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Original article

CLINICAL OUTCOMES FROM COVID-19 INFECTION IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE: 5 YEARS LATER

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Abstract

Introduction: Evidence of impact of COVID-19 infection on course of chronic obstructive pulmonary disease (COPD) is still limited.

Aim: To assess clinical outcomes of moderate COVID-19 infection in patients with moderate COPD by comparison of disease control, i.e., the frequency and severity of symptoms, level of health status impairment, values of spirometrc parameters and exacerbation risk, registered at two points in time: 2020 and 2025.

Material and methods: We performed a cross-sectional study including 74 patients with moderate COPD divided in two groups. The first group (COVID-19 group) included 37 COPD patients who had COVID-19 infection of moderate severity in 2020. The second group (non-COVID-19 group) included patients with COPD who did not have coronavirus disease in the period 2020-2025. The frequency and severity of symptoms and level of health impairment were assessed by COPD Assessment Test (CAT): lung function was assessed by spirometric measurements, and exacerbation risk was predicted by exacerbation rate registered in the previous year.

Results: In the COVID-19 group, we found a significantly lower mean CAT score in 2020 than the mean value registered in 2025 (18.3 ± 2.7 *vs.* 26.7 ± 4.3; $P = 0.000$). In addition, the mean CT score in the non-COVID-19 group registered in 2020 did not differ significantly compared to the mean value recorded in 2025 (17.8 ± 2.3 *vs.* 19.4 ± 3.; $P = 0.297$). The mean values of basic spirometric parameters registered in 2020 in the COVID-19 group were significantly higher than their mean values registered in 2025 while the difference between the mean values of these parameters in the non-COVID-19 group measured in 2020 and 2025 was statistically non-significant. The mean exacerbation rate registered in the COVID-19 group in the previous year before recruitment was significantly lower than the mean value registered five years later (0.63 ± 0.04 *vs.* 0.68 ± 0.03; $P = 0.000$), while the difference of the exacerbation rate in the non-COVID-19 group registered at the same points in time was non-significant (0.62 ± 0.07 *vs.* 0.64 ± 0.05; $P = 0.162$).

Conclusion: Our findings indicated significant impact of the COVID-19 infection on symptoms, patient's health and daily life, as well as on the lung function and exacerbation risk emphasizing a need of careful monitoring of these patients upon recovery from COVID-19 infection in order to minimize the impact of infection on COPD progression.

Keywords: chronic obstructive pulmonary disease, COVID-19 infection, exacerbation rate, lung function, symptoms

Introduction

Coronavirus disease 2019 (COVID-19) pandemic was caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), highly transmissible virus that may cause mild viral illness, as well as more severe cases which display systemic inflammation, pneumonia and acute severe respiratory failure[1,2]. In addition, the organ system affected by long COVID-19 may include the respiratory, cardiovascular, neurological, gastrointestinal, and musculoskeletal systems[3,4].

On the other hand, chronic obstructive pulmonary disease (COPD), a lung disease characterized by airway inflammation and remodeling with variable alveolar destruction development that is associated with inhalation of noxious particles and gases (tobacco smoke, occupational and environmental agents, etc.) became one of the most important public health problems at global level in the last decades. It is a significant cause of morbidity, disability and mortality [5,6,7].

Data from several studies indicated that COPD and COVID-19 had many negative interrelationships, i.e. COPD patients were more susceptible to acquire viral infections including SARS-CoV-2, outcomes of COVID-19 were worse in patients with COPD, etc. [8-12]. On the other side, the evidence of COVID-19 and COPD mainly was focused on the severity of COVID-19 and post-COVID syndrome. There is limited evidence about impact of COVID-19 on COPD control, including symptoms, lung function and exacerbation rate, in the medium-to long-term period.

In the present study we assessed the impact of coronavirus disease on the course of COPD five years upon recovery from COVID-19 infection.

Material and methods

Study design and setting

A cross-sectional study was performed at the Institute for Occupational Health (IOH) of RN Macedonia, Skopje, in the period March-September 2025. The consequences of COVID-19 infection were assessed in a group of COPD patients by comparison of the control of the disease, i.e. the frequency and severity of symptoms and the level of health status impairment, values of spirometrc parameters and exacerbation risk, registered at two points in time: 2020 and 2025.

Study population

Study population included 74 patients with COPD diagnosed and monitored at the IOH, divided in two groups. The first group included 37 COPD patients who had COVID-19 infection of moderate severity, diagnosed by polymerase chain reaction (PCR) test in 2020 (COVID-19 group) without a re-infection in the next period. The second group included patients with COPD who did not have coronavirus disease (non-COVID-19

group) in the period 2020-2025 matched to the patients of COVID-19 group by sex, age and COPD severity.

According to the combined assessment of COPD before 2023 ("ABCD" assessment tool), the disease in the subjects from both groups before the COVID-19 pandemic was classified as Group B, GOLD 2, i.e. COPD Assessment Test (CAT) score less than 10, 0-1 exacerbation in the previous year, forced expiratory volume in the first second (FEV_1) of 50-80% of its predicted value[13].

Moderate COVID-19 infection was defined by evidence of lower respiratory disease during clinical assessment and/or imaging by lung CT scan, with oxygen saturation measured by pulse oximetry ≥ 94% on room air[14,15].

All study subjects were informed about the purpose of the study and their written consent was obtained.

Study protocol

The study protocol included completion of a questionnaire on demographic and other characteristics of study subjects, completion of CAT, spirometric measurements, and exacerbation rate in the previous year. Data obtained in the period of stable disease in 2020, i.e. before the occurrence of coronavirus disease in study subjects from COVID-19 group, were contracted from their electronic medical history.

The questionnaire of demographic and other characteristics of study subjects included items on sex, age, smoking status, mean time after the established diagnosis of COPD , and chronic diseases diagnosed by a doctor. Smoking status (active smoker, ex-smoker, and non-smoker) was defined by the World Health Organization (WHO) criteria[16].

All study subjects completed the CAT, an 8-items questionnaire that quantifies the impact of COPD symptoms, i.e. cough, phlegm, chest tightness, breathlessness, and exercise tolerance, on the patient's health and daily life. The CAT score ranges from 0 to 40, classifying the impact of the disease as low (0-10), medium (11-20), high (21-30), and very high (31-40)[17].

Spirometric measurements included baseline (pre-bronchodilator) and post-bronchodilator spirometry. Baseline spirometry, including measures of forced vital capacity (FVC), FEV_1 and FEV_1/FVC ratio, was performed using spirometer Ganshorn SanoScope LF8 (Ganshorn Medizin Electronic GmbH, Germany) with recording the best result of three measurements in which the values of FEV_1 were within 5% of each other. The post-bronchodilator spirometry, recording the same parameters, was performed according to the actual recommendations, i.e. spirometric measurements were performed 20 minutes after administration of 400 μg salbutamol by metered dose inhaler through spacer[18,19].

Exacerbation rate in the previous year as an exacerbation risk predictor was contracted from the medical history of study subjects. High exacerbation risk was defined by two or more COPD exacerbations in the previous year[5].

Statistical analysis

All analyses were done using the Statistical Package for the Social Sciences (SPSS), version 26.0. Continuous variables were expressed as mean values with standard deviation (SD), and the nominal variables as numbers and percentages. Given the aim of the study,

univariate statistical models were used for testing the differences in prevalence and comparison of the means. Chi-square test (or Fisher's exact test where appropriate) was used for testing difference in the prevalence. Comparison of spirometric measurements was performed by independent-samples *T*-test. The level of significance was set at *P* value less than 0.05.

Results

Table 1 illustrates the demographic and other characteristics of study subjects.

Table 1. Characteristics of study subjects

Variable	COVID-19 group (n = 37)	Non-COVID-19 group (n = 37)	*P* value
Sex			
Males	21(56.8%)	20(54.1%)	0.815
Females	16(43.2%)	17(45.9%)	0.815
Age (years)			
Range	47-71	48-69	
Mean age	56.1 ± 5.8	58.3 ± 4.7	0.077
Smoking status			
Active smoker	10(27.1%)	9(24.3%)	0.790
Ex-smoker	21(56.8%)	23(62.1%)	0.637
Non-smoker	6(16.2%)	5(13.5%)	0.746
Period after diagnosis of COPD (years)			
Range	7-20	8-19	
Mean time	11.3 ± 2.9	10.8 ± 3.2	0.089
Comorbidities			
Arterial hypertension	14(37.8%)	16(43.2%)	0.636
IHD	5(13.5%)	6(16.2%)	0.744
DM type 2	6(16.2%)	7(18.9%)	0.760
Osteoarticular disorders	10(27.1%)	11(29.7%)	0.797
CAT scores documented in 2020			
Range	15-23	16-25	
Mean CAT score	18.3 ± 2.7	17.8 ± 2.3	0.394
Mean values of spirometric parameters measured in 2020 (% pred.)			
FVC	87.3 ± 7.8	88.9 ± 6.7	0.347
FEV_1	64.3 ± 5.7	65.9 ± 4.8	0.196
FEV_1/FVC ratio	0.64 ± 0.03	0.64 ± 0.02	1.000
Exacerbation risk			
Mean exacerbation rate in the previous 12 months (2019)	0.63 ± 0.04	0.62 ± 0.07	0.079

COPD: chronic obstructive pulmonary disease; IHD: ischemic heart disease; DM: diabetes mellitus; CAT: COPD Assessment Test; pred.: predicted; FVC: forced vital capacity; FEV_1: forced expiratory volume in the first second.

The mean CAT score in the COVID-19 group registered in 2020 was significantly lower than the mean value registered in 2025 (18.3 ± 2.7 *vs.* 26.7 ± 4.3; $P = 0.000$). On contrary, the mean CT score in the non-COVID-19 group registered in 2020 did not differ significantly compared to the mean value recorded in 2025 (17.8 ± 2.3 *vs.* 18.4 ± 2.6; $P = 0.297$) (Figure 1).

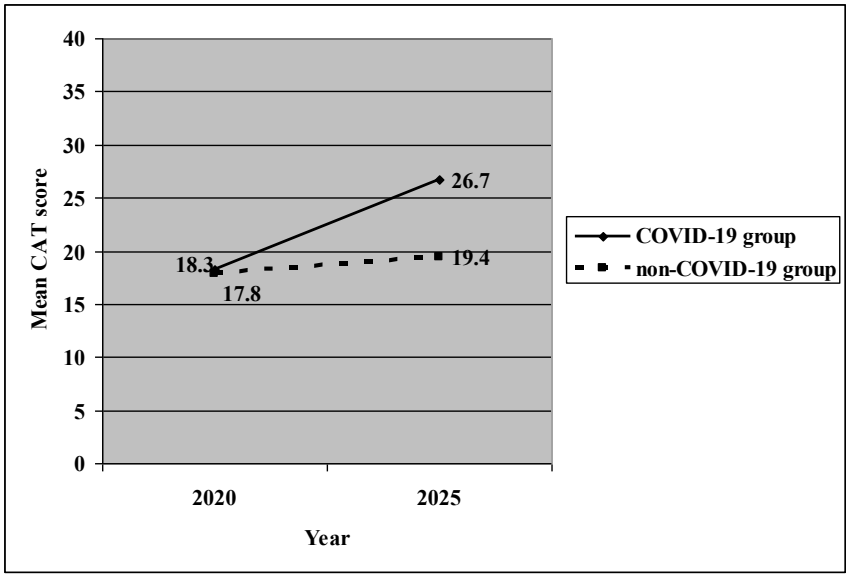

Fig. 1. Mean CAT scores registered in 2020 and 2025 in COVID-19 and non-COVID-19 group

The mean FVC value in the COVID-19 group measured in 2020 was significantly higher than the mean value registered in 2025 (87.3 ± 7.8 *vs.* 83.2 ± 5.9; $P = 0.013$). In contrast, the mean FVC value in the non-COVID-19 group measured in 2020 was similar to the mean value measured in 2025 (88.9 ± 6.7 *vs.* 87.8 ± 6.1; $P = 0.463$) (Figure 2).

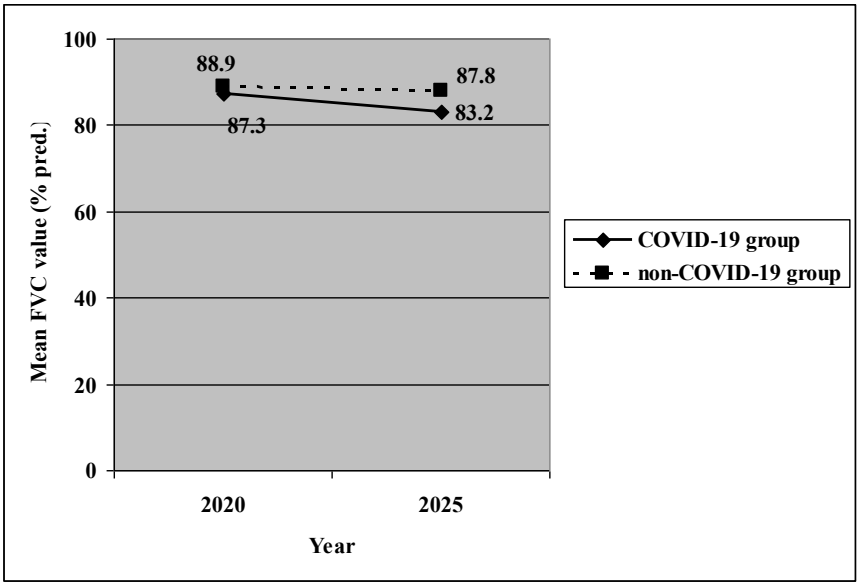

Fig. 2. Mean FVC value in 2020 and 2025 in COVID-19 and in non-COVID-19 group

The mean FEV_1 value in the COVID-19 group measured in 2020 was significantly higher than the mean value recorded in 2025 (64.3 ± 5.7 *vs.* 58.2 ± 4.4; $P = 0.000$). The mean FEV_1 value in the non-COVID-19 group measured in 2020 was non-significantly higher than the mean value measured in 2025 (65.9 ± 4.8 *vs.* 63.9 ± 4.6; $P = 0.071$) (Figure 3).

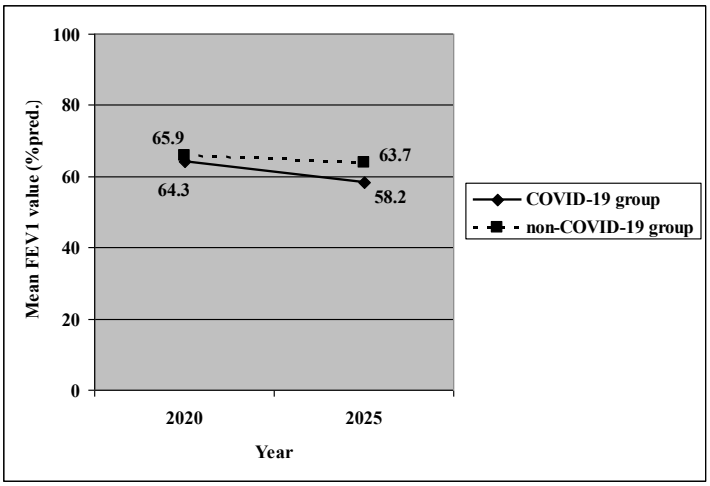

Fig. 3. Mean FEV_1value in 2020 and 2025 in COVID-19 and in non-COVID-19 group

The mean value of FEV_1/FVC ratio in the COVID-19 group measured in 2020 was significantly higher than the mean value registered in 2025 (0.64 ± 0.03 *vs.* 0.61 ± 0.02; $P = 0.000$). The mean value of FEV_1/FVC ratio in the non-COVID-19 group measured in 2020 was non-significantly higher than the mean value measured in 2025 (0.64 ± 0.02 *vs.* 0.63 ± 0.03; $P = 0.096$) (Figure 4).

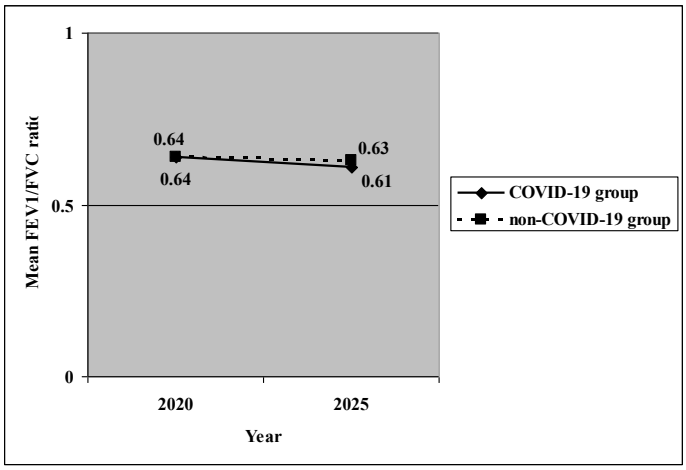

Fig. 4. Mean value of FEV_1/FVC ratio in 2020 and 2025 in COVID-19 and in non-COVID-19 group

The mean exacerbation rate in the COVID-19 group registered in 2019 was significantly lower than the mean value recorded in 2024 (0.63 ± 0.04 *vs.* 0.68 ± 0.03; $P = 0.000$). The mean exacerbation rate in the non-COVID-19 group registered in 2019 was slightly lower than the mean value registered in 2024 (0.62 ± 0.07 *vs.* 0.64 ± 0.05; $P = 0.162$) (Figure 5).

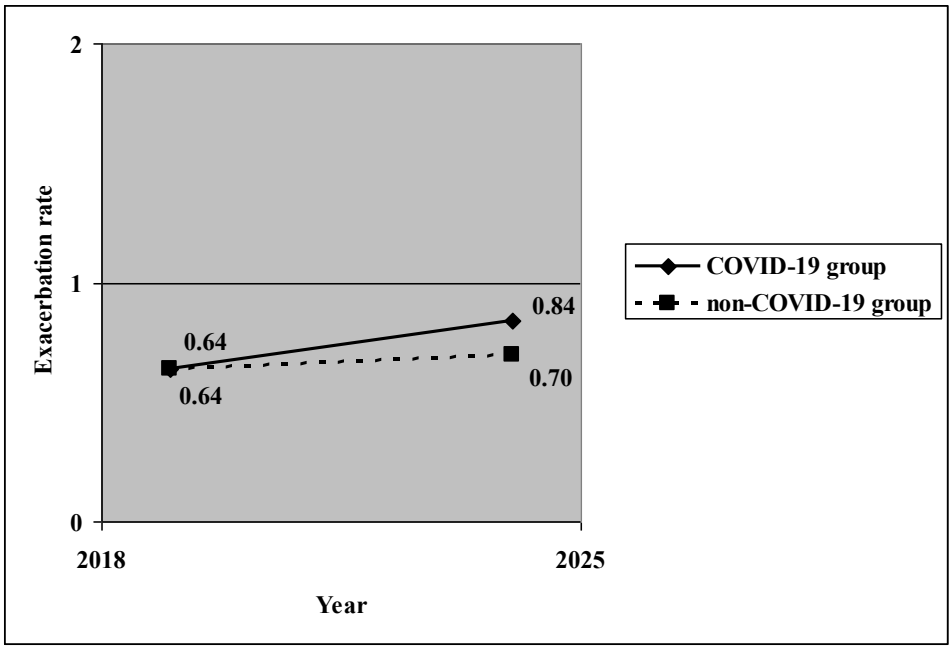

Fig. 5. Mean exacerbation rate in COVID-19 and non-COVID-19 group registered in 2019 and 2024

Discussion

Several studies indicated complex association between COPD and COVID-19 highlighting a need for careful management of COPD patients during the pandemic, as well as careful monitoring of these patients upon recovery from COVID-19 infection in order to minimize the impact of infection on COPD progression[20]. Risk factors for worse outcomes of COVID-19 infection in COPD patients include increasing age and cardiovascular comorbidities. On the other side, there is evidence that COPD itself is associated with worse outcomes, although the causes are still not clear. Possible reasons may be increased susceptibility to viral infection, pre-existing compromised lung function, pre-existing endothelial dysfunction that predisposes to vascular complications during COVID-19 infection, use of inhaled corticosteroids in the treatment of stable disease, etc.[21-25].

In the present study, we assessed the impact of COVID-19 infection in a group of COPD patients by comparison of the frequency and severity of symptoms and the level of health status impairment, values of spirometrc parameters and exacerbation risk, registered in 2020 and 2025. In addition, these parameters were compared at the same points in time in a group of COPD patients who did not have coronavirus disease (non-COVID-19 group) in the period 2020-2025 matched to COVID-19 group by sex, age and COPD severity.

COVID-19 and non-COVID-19 group had similar demographic characteristics. In both groups, more than 20% of participants were still active smokers while the frequency of ex-smokers varied from 50 to 60%. Similar findings were obtained in our previous surveys indicating low effectiveness of anti-smoking strategies and activities and a need of greater emphasis for tobacco smoking and environmental and occupational exposure to other respiratory irritants[26,27]. The frequency of comorbidities in both examined groups was also similar to their frequency registered in our previous studies[28,29].

We found significant difference in the CAT scores between the two groups. In the COVID-19 group, the mean CAT score documented in 2025 was significantly higher than the mean CAT score recorded in 2020 indicating significant impact of COVID-19 infection on symptoms and overall health status of study subjects. On the other hand, in the non-COVID-19 group, the mean CAT score documented in 2025 was slightly higher than its mean value registered in 2020. In the prospective cohort study with duration of around 25 months that assessed outcomes in COPD patients after recovery from COVID-19 infection of different severity, Kwok *et al.* registered symptomatic deterioration in patients who had severe coronavirus disease, as well as in COPD patients who had mild-moderate infection. The odds ratios (OR) for increase of the modified British Medical Research Council (mMRC) dyspnea scale, using the non-COVID-19 group for comparison, were around 3.5 for the mild-moderate COVID-19 group and around 5 for the severe COVID-19 group[30].

The impact of COVID-19 infection on spirometric parameters was also significant. In the COVID-19 group, the mean values of FVC, FEV_1 and FEV_1/FVC ratio registered in 2025 were significantly lower than their mean values registered in 2020. In addition, in the non-COVID-19 group the mean values of spirometric parameters registered in 2025 were lower than their mean values registered in 2020, but statistical significance was not reached for none of them. To date, we have not found data in the existing literature on changes of spirometric parameters in COPD patients after recovery from COVID-19 infection.

Our findings indicated that the exacerbation risk was also affected by the COVID-19 infection. The mean exacerbation rate in the previous year in the COVID-19 group registered in 2024 was found to be significantly higher than the mean exacerbation rate registered in 2019, while the mean exacerbation rate in the non-COVID-19 group registered in 2024 was higher than its value registered in 2019 but without statistical significance. In the study mentioned above, Kwok *et al*. registered increased annual exacerbation frequency in COPD patients upon recovery from COVID-19 infection with statistical significance in the group with severe coronavirus disease[10]. In addition, in the study including 3,445 COPD patients infected by COVID-19 in South Korea, Choi *et al.* registered increased frequency of both mild-to moderate and severe COPD exacerbations compared to pre-COVID-19 infection. Furthermore, among previously non-exacerbators, 11.2% of COPD patients transitioned to exacerbator after COVID-19 infection[31].

Findings of the present study should be interpreted in the context of its limitations. The small size of the examined groups, as well as the cross-sectional analysis, could have implications on the results obtained and their interpretation. In addition, CT scan was not performed in all study subjects from the COVID-19 group in 2025 for assessment of COVID-19 lung consequences, e.g. fibrosis, which could also account for symptoms deterioration and functional impairment. Furthermore, the study population included only patients with moderate COPD and the COVID-19 group included patients with moderate coronavirus disease; consequently, the results could not be representative for the COPD population at large. On the other side, the selection of subpopulation of COPD patients could be a strength of this study that enables better understanding of the impact of COVID-19 infection on the course of COPD as a heterogeneous lung condition.

Conclusion

In conclusion, in this cross-sectional study on assessment of the impact of moderate COVID-19 infection on the course of moderate COPD, we found significant influence of

the disease on symptoms, patient's health and daily life, as well as on lung function and exacerbation risk. Our findings indicated a need of careful monitoring of COPD patients upon recovery from COVID-19 infection and adequate intervention (escalation of COPD pharmacotherapy, vaccination, pulmonary rehabilitation, etc.) in order to minimize the impact of infection on COPD course and prognosis.

Conflict of interest statement. None declared.

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