitive functions in patients with COPD, is closely linked to the results of the CAT assessment test and the saturation of patients (Table 3). It is established that the increase in symptoms of COPD, expressed in an increase in points for the CAT test, is accompanied by a significant decrease in cognitive function. At the same time, saturation decrease in patients, on the contrary, contributes to a decrease in the MoCA test scores, which confirms the hypothesis about the role of hypoxia in cognitive impairments formation in COPD.

When assessing the impact of the clinical course of chronic obstructive pulmonary disease on cognitive function indicators in the MoCA test, patients were divided into subgroups depending on the severity of airflow restriction and the classification of clinical groups of patients (Table 4). It has been established that in more severe patients with pronounced symptoms of respiratory disorders (group D by GOLD), lower cognitive function indices are noted, mostly due to impaired attention and speech. Analyzing the effect of spirometry on cognitive function, it was found that an increase in the severity of the airflow rate limit is accompanied by a decrease in the total score, and visual attention and ability to delayed reproduction suffer from visual-executive and executive skills (Table 4).

Table 1: Group characteristics

| **Parameter** | **COPD (n=28)** | **Control (n=27)** | **P** |
|---|---|---|---|
| The frequency of exacerbations (per year) | 2 [1; 2] | - | |
| Smoking experience (years) | 40 [33,5; 44] | 27 [21; 36,5] | 0.15 |
| Pack-years index | 25 [16; 40] | 7 [5; 12] | 0.01 |
| CAT score | 25 [21; 28] | 3 [2; 3] | < 0.01 |
| Saturation (%) | 96 [95; 97] | 97 [97; 98] | < 0.01 |
| **Symptoms:** | | | |
| Cough | 68% (n=19) | 11% (n=3) | < 0.01 |
| Dyspnea | 93% (n=26) | 75 (n=2) | < 0.01 |
| Difficulty breathing | 43% (n=12) | 7% (n=2) | < 0.01 |
| Headaches | 29% (n=8) | 33% (n=9) | 0.78 |
| *Dizziness* | *25% (n=7)* | *7% (n=2)* | *0.14* |
| Movement disorders | 7% (n=2) | 7% (n=2) | 1.00 |
| Memory change | 29% (n=8) | 26% (n=7) | 1.00 |
| Coordinator violations | 18% (n=5) | 4% (n=1) | 0.19 |

| | | | |
|---|---|---|---|
| *Sleep disturbance* | *61% (n=17)* | *33% (n=9)* | *0.06* |
| Degradation of performance | 29% (n=8) | 19% (n=5) | 0.53 |
| Tinnitus | 21% (n=6) | 11% (n=3) | 0.47 |
| Emotional Instability | 14% (n=4) | 4% (n=1) | 0.35 |
| **Parameters of MoCA-test:** | | | |
| Visuospatial / Executive | 3 [3; 4] | 5 [4; 5] | < 0.01 |
| Naming | 3 [3; 3] | 3 [3; 3] | 0.99 |
| Attention | 5 [5; 6] | 6 [4; 6] | 0.44 |
| Language | 2 [0; 2] | 2 [2; 3] | 0.03 |
| Abstraction | 2 [0; 2] | 2 [2; 2] | 0.02 |
| Delayed recall | 4 [2; 4] | 4 [3; 5] | 0.08 |
| Orientation | 5 [5; 6] | 5 [5; 6] | 0.44 |

Table 2 – The total amount of MoCA-test scores, depending on cognitive impairment symptoms in patients with COPD

| **Symptoms:** | **Presence of complaints** | | **P** |
|---|---|---|---|
| | **Yes** | **No** | |
| Headaches | 24 [20; 27] | 18 [16; 27] | 0.218 |
| Dizziness | 18 [17; 27] | 24 [20; 27] | 0.189 |
| Movement disorders | 15 [13; 17] | 24 [20; 27] | 0.032 |
| Memory change | 18 [17; 22] | 25 [20; 28] | 0.016 |
| Coordinator violations | 17 [17; 17] | 24 [20; 27] | 0.010 |
| Sleep disturbance | 20 [17; 24] | 27 [24; 28] | <0.001 |
| Degradation of performance | 20 [17; 24] | 25 [20; 28] | 0.089 |
| Tinnitus | 26 [20; 27] | 23 [18; 27] | 0.806 |
| Emotion Instability | 20 [15; 25] | 24 [20; 27] | 0.186 |

Table 3: Correlation analysis

| **A pair of parameters** | **r by Spearman** | **p** |
|---|---|---|
| CAT score & Age | -0,22 | 0.26 |
| CAT score & Exacerbation Rate | 0,06 | 0.75 |
| CAT score & Smoking Experience | -0,13 | 0.50 |
| CAT score & Pack-Year Index | 0,04 | 0.84 |
| Saturation & Age | 0,39 | 0.04 |
| Saturation & Frequency Exacerbations | -0,26 | 0.18 |
| Saturation & Smoking Experience | -0,25 | 0.19 |
| Saturation & Pack-Year Index | -0,19 | 0.33 |
| MoCA-test – Total & Age | 0,01 | 0.97 |
| MoCA-test – Total & Frequency Exacerbations | -0,36 | 0.06 |
| Total Points & Smoking Experience | -0,08 | 0.70 |
| MoCA-test – Total & Pack-Years Index | -0,30 | 0.12 |
| MoCA-test – Total & CAT score | -0,58 | <0.01 |
| MoCA-test – Total & Saturation | 0,42 | 0.03 |

Table 4 - Indicators of MoCA-test depending on the course of COPD

| **Parameter** | **Group of pts by GOLD classification** | | **P** | **The severity of airflow limit by GOLD** | | | **P** |
|---|---|---|---|---|---|---|---|
| | **C** | **D** | | **2** | **3** | **4** | |
| Visuospatial / Executive | 4 [3; 5] | 3 [3; 4] | 0.17 | 4 [3; 5] | 3 [3; 4] | 3 [2; 3] | 0.02 |
| Naming | 3 [3; 3] | 3 [3; 3] | 1.00 | 3 [3; 3] | 3 [3; 3] | 3 [3; 3] | 1.00 |
| Attention | 6 [6; 6] | 5 [3; 5] | <0.01 | 6 [5; 6] | 5 [3; 6] | 3 [2; 3] | 0.01 |
| Language | 3 [2; 3] | 1 [0; 2] | 0.01 | 2 [1; 3] | 1 [0; 2] | 0 [0; 0] | 0.06 |
| Abstraction | 2 [0; 2] | 1 [0; 2] | 0.29 | 2 [0; 2] | 1 [0; 2] | 1 [1; 2] | 0.82 |
| Delayed recall | 4 [2; 5] | 3 [1; 4] | 0.24 | 4 [4; 5] | 2 [1; 3] | 1 [0; 1] | 0.01 |
| Orientation | 6 [5; 6] | 5 [5; 6] | 0.50 | 5 [5; 6] | 5 [5; 6] | 5 [5; 5] | 0.49 |
| Total | 28 [21; 28] | 20 [17; 25] | 0.01 | 27 [24; 28] | 20 [17; 24] | 15 [13; 17] | <0.01 |

## DISCUSSION

In recent years, there are more and more works aimed for determining the relationship of COPD with the development of cognitive impairment.[6] In such studies, standardized tools, such as the Montreal Cognitive Assessment Scale (MoCA test) and the Short Mental Status Assessment Scale (Mini – Mental State Examination, MMSE, are mainly used to check cognitive function. A number of papers indicating the benefits of the MoCA-test in the early diagnosis of cognitive impairment in patients with COPD compared with MMSE[7,8]. At present, the proportion of COPD patients suffering from cognitive impairment remains unclear, but in all the works there is a clear link between the decline in cognitive functions and COPD. So, in a paper published in Chest in 2012, Villeneuve S. notes that the proportion of COPD patients suffering from cognitive impairment was 3 times higher than in the control group[8]. In the article of Samareh F. the proportion of patients with cognitive impairment is already estimated at 52%, which indicates an even higher percentage and necessitates a broad study of this problem[9]. It is interesting to study the

structure of cognitive impairment. According to the literature, it is known that executive skills suffer more in patients with COPD. Similar results were obtained in our study. Along with an assessment of the overall connection between the development of cognitive impairment and the onset of COPD, it is very interesting to study the pathogenetic mechanisms and clinical markers associated with impaired mental status. In our work, the effect of clinical manifestations, which are reflected in an increase in points for a CAT test, and saturation on the level of cognitive functions, has been established. Similar results are obtained Miravitlles M., which indicates the existence of a correlation between the results of MMSE and CAT-test. Also Thakur N. show the relationship of hypoxemia with the development of cognitive impairment.[10,11] Among the possible mechanisms of impaired cognitive function is hypoxia, most researchers put in the first place, but there are other mechanisms, such as chronic hypercapnia, smoking and genetic predisposition.[9,12,13] The possible connection between the severity of the disease and the severity of cognitive impairment is also reflected in the literature.[4,14] Thus, cognitive impairment is widespread in patients with chronic obstructive pulmonary disease and can influence the clinical outcomes of the disease.[15] This indicates the need to introduce screening programs for patients with COPD for cognitive impairment, and the MoCA test can be used for this purpose. Patients with COPD, taking into account the effect of hypoxia on brain function, to prevent the development of cognitive impairment, pulmonary rehabilitation and prolonged oxygen therapy can be recommended, which can be recommended even with a slight decrease in blood oxygen saturation[11,14].

## CONCLUSION

In patients with chronic obstructive pulmonary disease observed cognitive functions decrease. At the same time, disease progression, an increase in the severity of bronchial obstruction and an increase in symptoms accompanies with progressive cognitive functions decrease. Compared with healthy patients with chronic obstructive pulmonary disease, they more often note sleep and memory disorders, these patients are more likely to have visuospatial and executive skills, mainly speech and the ability to abstraction suffer.

**Acknowledgments:** The authors declare no funding.
**Conflict of interest:** No conflict of interest.

## REFERENCES

1. Tudorache E, Fildan AP, Frandes M, et al. Aging and extrapulmonary effects of chronic obstructive pulmonary disease. Clin Interv Aging 2017;12:1281-7. http://dx.doi.org/10.2147/CIA.S145002
2. Ponomareva IB, Subbotin SV Possibilities of volumetric capnography method in the study of pulmonary functions in patients with COPD. Nauka molodykh (Eruditio juvenium) 2016;(1):68-73 (In Russian).
3. Uryasev OM, Konovalov OE, Kicha DI. The medical activity of patients with bronchial asthma. I.P. Pavlov Russian Medical Biological Herald 2013;(3):98-100 (In Russian). http://dx.doi.org/10.17816/PAVLOVJ2013398-100
4. Torres-Sánchez I, Rodríguez-Alzueta E, Cabrera-Martos I, et al. Cognitive impairment in COPD: a systematic review. J Bras Pneumol 2015;41(2):182-90. http://dx.doi.org/10.1590/S1806-37132015000004424
5. O'Driscoll C, Shaikh M Cross-Cultural Applicability of the Montreal Cognitive Assessment (MoCA): A Systematic Review. J Alzheimers Dis 2017;58(3):789-801. http://dx.doi.org/10.3233/JAD-161042
6. Poletaeva NB Cognitive dysfunction in COPD patients. Fundamental research 2013;9(6):1110-4 (In Russian).
7. Dag E, Bulcun E, Turkel Y, et al. Factors Influencing Cognitive Function in Subjects With COPD. Respir Care 2016;61(8):1044-50. http://dx.doi.org/10.4187/RESPCARE.04403
8. Villeneuve S, Pepin V, Rahayel S, et al. Mild cognitive impairment in moderate to severe COPD: a preliminary study. Chest 2012;142(6):1516-23. http://dx.doi.org/10.1378/CHEST.11-3035
9. Samareh Fekri M, Hashemi-Bajgani S-M, Naghibzadeh-Tahami A, Arabnejad F Cognitive Impairment among Patients with Chronic Obstructive Pulmonary Disease Compared to Normal Individuals. Tanaffos 2017;16(1):34-9
10. Miravitlles M, Molina J, Quintano JA, et al. Depressive status explains a significant amount of the variance in COPD assessment test (CAT) scores. Int J Chron Obstruct Pulmon Dis 2018;13:823-31. http://dx.doi.org/10.2147/COPD.S154791
11. Thakur N, Blanc PD, Julian LJ, et al. COPD and cognitive impairment: the role of hypoxemia and oxygen therapy. Int J Chron Obstruct Pulmon Dis 2010;5:263-9. http://dx.doi.org/10.1164/ajrccm-conference.2010.181.1_MeetingAbstracts.A4125
12. Wen X-H, Li Y, Han D, et al. The relationship between cognitive function and arterial partial pressure O2 in patients with COPD. Medicine (Baltimore) 2018;97(4):e9599. http://dx.doi.org/10.1097/MD.0000000000009599
13. Andrianopoulos V, Gloeckl R, Vogiatzis I, Kenn K Cognitive impairment in COPD: should cognitive evaluation be part of respiratory assessment? Breathe (Sheff) 2017;13(1):e1-e9. http://dx.doi.org/10.1183/20734735.001417
14. Roncero C, Campuzano A, Quintano J, et al. Cognitive status among patients with chronic obstructive pulmonary disease. Int J Chron Obstruct Pulmon Dis 2016;11(1):543-51. http://dx.doi.org/10.2147/COPD.S100850
15. Crişan AF, Oancea C, Timar B, et al. Cognitive impairment in chronic obstructive pulmonary disease. PLoS One 2014; 9(7): e102468. http://dx.doi.org/10.1371/journal.pone.0102468