Prevalence of asthma and COPD in a cohort of patients at the follow up after COVID-19 pneumonia

Alessia Verduri , Jonathan Hewitt , Ben Carter , Roberto Tonelli , Enrico Clini , Bianca Beghè

PII: S2531-0437(22)00127-1
DOI: https://doi.org/10.1016/j.pulmoe.2022.05.005
Reference: PULMOE 1757

To appear in: *Pulmonology*

Received date: 21 May 2022
Accepted date: 30 May 2022

Please cite this article as: Alessia Verduri , Jonathan Hewitt , Ben Carter , Roberto Tonelli , Enrico Clini , Bianca Beghè , Prevalence of asthma and COPD in a cohort of patients at the follow up after COVID-19 pneumonia, *Pulmonology* (2022), doi: https://doi.org/10.1016/j.pulmoe.2022.05.005

Letter-to-Editor

Prevalence of asthma and COPD in a cohort of patients at the follow up after COVID-19 pneumonia

Alessia Verduri[1], Jonathan Hewitt[2], Ben Carter[3], Roberto Tonelli[4], Enrico Clini[1], Bianca Beghè[1].

Affiliations

[1]Department of Surgical and Medical Sciences (SMECHIMAI), University of Modena and Reggio Emilia, and Respiratory Unit, University Hospital of Modena Policlinico, I

[2] Division of Population Medicine, Cardiff University, Wales-UK

[3] Department of Biostatistics and Health Informatics, Institute of Psychiatry, Psychology and Neuroscience, King's College London, England-UK

[4] Clinical and Experimental Medicine PhD School, University of Modena and Reggio, I

Corresponding author:

Prof. Enrico Clini, MD

University of Modena and Reggio Emilia, Modena (I)

Department of Surgical and Medical Sciences

Respiratory Unit, University Hospital of Modena Policlinico,

enrico.clini@unimore.it

To the Editor,

A relevant (but still unpredictable) proportion of patients after COVID-19, particularly those hospitalized with severe acute disease, may present persistent symptoms (i.e. long-COVID syndrome),[1] even clustering in specific clinical presentation (i.e. more dyspnea, fatigue, or anxiety/depression, etc).[2] Patients suffering from asthma and COPD have been considered less exposed to infection,[3] however, there is a lack of data on their prevalence in the long-COVID populations. We hypothesized that individuals with existing chronic airway disease could experience more long term symptoms and/or have respiratory functional impairment 6 months after discharge. Thus we aimed at: i) determining the prevalence of asthma and COPD at the follow-up in a cohort of patients recovering from COVID-19 pneumonia; ii) investigating their dyspnea grade, pulmonary function, and exercise tolerance.

A post-COVID service was established at the Respiratory Outpatient Clinic (University Hospital of Modena Policlinico) for all patients previously hospitalized and cases of SARS-CoV-2 infection not requiring admission for in-person follow up 3-6 months after discharge or recovery from viral infection. Out of 911 patients followed up between July 2020 and February 2022, 780 were hospitalized (85.6%). From the cohort of individuals previously hospitalized, we selected patients with existing diagnosis of asthma or COPD at hospital admission and newly diagnosed at the follow up according to the international guidelines[4,5]. Other individuals with asthma or COPD but not hospitalized for COVID-19, patients with confirmed interstitial lung disease, concomitant neuromuscular diseases, cognitive impairment or severe psychiatric disorders, and patients not able to perform follow up assessment were excluded.

This study summarises the clinical-functional assessment of 82 patients (10.5%) reviewed following hospital discharge. The mean time from discharge to follow up was 4 ±1.1 months. Out of 82 individuals, 41 were asthmatic patients and 41 COPD. The prevalence of asthma in the study cohort was 5.2%, and the same for COPD.

The characteristics of the participants and a summary of their COVID-19 admission are reported in **Table 1a**; patients with asthma and COPD were similar except for age and smoking history, as expected. Out of 41 patients with asthma, 3 (7.3%) were newly diagnosed, whereas 18 (44%) COPD patients had new diagnosis at the follow up. In patients with asthma, 18 (47%) were allergic, 19 (48%) obese, and 2 (5%) had bronchiectasis. The 23 patients with confirmed COPD were predominantly in GOLD 1-2 grades (87%). The newly diagnosed COPD patients were predominantly male (83%), all former or current smokers, and with similar grade of the disease.

Modified Medical Research Council (mMRC) dyspnea grade[6], spirometry and lung diffusing capacity (DL_{CO})[7] parameters, and six-minute walk distance (6MWT)[8,9] were collected at the follow up as outcomes (**Table 1b**). Persisting oxygen desaturation during exercise was observed in 9.7% of cases: 6 COPD patients with 3 newly diagnosed and 2 asthmatic patients with confirmed diagnosis.

According to the study purpose, we were able to show interesting findings.

First, data collection helped quantify the proportion of patients with diagnosis of asthma and COPD in a large cohort of people at the follow up after COVID-19 pneumonia. The prevalence of asthmatic patients is in line with that observed in the general population in Italy,[10] but it seems larger than previously reported data in a large cohort of COVID-19 patients.[11,12] On the other hand, COPD patients in our study cohort are less prevalent than in the general population, [13] which may support a different epidemiology within COVID-19 patients.[3] Notwithstanding, the follow-up service provided a new diagnosis of chronic respiratory disease, particularly COPD. This provided patients with an opportunity for an appropriate disease identification and care plan.

Second, a clinically meaningful post-COVID mMRC dyspnea score observed in 41.5% of the COPD patients, who were in mild GOLD grade of severity, confirms the findings of Huang *et al* in a large population of patients discharged in Wuhan and assessed six months later.[14] This emphasises that older age is not the only responsible factor for long-term residual dyspnea in COPD survivors.

Third, the reduction in DL_{CO} (mean 73.6% pred with <80%pred in 57.3% of cases) as a marker of residual lung damage following interstitial pneumonia was similar to that observed in unselected patients treated with respiratory support therapies (HFNC, NIV, intubation),[14-16] even though more frequent in COPD (75.6%) than in patients with asthma in our cohort.

Finally, the great proportion of people with asthma and obesity (43.9%), confirmed that this comorbidity makes asthma difficult to treat[17] and may also impact negatively on the patient's perception of good health in individuals recovering from COVID-19.

Considering major limitations (i.e. the single-center analysis and the lack of *pre-to-post* comparison of pulmonary function test in patients with existing diagnosis of asthma and COPD), the study results are informative. Indeed, the patients with asthma and COPD is a representative real-word disease-group, and the follow up assessment can be useful for unknown diagnoses of chronic respiratory disease. Therefore, the findings highlight the importance of a tight respiratory follow-up assessment in individuals recovering from COVID-19 pneumonia who should be

investigated for long-term symptoms including dyspnea, especially those underdiagnosed for having asthma or COPD.

Funding

EC have received research grant support from Chiesi Italia S.p.A. (letter of intent signed on 09/04/2021).

Consent for data publication

The consent for data publication was given by the Ethics Committee (CE 453/2020-OSS/AOUMO and CE EM453/2020-OSS/AOUMO).

Acknowledgments

None

Conflicts of interest

There are no conflicts of interest.

References

1. COVID-19 rapid guideline: managing the long-term effects of COVID-19. National Institute for Health and Care Excellence (NICE), Scottish Intercollegiate Guidelines Network (SIGN) and Royal College of General Practitioners (RCGP). NICE guideline [NG188] Published: 18 December 2020 Last updated: 11 November 2021. https://www.nice.org.uk/guidance/ng188
2. Carfi A, Bernabei R, Landi F, for the Gemelli against COVID-19 Post-acute Care Study Group. Persistent symptoms in patients after acute COVID-19. JAMA 2020; 324(6): 603-605.
3. Eger K, Bel EH. Asthma and COVID-19: do we finally have answers? Eur Respir J. 2021; 57(3): 2004451.
4. Vestbo J, Hurd SS, Agustí AG, Jones PW, Vogelmeier C, Anzueto A, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. Am J Respir Crit Care Med. 2013; 187(4): 347-365.
5. Global Initiative for Asthma. Global strategy for Asthma management and prevention, 2019. Available from www.ginasthma.org.
6. Fletcher CM. Standardised questionnaire on respiratory symptoms: a statement prepared and approved by the MRC Committee on the Aetiology of Chronic Bronchitis (MRC breathlessness score). Br Med J 1960; 2: 1662.
7. Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, *et al*. Standardization of spirometry. Eur Respir J 2005; 26(2): 319-338.
8. ATS Statement: Guidelines for the six-minute walk test. Am J Respir Crit Care Med 2002; 166: 111-117.
9. Enright PL, Sherrill DL. Reference equations for the six-minute walk in healthy adults. Am J Respir Crit Care Med. 1998; 158(5 Pt 1): 1384-1387.
10. de Marco R, Cappa V, Accordini S, Rava M, Antonicelli L, Bortolami O, et al. Trends in the prevalence of asthma and allergic rhinitis in Italy between 1991 and 2010. Eur Respir J. 2012 Apr;39(4):883-92.
11. Caminati M, Vultaggio A, Matucci A, Senna G, Almerigogna F, Bagnasco D, et al. Asthma in a large COVID-19 cohort: Prevalence, features, and determinants of COVID-19 disease severity. Respir Med. 2021; 176: 106261.

12. Yang J, Zheng Y, Gou X, Pu K, Chen Z, Guo Q, et al. Prevalence of comorbidities in the novel Wuhan coronavirus (COVID-19) infection: a systematic review and meta-analysis. Int J Infect Dis. 2020; 30136–3: S1201–9712.
13. Viegi G, Maio S, Fasola S, Baldacci S. Global Burden of Chronic Respiratory Diseases. J Aerosol Med Pulm Drug Deliv. 2020; 33(4): 171-177.
14. Huang C, Huang L, Wang Y, Li X, Ren L, Gu X, et al. 6-month consequences of COVID-19 in patients discharged from hospital: a cohort study. Lancet 2021; 397(10270): 220-232.
15. Fabbri L, Moss S, Khan FA, Chi W, Xia J, Robinson K, *et al*. Parenchymal lung abnormalities following hospitalisation for COVID-19 and viral pneumonitis: a systematic review and meta-analysis. Thorax 2022 Mar 25: thoraxjnl-2021-218275. doi: 10.1136/thoraxjnl-2021-218275. Online ahead of print.
16. Torres-Castro R, Vasconcello-Castillo L, Alsina-Restoy X, Solis-Navarro L, Burgos F, Puppo H, Vilaró J. Respiratory function in patients post-infection by COVID-19: a systematic review and meta-analysis. Pulmonology. 2021 Jul-Aug;27(4):328-337.
17. Moitra S, Carsin A, Abramson MJ, Accordini S, Amaral AFS, Anto J, *et al.* Long-term effect of asthma on the development of obesity among adults: an international cohort study, ECRHS. Thorax 2022 April 27: thoraxjnl-2021-217867. doi: 10.1136/thoraxjnl-2021-217867. Online ahead of print.

Table 1a. Characteristics of the study population on hospital admission.

	All patients N = 82	**Asthma N = 41**	**COPD N = 41**	**p-value**
Age[&], years	66 [34-88]	58 [34-83]	74 [58-88]	<0.0001
Male gender[&&]	53 [64.6]	23 [56.1]	30 [73.2]	0.17
Ethnicity, Caucasian	82 [100]	-	-	
Smoking history[&&]				<0.0001
Current smoker	5 [6.1]	1 [2.4]	4 [9.7]	
Former smoker	54 [66]	17 [41.5]	37 [90.2]	
Non-smoker	23 [28]	23 [56.1]	0 [0]	
BMI (pre-admission)[&]	28.6 [20-44]	29 [20-44]	28 [21-41]	0.31
BMI[&&] ≥ 30	30 [36.6]	18 [43.9]	12 [29.3]	0.25
Length of hospital stay[&] (days)	14 [1-94]	14 [1-94]	14 [2-45]	0.85
COT only[&&]	70 [85.3]	34 [83]	36 [88]	0.76
HFNC[&&]	5 [6.1]	3 [7.3]	2 [4.9]	1.00
NIV[&&]	7 [8.5]	4 [9.7]	3 [7.3]	1.00
Intubation/MV[&&]	4 [5]	3 [7.3]	1 [2.4]	0.62
O_2 at discharge[&&] **** COPD patients on pre-admission LTOT were excluded (n=5)***	5 [6.2]	2 [4.9]	3 [7.3]	0.048

Key: Data reported as mean and range or number and % as appropriate.

MV, mechanical ventilation

[&]*Analysis by Student-t test and* [&&]*Fisher's Exact test*

Abbreviations

BMI: Body Mass Index
LOS: Length of Stay
COT: Conventional Oxygen Therapy
HFNC: High Flow Nasal Cannula
NIV: Non-invasive Ventilation
MV: Mechanical Ventilation
O_2: Oxygen
LTOT: Long Term Oxygen Therapy

Table 1b. Follow-up assessment in the study population.

	All patients N = 82	**Asthma N = 41**	**COPD N = 41**	**p-value**
mMRC[&]	0.5 [0-3]	0.2 [0-2]	0.7 [0-3]	0.02
mMRC ≥ 1 point[&&]	22 [26.8]	5 [12.2]	17 [41.5]	0.005
FEV_1/FVC[&]	69.2 [35.6-86.4]	75.8 [59-86.4]	62.7 [35.6-70.5]	<0.0001
FEV_1[&] (%pred)	88.2 [27-145]	97.4 [42-138]	79 [27-145]	0.0002
TLC[&] (%pred)	111 [75-150]	109 [75-150]	112 [77-148]	0.36
TLC[&&] (<90%pred)	5 [6.1]	3 [7.3]	2 [4.9]	1.00
DL_{CO}[&] (%pred)	73.6 [25-128]	85 [37-128]	61 [25-119]	<0.0001
DL_{CO}[&&] (<80%pred)	47 [57.3]	16 [39]	31 [75.6]	0.002
6MWT[&] (meters)	425 [220-610]	452 [300-610]	399 [220-530]	0.003
6MWT[&] (%pred)	77 [46-98]	79 [56-97]	77 [46-98]	0.023
6MWT[&&], desaturation	10 [12.2]	2 [4.9]	8 [19.5]	0.048

Key: Data reported as mean and range or number and % as appropriate.

[&]*Analysis by Student-t test and* [&&]*Fisher's Exact test*

Abbreviations

mMRC: modified Medical Research Council

FEV_1: Forced Expiratory Volume in 1 Second

FVC: Forced Vital Capacity

TLC: Total Lung Capacity

DL_{CO}: Diffusing Lung Capacity for Carbon Monoxide

6MWT: 6-Minute Walk Test