Chronic Pulmonary Diseases and COVID-19

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Abstract
Over the past few months, coronavirus disease 2019 (COVID-19) has assumed the character of a pandemic, leading to significant global mortality mostly because of COVID-19–related pneumonia. Pneumonia is likely to progress more severely in patients with underlying chronic lung disease. The purpose of this review is to discuss the management strategies in patients with chronic lung disease such as chronic obstructive pulmonary disease, asthma, pleural diseases, and obstructive sleep apnea during the COVID-19 pandemic, with current literatures and international guidelines.

KEYWORDS: Chronic pulmonary disease, coronavirus disease 2019, management

INTRODUCTION
Coronavirus disease 2019 (COVID-19) was first seen in China in December 2019, and then it quickly spread all over the world. World Health Organization declared it as a pandemic on March 11, 2020. The most important cause of death in patients with COVID-19 is respiratory failure owing to pneumonia. Therefore, COVID-19 can be expected to be more frequent and more serious in people with chronic lung disease. In this review, the management of patients with lung diseases during pandemics is presented with international guidelines and literature.

Chronic Obstructive Pulmonary Disease and COVID-19
The presence of chronic obstructive pulmonary disease (COPD) is associated with an increased risk of mortality in patients with community-acquired pneumonia because of local/systemic inflammation, compromised host response, or increased mucus production in patients with COPD [1, 2]. In a study evaluating 1,099 laboratory-diagnosed patients with COVID-19 in China, COPD was detected in 1.1% patients [3]. In a meta-analysis evaluating the incidence of underlying diseases in patients with COVID-19 requiring hospitalization, 0.95% of patients were found to have COPD (95% confidence interval: 0.43-1.61) [4]. In another meta-analysis investigating the risk factors associated with patients with COVID-19, patients with COPD were found to have a 5.97-fold increased risk [5].

Smoking, which represents the most important risk factor for COPD, is also an established risk factor for COVID-19 infection. The aforementioned meta-analysis of patients with COVID-19 found that 7.63% of the patients were smokers [4]. Further work investigating the effect of COPD and smoking in patients with severe COVID-19 infection showed that smokers were 1.98 times more likely to have severe infection as compared with nonsmokers. In the same meta-analysis, there was a 4.38-fold increased risk of severe COVID-19 in patients with COPD [6].

Higher expression of angiotensin-converting enzyme 2 receptors has been reported in smokers and patients with COPD, facilitating the entry of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) into the cell. In this regard, it should be noted that a comparison between nonsmokers, ex-smokers, and current smokers indicated similar risk levels in the ex-smokers and in those who never smoked [7].

Treatment and follow-up recommendations for patients with COPD during the pandemic have been provided by both The Global Initiative for Chronic Obstructive Lung Disease (GOLD) and National Institute for health and care excellence (NICE) [8, 9]. Accordingly, patients’ visits should be made by telephone or email when feasible. It should also be ensured that a minimum of 30-day supply of medication is dispensed to each patient. Pulmonary function tests (PFT) should not be performed unless necessary.

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Ideally, an effective use of both oral and inhaler medications should be ensured in patients with COPD. Use of a nebulizer is not recommended during pandemic, whereas metered dose inhalers with spacer devices are preferred [10]. However, hand washing should be performed before and after using the inhaler device. Devices such as spacers and mouthpieces should be washed with soapy water and used personally [9]. Although inhaled corticosteroids are known to increase the risk of pneumonia, there is no evidence that they increase the risk of COVID-19. Therefore, it is recommended that patients with COPD continue their oral and inhaler corticosteroids during the COVID-19 pandemic [8]. Pulmonary rehabilitation can be sustained online at home. However, airway cleaning techniques should be applied in well-ventilated rooms away from the family members [9].

No changes are recommended in the home oxygen treatments and in the use of noninvasive mechanical ventilation (NIMV). NIMV should be carried out in well-ventilated rooms, again, away from the family members, if possible [9]. In hospitals, NIMV should be applied in negative pressure rooms using a bacteria filter and full-face mask. The mask must be worn first, and then the device must be turned on; when terminating the procedure, first, the device must be turned off, and then the mask should be removed. Filters should be used and replaced every 24 hours [11].

Asthma and COVID-19

Although viruses are known to trigger an asthma attack, there is no data suggesting that COVID-19 is more common in patients with asthma [12]. In one study involving 140 hospitalized patients in China, asthma was not considered to be a risk factor for COVID-19 [13].

Global Initiative for Asthma made recommendations for the management of patients with asthma during the COVID-19 pandemic. Patients with asthma have been recommended to continue their current medications, including inhaled corticosteroids. Along with the inhaled treatments, chronic oral steroid therapy should be used at the lowest effective dose. Use of spacers instead of nebulization treatment will reduce the risk of transmission in acute attacks. Routine PFT should be postponed [14].

| MAIN POINTS |
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| • Smoking and COPD are established risk factor for COVID-19 infection. |
| • Use of a nebulizer is not recommended during pandemic, whereas metered dose inhalers with spacer devices are preferred. |
| • Patients with asthma have been recommended to continue their current medications, including inhaled corticosteroids. |
| • COVID-19 infection is associated with an increased tendency of thrombosis in both arterial and venous systems owing to inflammation, endothelial dysfunction, hypoxemia, and stasis. |
| • CPAP should be used in negatively pressurized or isolated rooms. |

The Canadian Thoracic Society proposed continued treatment with anti-IgE and anti-IL-5 monoclonal antibodies during the COVID-19 pandemic [15]. In addition, possible side effects and drug interactions have been reported by the Turkish National Society of Allergy and Clinical Immunology for the drugs commonly used during the pandemic [16].

Although symptoms suggestive of an asthma attack, such as cough and shortness of breath, can also occur in patients with COVID-19 infection, other manifestations such as high fever as well as the loss of smell and taste sensation may indicate possible SARS-CoV-2 infection. Such patients with the latter group of symptoms should be advised to seek medical assistance [17].

Interstitial Lung Disease and COVID-19

A significant proportion of patients with interstitial lung disease (ILD) are at an increased risk of COVID-19 infection because of a number of factors such as advanced age and side effects of medical treatments administered. This necessitates close adherence to social isolation. Follow-up of the patients with ILD can be performed by phone or email. Routine PFT as well as bronchoscopic and tomographic follow-up examinations should be postponed. Patients with fever should be evaluated for possible COVID-19 infection.

Antifibrotic agents used for the treatment of idiopathic pulmonary fibrosis (IPF) do not seem to pose additional risks and therefore should not be stopped. It is not a problem if the patients taking antifibrotic medication diagnosed with COVID-19 not take their medication for a short time (4-8 weeks). It should also be kept in mind that antifibrotic drugs can be associated with elevated liver enzymes levels [18].

In the newly diagnosed patients with IPF, antifibrotic treatment can be started on the basis of PFTs and blood tests performed within the last 6 months. In patients with ILD, receiving immunosuppressive therapy, the lowest effective dose should be continued.

Lymphocytopenia, which can occur in patients with sarcoidosis, does not pose a special risk and does not require discontinuation of the immunosuppressive therapy [18].

Treatments for slowly progressing ILD such as chronic hypersensitivity pneumonitis can be delayed throughout the pandemic, and if required, prednisolone at a maximum dose of 20 mg can be started. In the patients with rapidly progressing ILD, for example, vasculitis, intravenous cyclophosphamide can be used in case of steroid failure or inefficacy. Prophylactic antibiotics should also be given to the patients who require intravenous treatment. Rituximab use should be postponed until the termination of the pandemic [18].

Acute respiratory distress syndrome (ARDS) can be associated with fibrosis in patients with genetic predisposition. It has been established that some patients may develop ARDS when infected with COVID-19 and therefore may need extended follow-up after the pandemic for possible fibrotic changes.

Lung Cancer and COVID-19

Cancer patients are fragile due to age, immunosuppressive therapy, and comorbidity. In one series, 18 of the 1,590 pa-
tients with confirmed COVID-19 had a history of cancer. In addition, these patients had a higher risk and worse prognosis of COVID-19 infection [19].

During the pandemic, an optimum balance between COVID-19 risk and cancer progression risk should be sought, with minimization of hospital admissions. Furthermore, the most appropriate and minimally invasive methods should be chosen for diagnosis and staging. Before proceeding, consideration should be given to whether delaying the diagnostic work-up and staging procedures will compromise the outcome. It may be best to avoid bronchoscopy and endobronchial ultrasonography in patients with a low risk of cancer. When indicated, positron emission tomography should be used to identify alternative biopsy targets. Before surgery, if possible, the pulmonary functions should be evaluated with simple spirometry or a shuttle walk test instead of full PFT [20].

A staging system has been proposed by some authors to evaluate the risk of infection in patients with lung cancer requiring surgery. The authors evaluated patients under the age of 70 years and with less than 2 comorbidities as low risk of infection. They interpreted patients with T4 (size of the main tumor), N2 (the location of lymph nodes containing cancer), or oligometastases as high risk of progression. Surgery is recommended when the risk of infection is low. Nonsurgical options should be considered in high risk of progression and high risk of COVID-19 infection. In patients with low risk of progression and high risk of infection, an individualized approach should be chosen, and if possible, definitive treatment must be delayed for 3 months [21].

Delaying radiotherapy should be considered in patients with stage 1-2 of the disease. If feasible, hypofractionated regimens should be preferred. Whether to give chemotheraphy during the period of pandemic should be decided according to the tumor biology [20].

The radiological manifestations of COVID-19 may resemble the progression of lung cancer. Pneumonitis can also be induced by immune checkpoint inhibitor therapy [22]. Therefore, clinicians should maintain a high level of attention when deciding the treatment.

**Pleural Disease and COVID-19**

**Pleural Effusion**
The main principle is that diagnostic procedures should be continued in patients with suspected cancer. In this regard, cytological examination of the pleural fluid seems to represent the most appropriate method. If it cannot be performed, needle biopsy under ultrasound or thoracoscopic guidance can be tried. Worsening dyspnea in a patient with malignant pleural effusion may necessitate drainage using pleural catheters or aspiration. Talc pleurodesis using a thoracic tube should be avoided [23]. In patients with suspected or confirmed empyema, usual treatment is indicated. It should be kept in mind that pleural effusion is a rare occurrence during the course of COVID-19 infection [24].

**Pneumothorax**
In patients with primary spontaneous pneumothorax, conservative management should be considered if the symptoms are minimal. Chest tube placement may be required for more severe cases. In patients with persistent air leak, a closed system should be used [23].

**Venous Thromboembolic Disease and COVID-19**
COVID-19 infection is associated with an increased tendency of thrombosis in both arterial and venous systems owing to inflammation, endothelial dysfunction, hypoxemia, and stasis [25]. The risk of venous thromboembolism (VTE) is increased in patients infected with COVID-19, especially in the critically ill patients requiring admission to the intensive care unit [26]. As such, abnormal coagulation parameters are associated with poor prognosis in patients with COVID-19 infection [27].

Clinicians should suspect VTE when sudden worsening of hypoxemia and tachycardia develop or the blood pressure drops in patients infected with COVID-19. When embolism is suspected, computed tomography (CT) pulmonary angiography should preferably be performed instead of standard noncontrast CT [28]. Duplex ultrasonography should be utilized when clinical suspicion of pulmonary embolism (PE) is high and CT PE is unobtainable or when there is clinical suspicion of deep venous thrombosis [29]. Anticoagulant doses recommended by the British Thoracic Society for VTE include enoxaparin 0.4 mg once a day for standard-risk patients with creatinine clearance (CrCl) >30 mL/min and 0.4 mg enoxaparin twice a day for high-risk patients with CrCl >30 mL/min. It would be safe to increase the duration of thromboprophylaxis to 4 weeks in the high-risk patients with COVID-19 pneumonia. In case of VTE suspicion, treatment dose low molecular weight heparin should be given. The recommended duration of treatment is generally 3 months [30].

**Obstructive Sleep Apnea and COVID-19**
Despite published reports on the relationship between obesity and SARS-CoV-2 infection requiring mechanical ventilation, until now, no studies have been conducted to determine whether the patients with obstructive sleep apnea (OSA) are at an increased risk of COVID-19 infection [31].

Patients with OSA using continuous positive airway pressure (CPAP) at home should continue to use it in the same way. However, if the symptoms of COVID-19 are observed, they should contact their physician and isolate themselves from the household. The effect of CPAP in terms of the facilitation of virus spread to other family members is currently unknown. Therefore, patients with COVID-19 symptoms should change their bedrooms or stop using CPAP if necessary. When using CPAP, hygiene should be practiced meticulously, device filters should be replaced as scheduled, and the surface of the device, mask, and filter should be cleaned using soapy water. Mask and device should never be shared [32].

Polysomnography (PSG) examinations should be postponed. Disposable devices should be preferred if home PSG testing is performed [33].

Patients on routine CPAP therapy should remember to bring their CPAP machines in case a hospital visit is required because of suspected COVID-19 infection. However, CPAP should be used under the supervision of the medical staff.
The treating physician should evaluate the need for CPAP during the pandemic. For example, a patient with mild OSA symptoms may not need CPAP. In addition, when available, CPAP should be used in negatively pressurized or isolated rooms, with the addition of bacterial/viral filters. Moreover, a heat moisture exchanger could be used instead of humidifier attachment [34].

CONCLUSION

The patients with chronic lung diseases are those who may be more affected in the pandemic. Therefore, treatments used by these patients should be continued. They should be monitored as much as possible by email or telephone.

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