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More Data on Risks and Outcomes of COVID-19 in Asthma, COPD, and Bronchiectasis



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From the start of the coronavirus disease 2019 (COVID-19) pandemic, there has been concern that patients with chronic respiratory disease (CRD) would be at a greater risk of infection with more adverse outcomes from severe acute respiratory syndrome coronavirus 2 infection. A year on now, several observational studies have just been published, which bring some clarity regarding these risks with regard to asthma and chronic obstructive pulmonary disease (COPD), and also bronchiectasis.

We start with the report from China published in the current issue of the *Journal of Allergy and Clinical Immunology: In Practice*,¹ that analyzed the outcome of the 2.8% of the 39,420 laboratory-confirmed hospitalized patients with COVID-19 who were diagnosed with CRD, using electronic medical records. More than half had COPD followed by bronchiectasis and asthma. Patients with COPD and asthma were more likely to develop more severe COVID by reaching a composite end point of need for invasive ventilation, admission to intensive care unit, or death within 30 days of admission, after taking into account confounding factors such as age, sex, and presence of other comorbidities. However, these conditions were not associated with a greater likelihood of dying from COVID-19 compared with those without CRD.

Two other large studies from the United Kingdom also using electronic medical records have just been published. In the analysis of 75,463 hospitalized COVID-19 patients,² 26.8% of patients had CRD, with 10.4% consisting of asthma and 13.6% with chronic pulmonary disease without asthma. This proportion of CRD, which is higher than the national UK prevalence for CRD, indicates that the susceptibility to catching COVID-19 was higher in this group. Although the latter group of “chronic pulmonary disease without asthma” was not specifically described, the asthma group was subanalyzed in terms of age and asthma severity, with a severe asthma category defined as those prescribed inhaled corticosteroid (ICS) plus a long-acting β -agonist (LABA) plus another maintenance asthma medication. Patients with asthma older than

16 years were more likely to receive critical care than patients without an underlying respiratory condition, and those aged 16 to 49 years with severe asthma had an increased mortality compared with those with no asthma. In patients 50 years and older, use of ICS within 2 weeks of being admitted to hospital was associated with a decreased mortality in those with asthma, compared with those without an underlying respiratory condition. Patients 50 years or older with CRD (with or without asthma) were less likely than those without a respiratory condition to receive critical care, but they had an increased mortality risk.

In another cohort study in England, general practice records of 14,479 people admitted to hospital with COVID-19 out of a population of 8.3 million people were analyzed.³ Although the prevalence of any respiratory disease in that population was 15.4%, that in those hospitalized COVID-19-positive patients was 25.5%. This risk of hospitalization was increased in those with a diagnosis of asthma (hazard ratio [HR] of 1.18) and was higher in severe asthma (HR, 1.29) and COPD (HR, 1.54). The risk of death for severe asthma (HR, 1.08) was increased but not in asthma (HR, 0.99), and was higher in COPD (HR, 1.54). This increased risk of death in severe asthma has already been reported in another UK cohort, particularly in those prescribed high-dose ICS.⁴

Two other studies in asthma have also been recently published. A study from Korea⁵ examined data taken from the National Health Insurance scheme of 7590 patients with COVID-19 of whom 2.9% had asthma. They reported no association between asthma, asthma medication, or asthma severity and clinical outcomes of COVID-19, although there was an increased death rate in the patients with asthma compared the other patients with COVID-19 (7.8% vs 2.8%). In a study from Spain,⁶ the medical records of 1006 COVID-19-infected people from a population of 71,182 patients with asthma showed a higher prevalence of comorbidities such as hypertension, dyslipidemia, diabetes, and obesity compared with those who were not infected. Those who were admitted to hospital had more comorbidities. There was an increased mortality in the asthmatic patients with COVID-19 compared with subjects without asthma with COVID-19.

Overall, these studies published this year indicate that asthma presents an increased risk of COVID-19 infection, with an increased propensity for more severe COVID-19 infection and for increased risk of death in those with severe asthma, although this risk is not as high as that reported for COPD. Two meta-analyses of published studies conducted worldwide, reported in early 2021, found no evidence of increased risk of diagnosis, hospitalization, and severity, but with protective effect on mortality from COVID-19 in patients with asthma.^{7,8} However, a major issue with this analysis is the tremendous heterogeneity of diagnosis and classification of asthma across these different countries and the lack of detail on the asthma severity and

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Conflict of interest: K. F. Chung has received honoraria for participating on Advisory Board meetings of GlaxoSmithKline, AstraZeneca, Roche, Novartis, Merck, Nacion, and Shionogi regarding treatments for asthma, chronic obstructive pulmonary disease, and chronic cough and has also been remunerated for speaking engagements.

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treatments. These could have contributed to these more reassuring observations, contrasting with the observations from the large single-country cohorts of China and the United Kingdom as described above.

With regard to COPD, a Korean report using National Health Insurance scheme found a greater proportion of patients with COPD compared with patients without COPD with COVID to receiving critical care and mechanical ventilation. COPD was also an independent risk factor for all-cause mortality.⁹ In a meta-analysis of 39 worldwide studies, those with a diagnosis of COPD were associated with an increase in poor clinical outcomes in those infected with COVID-19, with increased odds of hospitalization, intensive care admission, and mortality.¹⁰

The study of Guan et al¹ also classified patients with bronchiectasis and found them to be less likely to reach the composite end point of severe disease at day 30 compared with those without bronchiectasis, with some reduced likelihood of death. This is surprising as acknowledged by the authors. The diagnosis of bronchiectasis was made on a radiological basis without any consideration of accompanying symptoms associated with clinical bronchiectasis, and therefore the presence of clinical bronchiectasis in this cohort might be in doubt.

In contrast, in the UK study of Aveyard et al,³ the diagnosis of bronchiectasis taken from general practice records was associated with an HR of hospitalization of 1.34 and of death of 1.12 with COVID-19 infection. In an analysis of the Korean National Health Insurance scheme, of a cohort of 8070 COVID-19–infected patients, 132 (1.6%) had bronchiectasis against 1.4% in matched cohorts, with an increased 1.22 odds ratio of getting infected.¹¹ These patients were older and more frequently had pulmonary (eg, asthma or COPD) and nonpulmonary (diabetes, hypertension, and heart failure) comorbidities. They had more severe COVID-19 infection, with a greater need for supplementary oxygen, extracorporeal membrane oxygenation, and higher mortality.

For the management of these respiratory conditions that show different risk of worse disease or even risk of death with COVID-19, it is important that their condition be optimally treated. For asthma, particularly those with poorly-controlled asthma, management with ICS and LABA and other medications should be maximized. There has been conflicting evidence regarding the association of ICS treatment and outcome of COVID-19–infected asthmatic patients (good outcome in^{2,6}; poor outcome in^{3,4}), but observational studies cannot determine cause and effect. This should not be used as an argument to limit the use of corticosteroids (both inhaled and oral) in managing asthma. For those on biologic therapies targeting type 2 inflammation, this treatment may be associated with some protective effect on the clinical course of COVID-19.⁶ Optimization of management of COPD and bronchiectasis also needs to be undertaken. Cigarette smoking or secondary exposure to smoke should be discontinued or avoided.

With the increased risk of patients with CRD catching COVID-19, it would be essential for these patients to adhere to public health measures including physical distancing, regular use of face masks, hand washing, avoiding crowded places, and limiting meetings with groups of people. In fact, the shielding policy adopted in various countries for those with at-risk diseases has helped to reduce the prevalence of COVID-19 in these groups. But outside the shielding period, these public health measures need to be continued in this new era of coexistence with the severe acute respiratory syndrome coronavirus 2 virus. Finally, COVID-19 vaccination remains a priority and should be offered to this vulnerable group of CRD. It might be argued, for asthma, that those with more severe asthma, particularly those needing regular or continuous oral steroids or experiencing exacerbations, are most in need of vaccination, but this would also be beneficial for the nonsevere asthmatic patients.

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