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Statement

Statement from the Japanese Respiratory Society: Working diagnosis and initial management of COPD during the COVID-19 pandemic

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ABSTRACT

The Japanese Respiratory Society (JRS) has recommended spirometry for the diagnosis of respiratory diseases. It is indispensable for the confirmation of airflow obstruction by spirometry in chronic obstructive pulmonary disease (COPD) diagnosis. However, the coronavirus disease 2019 (COVID-19) pandemic has made it difficult for many clinics to perform spirometry as it may lead to possible aerosol infections. Thus, the diagnosis of COPD, especially in the early stage, has become difficult. To overcome this situation, JRS issued a “Flowchart of Working Diagnosis and Management of COPD during the COVID-19 Pandemic”. This flowchart may help physicians provisionally diagnose COPD patients without performing spirometry, offering them appropriate intervention even in epidemic and pandemic situations.

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1. Introduction

The coronavirus disease 2019 (COVID-19) has had a tremendous impact on clinics all over the world. Recently, aerosol infection is considered as one of the modes of transmission of the disease, in addition to droplet and contact infection [1]. Approximately, 39%, 20%, 13% of children, adults, and elderly infected with severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2) are asymptomatic, respectively. However, the

Abbreviations: ACE2, angiotensin converting enzyme 2; ACO, asthma COPD overlap; CAT, COPD assessment test; COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; ICS, inhaled corticosteroid; JRS, Japanese Respiratory Society; LABA, long-acting β-agonist; LAMA, long-acting muscarinic antagonist; SARS-Cov-2, severe acute respiratory syndrome coronavirus 2.

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transmission from asymptomatic individuals was estimated to account for more than half of all transmissions. Therefore, medical staff needs to pay attention to asymptomatic pathogen carriers [2,3]. When COVID-19 asymptomatic patients visit the hospital, medical examinations that may cause the patients to cough, such as spirometry, can result in in-hospital outbreaks through aerosol transmission. Although the Japanese Respiratory Society (JRS) typically promotes spirometry for the precise diagnosis of pulmonary diseases, including COPD, under the current pandemic phase of COVID-19, new diagnostic and management strategies without spirometry are required.

1.1. COVID-19 and COPD

The SARS-Cov-2 virus invades the cells using angiotensin-converting enzyme 2 (ACE2) on the cell surface. ACE2 is upregulated in the lower respiratory tract of smokers, especially in COPD patients [4]. Additionally, COPD has been reported to be an aggravating factor for COVID-19 [5]. Therefore, despite the difficulty in performing spirometry, it is important to diagnose COPD at an early stage and encourage COPD patients to quit smoking. This should be done in order to reduce the number of patients who become severely ill with COVID-19. In addition, it is expected that the initiation of medical intervention for treatment-naive COPD patients may prevent aggravation of already-present COVID-19 in COPD patients.

2. Working diagnosis

Against this background, the JRS created a Japanese flowchart, entitled “Flowchart of Working Diagnosis and Management of COPD during Pandemic of COVID-19” and issued it on its website in January 2021. In this article, we present the English-language version (Fig. 1). This flowchart is used for individuals suspected of having COPD in clinics and at annual health check-ups. After a provisional COPD diagnosis is made without performing spirometry, initial treatment is initiated according to symptom severity. Subsequently, the effect of initial treatment is evaluated 1–4 weeks later. Spirometry is recommended to be performed after the pandemic is over, in order to confirm whether the patient has an airflow obstruction.

First, in this flowchart, “individuals aged ≥50 years with a history of smoking” are targeted [6]. Further, each individual is screened using a COPD-Q or COPD-PS™ [7,8]. For individuals with a score above the cut-off, chest X-ray and blood sampling in particular blood eosinophil counts should be performed in order to identify inhaled corticosteroids (ICS) responders or those who might have asthma. In patients with bronchial asthma, concomitant use of ICS is essential to prevent death. However, ICS pose an increased risk of infection and can be a disadvantage for COPD patients who do not require them. Therefore, it is necessary to carefully judge the complication of asthma. In this flowchart, asthmatic characteristics such as daily fluctuations of symptoms, history of asthma, and worsening of symptoms outside of exercise are checked. When individuals have no check items related to asthma and no findings suggesting a disease other than COPD, they are provisionally diagnosed as having COPD. If the individual has any check items related to asthma and no evidence of other diseases, asthma or asthma COPD overlap (ACO) is probable. Here, the characteristics of COPD are reassessed in order to identify the individuals with COPD among those who are suspected as having asthma, that is, ACO. If the individual has prolonged exhalation, hyperinflation of the lung field on chest X-ray, or a low attenuation area on chest computed tomography imaging, they are provisionally diagnosed as having ACO. If the individuals do not have COPD characteristics, other diseases, including asthma, are suspected.

3. Symptom assessment and management procedures

In the flowchart, the symptom severity in the individuals who have been provisionally diagnosed as having COPD with/without asthma is evaluated by using a COPD assessment test (CAT) [9]. Thereafter, the treatment is chosen according to the CAT score and presence/absence of asthma (Fig. 1). It is also essential to instruct all individuals to quit smoking.

1) CAT ≥ 10 points, or dyspnea when walking at own pace on level ground: We recommend dual bronchodilation therapy using long-acting muscarinic receptor antagonist (LAMA) and β2-agonist (LABA). This is because the individual is thought to have moderate-to-severe respiratory symptoms. The 2020 American Thoracic Society guidelines strongly recommend the use of LAMA/LABA combination drugs for COPD patients who complain of respiratory symptoms [10]. In particular, we recommend LAMA/LABA/ICS for patients who have been provisionally diagnosed as having ACO. In cases where peripheral blood eosinophils are 300 cells/μL or 5% or more, the effect of preventing exacerbation of ICS can be expected in COPD patients with repeat exacerbations [10].

2) CAT 5–9 points, or dyspnea when walking up a slight hill or stairs: We recommend bronchodilation therapy using LAMA or LABA alone. This is because the individual is thought to have mild respiratory symptoms. If there are no limitations for the use of LAMA (prostatic hyperplasia with dysuria, angle-closure glaucoma), LAMA will be more effective than LABA in preventing exacerbation. We recommend that ICS/LABA be started in patients who are provisionally diagnosed with ACO.

3) CAT 0–4 points, or no dyspnea when walking up a slight hill or stairs: Symptoms are considered to be minor, and doctor follow-up is recommended. The patient must be counseled to quit smoking.

Considering the peculiarity of prioritizing diagnostic treatment without making a definitive diagnosis by using spirometry, early evaluation of the therapeutic effects of initial treatment is essential. The minimal clinically important difference of CAT is 2 points. Therefore, if the CAT score drops by 2 points or more after 1–4 weeks of initial therapy, we recommend the continuation of treatment. If no improvement is observed, we recommend the reconfirmation of the scrutiny of other respiratory and heart diseases.

In any event, after the pandemic spirometry is essential to confirm the presence of airflow obstruction.
This flowchart was made in order to make early diagnoses and manage COPD patients without using spirometry. However, further studies are required for the verification of the effectiveness of the flowchart. If the effectiveness of this chart is confirmed, we believe that it may also be useful in the future for the diagnosis and management of COPD in small clinics that do not have spirometers. We expect that this flowchart will be widely used to help in the medical care of COPD.

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Shigeo Muro: review, editing.
Akihito Yokoyama: review, supervision.
Shu Hashimoto: conceptualization, supervision, review.

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Conflict of Interest
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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.resinv.2021.03.004.

REFERENCES

[1] Jarvis MC. Aerosol transmission of SARS-cov-2: physical principals and implications. Front Publ Health 2020;8:590041.
[2] Bellino S, Punzo O, Rota MC, Manso MD, Urdiales AM, Andrianou X, et al. COVID-19 disease severity risk factors for pediatric patients in Italy. Pediatrics 2020;146:e2020009399.
[3] Johansson MA, Quandelacy TM, Kada S, Prasad PV, Steele M, Brooks JT, et al. SARS-Cov-2 transmission from people without COVID-19 symptoms. JAMA Network Open 2021;4:e2035057.
[4] Leung JM, Niikura M, Yang CW, Sin DD. COVID-19 and COPD. Eur Respir J 2020;56:2002108.
[5] Grasselli G, Greco M, Zanella A, Albano G, Antonelli M, Bellani G, et al. Risk factors associated with mortality among patients with COVID-19 in intensive care units in Lombardy, Italy. JAMA Intern Med 2020;180:1345–55.
[6] Osaka D, Shibata Y, Abe S, Inoue S, Tokairin Y, Igarashi A, et al. Relationship between habit of cigarette smoking and airflow limitation in healthy Japanese individuals: the Takahata study. Intern Med 2010;49:1489–99.
[7] Samukawa T, Matsumoto K, Tsukuya G, Koriyama C, Fukuyama S, Uchida A, et al. Development of a self-scored persistent airflow obstruction screening questionnaire in a general Japanese population: the Hisayama study. Int J Chronic Obstr Pulm Dis 2017;12:1469–81.
[8] Tsukuya G, Matsumoto K, Fukuyama S, Crawford B, Nakanishi Y, Ichinose M, et al. Validation of a COPD screening questionnaire and establishment of diagnostic cut-points in a Japanese general population: the Hisayama study. Allergol Int 2015;64:49–53.
[9] Jones PW, Harding G, Berry P, Wiklund I, Chen WH, Kline Leidy N. Development of first validation of the COPD assessment test. Eur Respir J 2009;34:648–54.
[10] Nici L, Mammem MJ, Charbek E, Alexander PE, Au DH, Boyd CM, et al. Pharmacologic management of chronic obstructive pulmonary disease. An Official American Thoracic Society Clinical Practice Guideline. Am J Respir Crit Care Med 2020;201:e56–69.