



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Available online at
ScienceDirect
www.sciencedirect.com

Elsevier Masson France
EM|consulte
www.em-consulte.com



Editorial

Chronic obstructive pulmonary disease and the COVID-19 pandemic: Reciprocal challenges



ARTICLE INFO

Keywords:
 COPD
 COVID-19
 Infection

The coronavirus disease 2019 (COVID-19) pandemic caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is an international public health emergency challenging our health system. Pneumonia is one of the main hallmarks of severe COVID-19, with high risks of severe hypoxemia and acute respiratory distress syndrome. An excess prevalence and severity of COVID-19 in patients with chronic obstructive pulmonary disease (COPD) was anticipated. However, based on currently available data, COPD does not appear as a frequent comorbidity in patients with COVID-19. It could even be less frequent in patients with COVID-19 than in the general population of similar age and gender characteristics, but this remains to be confirmed [1–4]. Conversely, COPD seems clearly associated with a greater severity in patients with COVID-19 [5–9].

Regarding the prevalence of COPD in patients with COVID-19, it has to be pointed out first that currently available data is sparse, mostly from hospitalized patients, and has to be considered cautiously. A systematic review and meta-analysis including 10 studies from 3,403 hospitalized patients for COVID-19 in Asia found that COPD rate was 0.95% [1], whereas the prevalence of hypertension (16%), cardiovascular disease (12%) and diabetes (8%) was much higher. Of note, COPD comorbidity was reported in 5 studies only. In a retrospective case series of 1,591 COVID-19 patients referred to intensive care units (ICU) in Lombardy, Italy, the rate of patients with COPD was 4% [2]. Among 393 patients hospitalized for COVID-19 in New York City, the rate of patients with COPD was 5.1%, whereas other comorbidities were much more frequent including hypertension (50%), obesity (36%), diabetes (25%), coronary artery disease (14%), and asthma (12%) [3]. Before drawing any conclusion regarding the relatively low prevalence of COPD compared to other comorbidities in patients with COVID-19, we definitely need more data, especially comparing this prevalence to what is observed in general population samples of the same geographical, age and gender structure, using similar diagnostic criteria. In currently available studies, COPD is identified through known diagnosis, which might lead to marked underestimation. Other speculative explanations for this low prevalence of COPD include a potentially stricter compliance to preventive measures including

avoiding close contact, quarantine, and general measures like hand-washing. A potential benefit from inhaled treatments including corticosteroids has also been proposed, but needs to be demonstrated [4].

Regarding the severity of COVID-19, current data clearly indicates a higher risk of severe infection in patients with COPD. A meta-analysis including 6 studies with 1,592 patients from Asia found an odd-ratio (OR) for severe COVID-19 of 5.69 in COPD patients [5]. Another meta-analysis also found an OR of 4.38 for the development of severe COVID-19 in patients with COPD [6]. In 339 consecutive over 60 years old patients hospitalized for COVID-19 in Wuhan, COPD was a predictor of death with a hazard ratio of 2.24 [7]. Interestingly, a meta-analysis focusing on comorbidities in 1,558 patients found that the highest OR for severe COVID-19 was for COPD (OR=5.97), compared to lower OR in more common comorbidities like hypertension (OR=2.29), diabetes (OR=2.47), cardiovascular disease (OR=2.93) and cerebrovascular disease (OR=3.89) [8]. In these studies, severe infection was defined by acute respiratory failure and/or requirement of ICU. A higher expression of angiotensin converting enzyme 2 (ACE-2), the receptor for SARS-CoV-2, has been reported in the small airway epithelium of patients with COPD with a significant inverse relationship between ACE-2 gene expression and FEV₁% [9]. However, the relevance of these findings to the severity of COVID-19 in COPD remains to be demonstrated.

So far, no specific antiviral therapy has been shown to be effective in COVID-19 [10]. There is no specific data assessing specific therapeutic management of COPD patients with COVID-19. The following propositions for clinical practice are based on expert opinions from the COPD group of the French Language Respiratory Society (Société de Pneumologie de Langue Française, SPLF). When nebulization with short-acting bronchodilators is needed, a protective mask (Filtering Facepiece Particles, FFP2) has to be used by caregivers within 3 hours of nebulization to avoid viral contamination. Whenever possible, non-nebulized inhaled treatments should be preferred using, e.g., metered-dose inhalers + spacers or dry-powder inhalers, as appropriate based on availability and patients' experience, condition and inspiratory flow. When needed, oxygen therapy should be used as usual to maintain a SpO₂ of more than 88–90%. Arterial blood gas should be performed in all COPD patients with signs of respiratory failure. Hypercapnic acidosis (pH < 7.35) should lead to consider ventilatory support including non-invasive ventilation (NIV), invasive ventilation or high-flow oxygen therapy. If NIV is used, a mask with no leak and dual limb breathing circuits should be used to prevent viral contamination. In severe

hypoxemia with no hypercapnia, invasive ventilation or high-flow oxygen therapy should be preferred. The effects of systemic corticosteroids on COVID-19 are still controversial [10], but systemic corticosteroids can be used for COPD exacerbations in patients with COVID-19, if needed. As for other patients with COVID-19, prophylactic low-molecular-weight heparin should be used to prevent thromboembolism in the absence of contraindication and the diagnosis of associated acute pulmonary embolism should be carefully considered in case of severe or aggravating conditions.

In COPD exacerbation with no COVID-19, usual therapeutic guidelines should be followed during the COVID-19 pandemic [11].

Stable COPD patients should maintain their regular therapy as recommended by GOLD COVID-19 guidance [12]. There is no evidence to support that inhaled corticosteroids should be avoided during the COVID-19 pandemic. Oxygen therapy should be provided if needed following standard recommendations and using appropriate protective measures for contacts. Specifically, public health recommendations to minimize the risk of infection have to be strictly implemented including handwashing, wearing a mask and reduction of contact. Physical activity should be maintained as much as possible, at home in case of quarantine. Regular follow-up, support and management have to be maintained and probably reinforced in this context of COVID-19 pandemic, involving general practitioners, pulmonologists, physiotherapists, rehabilitation, smoking cessation interventions, psychologists, dietitians etc, as appropriate. This pandemic could also be viewed as an opportunity to develop telemedicine strategies in order to provide efficient management while minimizing the risk of viral contamination [13]. Another point to consider is the strict limitation of lung transplantation to urgent cases only during the pandemic, leading to delay lung transplantation for COPD patients with potential deleterious effects.

A highly deleterious consequence of this pandemic is the suspension of many clinical trials in various diseases including COPD. Depending on the evolution of the pandemic and subsequent economic crisis, we can anticipate a downstream effect delaying the development of innovative treatments within the next years. From a COPD research perspective, it will be particularly interesting to assess in ongoing observational COPD cohorts and post-COVID follow-up studies the impact of this pandemic on the natural history of COPD, taking into account all aspects including respiratory symptoms, exacerbation, lung function, consequences of decreased physical activity, and also mental and social impact.

As the COVID-19 pandemic puts high pressure on our health system, providing COPD patients with sufficiently careful attention is a real challenge. It is our responsibility to maintain and reinforce follow-up and close management for these patients, with the aim of limiting collateral effects that could be induced by non-optimal management of COPD during and after the pandemic.

Disclosure of interest

GD reports grants and personal fees from BTG/PneumRx, and personal fees from Boehringer Ingelheim, AstraZeneca, Chiesi, Novartis, and Nuvaira, outside the submitted work.

MZ reports grants and personal fees from Boehringer Ingelheim, personal fees from Novartis, personal fees from Chiesi and GSK, outside the submitted work.

PRB reports personal fees from Astra-Zeneca, Boehringer Ingelheim, CHiesi, GSK, Novartis, Pfizer, Teva, Vertex, Zambon, outside the submitted work.

TP reports personal fees from Boehringer Ingelheim, Chiesi, Novartis, GSK, and research grant from AstraZeneca, all outside the submitted work.

LB reports grants and personal fees from Chiesi, grants from Astra Zeneca, personal fees from GSK, outside the submitted work.

JGB reports personal fees from Resmed, Air Liquide, Lowenstein, Philips and Breas outside the submitted work.

NR reports grants and personal fees from Boehringer Ingelheim, Novartis, Pfizer and personal fees from Teva, GSK, AstraZeneca, Chiesi, Mundipharma, Cipla, Sanofi, Sandoz, 3M, Trudell, Zambon.

References

- [1] Emami A, Javanmardi F, Pirbonyeh N, Akbari A. Prevalence of Underlying Diseases in Hospitalized Patients with COVID-19: a Systematic Review and Meta-Analysis. *Arch Acad Emerg Med* 2020;8:e35.
- [2] Grasselli G, Zangrillo A, Zanella A, Antonelli M, Cabrini L, Castelli A, et al. COVID-19 Lombardy ICU Network. baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy Region, Italy. *JAMA* 2020 [Epub ahead of print].
- [3] Goyal P, Choi JJ, Pinheiro LC, Schenck EJ, Chen R, Jabri A, et al. Clinical characteristics of Covid-19 in New York City. *N Engl J Med* 2020 [Epub ahead of print].
- [4] Halpin DMG, Faner R, Sibila O, Badia JR, Agusti A. Do chronic respiratory diseases or their treatment affect the risk of SARS-CoV-2 infection? *Lancet Respir Med* 2020 [Epub ahead of print].
- [5] Lippi G, Henry BM. Chronic obstructive pulmonary disease is associated with severe coronavirus disease 2019 (COVID-19). *Respir Med* 2020 [Epub ahead of print].
- [6] Zhao Q, Meng M, Kumar R, Wu Y, Huang J, Lian N, et al. The impact of COPD and smoking history on the severity of Covid-19: A systemic review and meta-analysis. *J Med Virol* 2020 [Epub ahead of print].
- [7] Wang L, He W, Yu X, Hu D, Bao M, Liu H, et al. Coronavirus disease 2019 in elderly patients: characteristics and prognostic factors based on 4-week follow-up. *J Infect* 2020 [Epub ahead of print].
- [8] Wang B, Li R, Lu Z, Huang Y. Does comorbidity increase the risk of patients with COVID-19: evidence from meta-analysis. *Aging (Albany NY)* 2020;12:6049–57.
- [9] Leung JM, Yang CX, Tam A, Shaipanich T, Hackett TL, Singhera GK, et al. ACE-2 Expression in the Small Airway Epithelia of Smokers and COPD Patients: Implications for COVID-19. *Eur Respir J* 2020 [Epub ahead of print].
- [10] Sanders JM, Monogue ML, Jodlowski TZ, Cutrell JB. Pharmacologic treatments for coronavirus disease 2019 (COVID-19): a review. *JAMA* 2020 [Epub ahead of print].
- [11] Jouneau S, Dres M, Guerder A, Bele N, Bellocq A, Bernady A, et al. Management of acute exacerbations of chronic obstructive pulmonary disease (COPD). Guidelines from the Société de pneumologie de langue française (summary). *Rev Mal Respir* 2017;34:282–322.
- [12] <https://goldcopd.org/gold-covid-19-guidance/> [accessed on Apr 23, 2020].
- [13] Portnoy J, Waller M, Elliott T. Telemedicine in the Era of COVID-19. *J Allergy Clin Immunol Pract* 2020 [Epub ahead of print].

G. Deslée^{a,*}

M. Zysman^b

P.-R. Burgel^c

T. Perez^d

L. Boyer^e

J. Gonzalez^f

N. Roche^c, on behalf of the COPD Group of the French Language Respiratory Society (Société de Pneumologie de Langue Française, SPLF)

^a Service de Pneumologie, inserm U1250, CHU Reims, Université Reims Champagne Ardenne, Reims, France

^b Service des Maladies Respiratoires, CHU Bordeaux, Univ-Bordeaux, Centre de Recherche cardio-thoracique de Bordeaux, U1045, CIC 1401, Pessac, France

^c Service de Pneumologie, AP-HP Paris, Institut Cochin, inserm U1016, Université de Paris, Paris, France

^d Service de Pneumologie, CHU Lille, Institut Pasteur de Lille, U1019-UMR9017-CIL-Centre d'Infection et d'Immunité de Lille, Lille, France

^e Département de physiologie-explorations fonctionnelles, AP-HP Hôpital Henri-Mondor, Inserm U955, Créteil, France

^f Sorbonne Université, inserm, UMRS1158 Neurophysiologie Respiratoire Expérimentale et

*Clinique; AP-HP, Groupe Hospitalier Universitaire
AP-HP-Sorbonne Université, site Pitié-Salpêtrière,
Service de Pneumologie, Médecine Intensive et
Réanimation (Département R3S), Paris, France*

* Corresponding author at: Service de
Pneumologie, inserm U1250, Hôpital Maison
Blanche, 45, rue Cognacq-Jay, 51092 Reims, France.
E-mail address: gdeslee@chu-reims.fr (G. Deslée)

Received 23 April 2020

Received in revised form 27 April 2020

Accepted 29 April 2020

Available online 11 May 2020