



Editorial

COPD & COVID-19

EPOC y COVID-19



The COVID-19 pandemic has led to many difficulties with the diagnosis and routine management of COPD as well as raising concerns about the management and outcomes for patients with COPD who develop COVID-19. Patients themselves are anxious about developing COVID-19, worried about being denied care, about coping with the symptoms and dying.¹ In November 2020 the Global initiative for the management of chronic Obstructive Lung Disease (GOLD) committee published its 2021 Report on the management of COPD.² The Report contains some important updates to the recommendations on the diagnosis, assessment and management of COPD, but the most significant change is the inclusion of a new chapter on COPD and COVID-19 which reviews the current evidence about COPD and COVID-19 and makes provisional recommendations based on the current state of knowledge.³

Patients with COPD do not seem to be at greatly increased risk of infection with SARS-CoV-2, possibly reflecting, at least in part, the effect of protective strategies. Most studies of symptomatic people in the community tested for SARS-CoV-2 have not shown chronic respiratory disease as an independent risk factor for testing positive,^{4,5} although at least one has.⁶ Patients with COPD are at a slightly increased risk of hospitalization for COVID-19 but the evidence about the risk of developing severe disease and death are contradictory: COPD has been reported to independently increase the risk of severe disease or death in some series^{7–10} but not all.^{6,11,12} Overall the magnitude of these risks seems to be lower than might be expected.¹³

GOLD recommends that patients with COPD should follow basic infection control measures and whenever possible should wear masks. In most cases, a loose face covering, or even a face shield is tolerable and effective,^{14,15} but wearing a surgical mask does not appear to affect ventilation even in patients with severe airflow limitation.⁴

Many health systems have reduced face-to-face visits during the pandemic and introduced remote consultations using online, phone and video-links. GOLD has produced a tool to support remote review of COPD patients (www.goldcopd.org). Spirometry should be restricted to urgent or essential situations such as prior to surgery. When routine spirometry is not available, home measurement of peak expiratory flow (PEF) combined with validated patient questionnaires can be used to support or refute a possible diagnosis of COPD. However, PEF does not correlate well with the results of spirometry,^{5,6,16} has low specificity¹⁷ and cannot differentiate obstructive and restrictive lung function abnormalities.

The use of inhaled corticosteroids (ICS) in the treatment of COPD during the COVID-19 pandemic has been questioned. ICS have an overall protective effect against exacerbations in COPD patients with a history of exacerbations; however, their use is also associated with an increased risk of pneumonia. There are theoretical reasons why they may be beneficial,⁷ but a systematic review identified no clinical studies concerning the relationship between ICS use in COPD and clinical outcomes from coronavirus infections.⁸ A more recent study suggested ICS use in COPD was not protective against coronavirus infection and raised the possibility that it increased the risk of developing COVID-19,⁹ but the results are likely to be confounded by the indication for ICS.¹⁰ The GOLD Report concludes that there are no conclusive data to support alteration of maintenance COPD pharmacological treatment including ICS, either to reduce the risk of developing COVID-19, or conversely because of concerns that pharmacological treatment may increase the risk of developing COVID-19.

Many pulmonary rehabilitation programmes have been suspended during the pandemic to reduce risks of spreading SARS-CoV-2. Patients should be encouraged to keep active at home and can be supported by home-based rehabilitation which, although probably less effective than traditional programmes² is likely to be better than nothing. Technology-based solutions¹¹ may be useful to support home rehabilitation.

Coronaviruses are among the viruses that trigger COPD exacerbations¹² and COPD patients with SARS-COV2 infection presenting with respiratory symptoms requiring changes in their maintenance medications would fulfil the definition of an exacerbation.² Differentiating the symptoms of COVID-19 infection from the usual symptoms of COPD or an exacerbation can be challenging. Cough and breathlessness are found in over 60% of patients with COVID-19 but are usually also accompanied by fever (>60% of patients) as well as fatigue, confusion, diarrhoea, nausea, vomiting, muscle aches and pains, anosmia, dysgeusia and headaches. These additional symptoms may suggest a diagnosis of COVID-19¹⁸ and testing for SARS-CoV-2 should be considered.

Chest radiography is insensitive in mild or early COVID-19 infection.¹⁹ It is indicated in patients with COPD with moderate to severe symptoms of COVID-19 and for those with evidence of worsening respiratory status.²⁰ COVID-19 pneumonia changes are mostly bilateral.²¹ Chest radiography can be useful for excluding or confirming alternative diagnoses (e.g., lobar pneumonia, pneumothorax, or pleural effusion). Point-of-care lung ultrasound can

also be used to detect the pulmonary manifestations of COVID-19.²² Patients with COVID-19 are at increased risk of venous thromboembolism (VTE)^{23–26} and chest CT angiography should be performed if pulmonary embolism is suspected.

Bacterial co-infections appear infrequent in COVID-19²⁷; however, the risk of co-infections increases with the severity of COVID-19 and bacterial co-infections have been detected in up to 46% of COVID-19 patients admitted to an ICU.²⁸ Current WHO guidelines recommend broad-spectrum antibiotics in severe COVID-19 patients, and in milder COVID-19 infections when there is clinical suspicion of a bacterial infection.²⁹ Antibiotics should be used in COPD exacerbations according to the usual indications² whether or not there is evidence of SARS-CoV-2 infection.

Caution has been raised about the widespread use of systemic corticosteroids in patients with COVID-19,^{30,31} but systemic steroids should be used in COPD exacerbations according to the usual indications^{2,29} whether or not there is evidence of SARS-CoV-2 infection as there is no evidence that this approach modifies the susceptibility to SARS-CoV2 infection or worsens outcomes.

Patients who develop moderate to severe COVID-19, including hospitalization and pneumonia, should be treated with the evolving pharmacotherapeutic approaches for COVID-19, as appropriate, including dexamethasone. High flow nasal therapy (HFNT) should be considered in preference to non-invasive ventilation (NIV) for acute hypoxaemic respiratory failure despite conventional oxygen therapy as it may have a lower failure rate^{32–34} and NIV has the potential to worsen lung injury as a result of high transpulmonary pressures and tidal volumes.³⁵ Patients on HFNT or NIV should be monitored closely for worsening and early intubation and IMV with adoption of a protective lung strategy, similar to that used in other forms of ARDS, should be considered.^{36,37}

COVID-19 is associated with a hypercoagulable state²³ and VTE is common.³⁸ Patients with COPD are already at increased risk of VTE^{39,40} and those hospitalized with COVID-19 should receive pharmacologic intermediate-intensity (i.e. twice daily LMWH rather than once daily) or even a therapeutic-intensity dose strategy for thromboprophylaxis.⁴¹

Rehabilitation should be provided to all COPD patients with COVID-19, particularly to those that have been more severely affected or required ICU admission. Rehabilitation and oxygen needs should be assessed at discharge, and 6–8 weeks later if they have had severe COVID-19.⁴²

GOLD concludes that clinicians should maintain a high level of suspicion of COVID-19 in patients with COPD presenting with new or worsening respiratory symptoms, fever, and/or any other symptoms that could be COVID related and should test for SARS-CoV-2. Patients should keep taking their oral and inhaled respiratory medications for COPD as directed, as there is no evidence that COPD medications should be changed during this COVID-19 pandemic.

References

- Philip KEJ, Lonergan B, Cumella A, Farrington-Douglas J, Laffan M, Hopkinson NS. COVID-19 related concerns of people with long-term respiratory conditions: a qualitative study. *BMC Pulm Med.* 2020;20:319.
- Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. 2021 Report [Available from: <http://www.goldcopd.org/>].
- Halpin DMG, Criner GJ, Papi A, Singh D, Anzueto A, Martinez FJ, et al. Global Initiative for the Diagnosis, Management, and Prevention of Chronic Obstructive Lung Disease. The 2020 GOLD Science Committee Report on COVID-19 and chronic obstructive pulmonary disease. *Am J Respir Crit Care Med.* 2021;203:24–36.
- Samannan R, Holt G, Calderon-Candelario R, Mirsaeidi M, Campos M. Effect of face masks on gas exchange in healthy persons and patients with COPD. *Ann Am Thorac Soc.* 2020.
- Aggarwal AN, Gupta D, Jindal SK. The relationship between FEV1 and peak expiratory flow in patients with airways obstruction is poor. *Chest.* 2006;130:1454–61.
- Pothirat C, Chaiwong W, Phetsuk N, Liwsrisakun C, Bumroongkit C, Deesomchok A, et al. Peak expiratory flow rate as a surrogate for forced expiratory volume in 1 second in COPD severity classification in Thailand. *Int J Chron Obstruct Pulmon Dis.* 2015;10:1213–8.
- Higham A, Mathioudakis A, Vestbo J, Singh D. COVID-19 and COPD: a narrative review of the basic science and clinical outcomes. *Eur Respir Rev.* 2020;29:200199.
- Halpin DMG, Singh D, Hadfield RM. Inhaled corticosteroids and COVID-19: a systematic review and clinical perspective. *Eur Respir J.* 2020;55:2001009.
- Schultze A, Walker AJ, MacKenna B, Morton CE, Bhaskaran K, Brown JP, et al. Risk of COVID-19-related death among patients with chronic obstructive pulmonary disease or asthma prescribed inhaled corticosteroids: an observational cohort study using the OpenSAFELY platform. *Lancet Respir Med.* 2020;8:1106–20.
- Singh D, Halpin DMG. Inhaled corticosteroids and COVID-19-related mortality: confounding or clarifying? *Lancet Respir Med.* 2020;8:1065–6.
- Demeyer H, Louvaris Z, Frei A, Rabinovich RA, de Jong C, Gimeno-Santos E, et al. Physical activity is increased by a 12-week semiautomated telecoaching programme in patients with COPD: a multicentre randomised controlled trial. *Thorax.* 2017;72:415–23.
- Hewitt R, Farne H, Ritchie A, Luke E, Johnston SL, Mallia P. The role of viral infections in exacerbations of chronic obstructive pulmonary disease and asthma. *Thorax.* 2016;71:158–74.
- 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;8:436–8.
- Perencevich EN, Diekema DJ, Edmond MB. Moving personal protective equipment into the community: face shields and containment of COVID-19. *JAMA.* 2020;323:2252–3.
- US Centers for Disease Control. Considerations for Wearing Masks. Help Slow the Spread of COVID-19 2020 [Available from: <https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/cloth-face-cover-guidance.html>].
- Llewellyn P, Sawyer G, Lewis S, Cheng S, Weatherall M, Fitzharris P, et al. The relationship between FEV1 and PEF in the assessment of the severity of airways obstruction. *Respirology.* 2002;7:333–7.
- Jackson H, Hubbard R. Detecting chronic obstructive pulmonary disease using peak flow rate: cross sectional survey. *BMJ.* 2003;327:653–4.
- Docherty AB, Harrison EM, Green CA, Hardwick HE, Pius R, Norman L, et al. Features of 20 133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: prospective observational cohort study. *BMJ.* 2020;369:m1985.
- Wong HYF, Lam HYS, Fong AH, Leung ST, Chin TW, Lo CSY, et al. Frequency and distribution of chest radiographic findings in patients positive for COVID-19. *Radiology.* 2020;296:E72–8.
- Rubin GD, Ryerson CJ, Haramati LB, Sverzellati N, Kanne JP, Raouf S, et al. The role of chest imaging in patient management during the COVID-19 pandemic: a multinational consensus statement from the Fleischner Society. *Radiology.* 2020;296:172–80.
- Rodríguez-Morales AJ, Cardona-Ospina JA, Gutiérrez-Ocampo E, Villamizar-Pena R, Holguin-Rivera Y, Escalera-Antezana JP, et al. Clinical, laboratory and imaging features of COVID-19: a systematic review and meta-analysis. *Travel Med Infect Dis.* 2020;34:101623.
- Kulkarni S, Down B, Jha S. Point-of-care lung ultrasound in intensive care during the COVID-19 pandemic. *Clin Radiol.* 2020;75, 710.e1–e4.
- Han H, Yang L, Liu R, Liu F, Wu KL, Li J, et al. Prominent changes in blood coagulation of patients with SARS-CoV-2 infection. *Clin Chem Lab Med.* 2020;58:1116–20.
- Driggin E, Madhavan MV, Bikdeli B, Chuich T, Laracy J, Biondi-Zoccai G, et al. Cardiovascular considerations for patients, health care workers, and health systems during the COVID-19 pandemic. *J Am Coll Cardiol.* 2020;75:2352–71.
- Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med.* 2020;382:1708–20.
- Helms J, Tacquard C, Severac F, Leonard-Lorant I, Ohana M, Delabranche X, et al. High risk of thrombosis in patients with severe SARS-CoV-2 infection: a multicenter prospective cohort study. *Intensive Care Med.* 2020;46:1089–98.
- Rawson TM, Moore LSP, Zhu N, Ranganathan N, Skolimowska K, Gilchrist M, et al. Bacterial and fungal co-infection in individuals with coronavirus: a rapid review to support COVID-19 antimicrobial prescribing. *Clin Infect Dis.* 2020:ciaa530.
- Verroken A, Scohy A, Gerard L, Wittebole X, Collienne C, Laterre PF. Co-infections in COVID-19 critically ill and antibiotic management: a prospective cohort analysis. *Crit Care.* 2020;24:410.
- World Health Organization. Clinical management of COVID-19. interim guidance. 27 May 2020 [Available from: <https://www.who.int/publications/i/item/clinical-management-of-covid-19>].
- Shang L, Zhao J, Hu Y, Du R, Cao B. On the use of corticosteroids for 2019-nCoV pneumonia. *Lancet.* 2020;395:683–4.
- Dagens A, Sigfrid L, Cai E, Lipworth S, Cheng V, Harris E, et al. Scope, quality, and inclusivity of clinical guidelines produced early in the covid-19 pandemic: rapid review. *BMJ.* 2020;369:m1936.
- Frat JP, Thille AW, Mercat A, Girault C, Ragot S, Perbet S, et al. High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure. *N Engl J Med.* 2015;372:2185–96.
- Ni YN, Luo J, Yu H, Liu D, Liang BM, Liang ZA. The effect of high-flow nasal cannula in reducing the mortality and the rate of endotracheal intubation when used before mechanical ventilation compared with conventional oxygen therapy and noninvasive positive pressure ventilation. A systematic review and meta-analysis. *Am J Emerg Med.* 2018;36:226–33.

34. Alhazzani W, Moller MH, Arabi YM, Loeb M, Gong MN, Fan E, et al. Surviving sepsis campaign: guidelines on the management of critically ill adults with coronavirus disease 2019 (COVID-19). *Crit Care Med.* 2020;48:e440–69.
35. Slutsky AS, Ranieri VM. Ventilator-induced lung injury. *N Engl J Med.* 2013;369:2126–36.
36. Berlin DA, Gulick RM, Martinez FJ. Severe Covid-19. *N Engl J Med.* 2020.
37. Fan E, Beitler JR, Brochard L, Calfee CS, Ferguson ND, Slutsky AS, et al. COVID-19-associated acute respiratory distress syndrome: is a different approach to management warranted? *Lancet Respir Med.* 2020;8:816–21.
38. Dobesh PP, Trujillo TC. Coagulopathy, venous thromboembolism, and anticoagulation in patients with COVID-19. *Pharmacotherapy.* 2020.
39. Ambrosetti M, Ageno W, Spanevello A, Salerno M, Pedretti RF. Prevalence and prevention of venous thromboembolism in patients with acute exacerbations of COPD. *Thromb Res.* 2003;112:203–7.
40. Kim V, Goel N, Gangar J, Zhao H, Ciccolella DE, Silverman EK, et al. Risk factors for venous thromboembolism in chronic obstructive pulmonary disease. *Chronic Obstr Pulm Dis.* 2014;1:239–49.
41. Paranjpe I, Fuster V, Lala A, Russak AJ, Glicksberg BS, Levin MA, et al. Association of treatment dose anticoagulation with in-hospital survival among hospitalized patients with COVID-19. *J Am Coll Cardiol.* 2020;76:122–4.
42. Spruit MA, Holland AE, Singh SJ, Tonia T, Wilson KC, Troosters T. COVID-19: interim guidance on rehabilitation in the hospital and post-hospital phase from a European Respiratory Society and American Thoracic Society-coordinated International Task Force. *Eur Respir J.* 2020;2002197.

David M.G. Halpin^a, Claus F. Vogelmeier^b, Alvar A. Agusti^{c,*}

^a *University of Exeter Medical School, College of Medicine and Health, University of Exeter, Exeter, UK*

^b *Department of Medicine, Pulmonary and Critical Care Medicine, University Medical Center Giessen and Marburg, Philipps-University Marburg, Germany*

^c *Respiratory Institute, Hospital Clinic, IDIBAPS, University of Barcelona and National Spanish Network for Respiratory Research (CIBERES), Barcelona, Spain*

* Corresponding author.

E-mail address: aagusti@clinic.cat (A.A. Agusti).