

Impact of bronchiectasis on susceptibility to and severity of COVID-19: a nationwide cohort study

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To the Editor

The infection caused by novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which is called coronavirus disease 2019 (COVID-19), has spread rapidly worldwide since December 2019.¹ Although there is conflicting evidence on whether patients with chronic respiratory diseases are more susceptible to COVID-19, these patients exhibit a more severe presentation and higher mortality compared with those without chronic respiratory diseases.^{2–4} A meta-analysis revealed that approximately 2% of patients with COVID-19 have concomitant pulmonary disease, which is associated with worse outcomes.⁵ In agreement with this analysis, several follow-up studies revealed that patients with asthma, chronic obstructive pulmonary disease (COPD), and other chronic respiratory diseases harboured severe clinical manifestations with higher mortality compared with those without chronic respiratory diseases.^{6,7} However, previous research has not addressed these issues in patients with bronchiectasis. In this study, we performed a nested case-control study using nationally representative data from the COVID-19 cohort and matched cohort in South Korea to evaluate whether the prevalence of bronchiectasis is higher in the COVID-19 cohort than in the matched cohort. We also compared clinical course and mortality of COVID-19 in patients with bronchiectasis and those without bronchiectasis.

The Korean National Health Insurance Service (NHIS) provided researchers with an anonymised national cohort for the evaluation of COVID-19, which comprised the COVID-19 cohort (8070 patients with a confirmed diagnosis of COVID-19 after January 2020) and the matched cohort (121,050 age-, sex-, and residence-matched

patients not infected with COVID-19). The data in this cohort were combined with claims-based data from the NHIS between January 2015 and May 2020. Hence, the datasets analysed in this study included personal data as well as inpatient and outpatient records from the past 5 years.⁸ The institutional review board of our institution approved this study (application No. HYUH 2020-06-029). Since the NHIS database was constructed after anonymisation, the need for informed consent from the participants was waived.

Laboratory confirmation of SARS-CoV-2 infection was defined as a positive result on real-time reverse-transcriptase polymerase chain reaction assay of nasal or pharyngeal swabs, in accordance with the guidelines for laboratory diagnosis of COVID-19 in Korea.⁹ Bronchiectasis was defined as ≥ 2 claims under the International Classification of Diseases 10th revision (ICD-10) diagnosis code J47 during the study period (from January 2015 to May 2020). Additionally, other comorbidities were also defined as ≥ 2 claims under ICD-10 codes as major diagnosis codes during the study period. The ICD-10 codes for definition can be found in our previously published study, except for lung cancer (ICD-10 diagnosis code C34).¹⁰ Severe COVID-19 was defined as (1) patients who required supplemental oxygen therapy, mechanical ventilator (MV) treatment, extracorporeal membrane oxygenation (ECMO), or intensive care unit (ICU) admission, or (2) patients who died after a confirmed COVID-19 diagnosis.

The rate of bronchiectasis was 1.6% in the COVID-19 cohort ($n=132/8070$) and 1.4% in the matched cohort ($n=1630/121,050$) ($p=0.030$) with a 1.22-fold increased odds ratio (95% confidence interval = 1.01–1.45) of the prevalence of bronchiectasis

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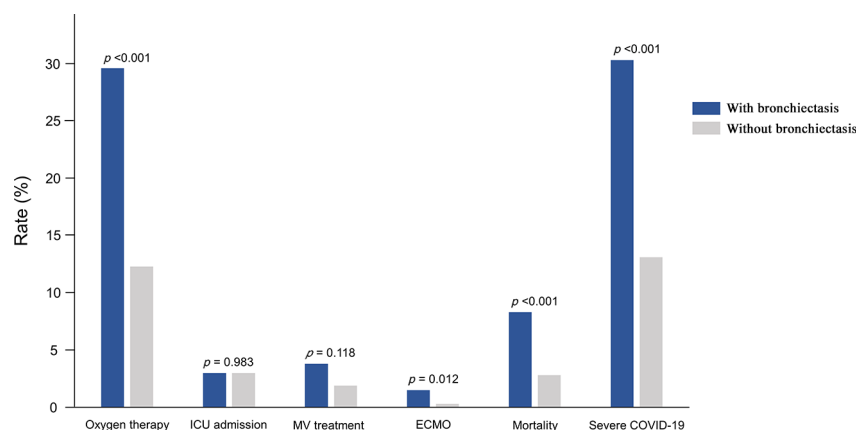


Figure 1. Comparison of the most severe clinical course between the COVID-19 patients with bronchiectasis and those without bronchiectasis. Patients receiving oxygen therapy did not include cases receiving MV treatment or ECMO and mortality cases; those receiving MV treatment did not include cases receiving ECMO and mortality cases; those receiving ECMO did not include mortality cases. COVID-19, coronavirus disease 2019; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; MV, mechanical ventilation.

in the COVID-19 cohort relative to the matched cohort. Of the 8070 patients with COVID-19, 132 (1.6%) had bronchiectasis and 7938 (98.4%) did not have bronchiectasis. COVID-19 patients with bronchiectasis were significantly older ($p < 0.001$) and more frequently exhibited pulmonary comorbidities, including asthma (62.1% *versus* 30.4%) and COPD (57.6% *versus* 17.8%), than those without bronchiectasis. Additionally, COVID-19 patients with bronchiectasis also had more frequent extra-pulmonary comorbidities, including hypertension (52.3% *versus* 27.0%), diabetes mellitus (61.4% *versus* 31.0%), and heart failure (27.3% *versus* 10.1%), than those without bronchiectasis ($p < 0.001$ for all).

Figure 1 compares the most severe clinical course between the COVID-19 patients with bronchiectasis and those without bronchiectasis. The proportion of patients with severe COVID-19 was significantly higher in patients with bronchiectasis than in those without bronchiectasis [30.3% (40/132) *versus* 13.1% (1039/7938), $p < 0.001$]. COVID-19 patients with bronchiectasis required significantly more oxygen (cases receiving MV or ECMO and mortality cases were not included) (29.6% *versus* 12.3%, $p < 0.001$) and ECMO (mortality cases were not included) (1.5% *versus* 0.3%, $p = 0.012$), and had significantly higher mortality (8.3% *versus* 2.8%, $p < 0.001$) than those without bronchiectasis. The rates of ICU admission (3.0% *versus* 3.0%, $p = 0.983$) and MV treatment (cases receiving ECMO and mortality

cases were not included) (3.8% *versus* 1.9%, $p = 0.118$) were not significantly different between the two groups.

The first notable finding of this study is that the rate of COVID-19 was relatively higher in patients with bronchiectasis than those without bronchiectasis. Considering that age-, sex-, and residence-matching was done before comparison, this study provides evidence suggesting that bronchiectasis patients may be more vulnerable to COVID-19. Accordingly, our study findings indicate that bronchiectasis patients should be more cautious about social activities or travel in areas where COVID-19 is prevalent.¹¹

Another notable finding is that COVID-19 patients with bronchiectasis suffered from more severe infection than those without bronchiectasis. In this study, COVID-19 patients with bronchiectasis exhibited a much higher rate of supplemental oxygen, ECMO, and higher mortality than those without bronchiectasis. Considering similar ICU admission rates, COVID-19 patients with bronchiectasis revealed worse clinical course finally than those without bronchiectasis although both groups had similar severity when admitted to ICU initially. Impaired mucociliary clearance and chronic inflammation in the airway of patients with bronchiectasis is likely to increase their susceptibility to and severity of COVID-19. Additionally, COVID-19 could exacerbate bronchiectasis. Interestingly, COVID-19 patients with

bronchiectasis showed a significantly higher prevalence of COPD (57.6% *versus* 19.3%) and asthma (62.1% *versus* 17.2%) than the overall population with bronchiectasis in South Korea.¹⁰ Although asthmatics were suggested to be protected from COVID-19,¹² this study showed significantly higher asthma rate in COVID-19 patients with bronchiectasis than those without bronchiectasis. Bronchiectasis may serve as a leverage to more severe COVID-19 in asthmatics; however, future research is necessary to clarify the mechanistic link. Previous research revealed that patients with COPD or asthma showed more severe clinical course and worse outcome if they have comorbid bronchiectasis.¹³ In line with the study, comorbid airway disease may play a major role in poorer clinical outcomes in bronchiectasis patients with COVID-19.

The major strength of this study is that it is the first real-world report on the impact of bronchiectasis on the susceptibility to and severity of COVID-19. Nonetheless, there are also several limitations to this study. First, since the NHIS database for COVID-19 did not provide data on smoking history, pulmonary function tests, laboratory findings, medications, and the duration of hospital stay, we could not include this information in our study results. Second, for the same reason above-mentioned, this study could not provide information about bronchiectasis in detail: aetiology of bronchiectasis, exacerbation history, and *Pseudomonas* colonisation in sputum. Accordingly, reports from international bronchiectasis registries are warranted shortly. Third, as the number of COVID-19 patients with bronchiectasis was small (1.3% of all study population), we could not establish a well-fitted regression analysis model accounting whether increased prevalence and more severe clinical course of COVID-19 did not result from comorbidities in bronchiectasis patients. Fourth, COVID-19 patients with bronchiectasis were older and had more comorbidities than those without bronchiectasis. Although it was a natural phenomenon that patients with bronchiectasis were older and had more comorbidities, this may have affected the more severe clinical presentations and poor clinical outcomes.

In conclusion, patients with bronchiectasis may be more prone to COVID-19 infection than those without bronchiectasis. Additionally, COVID-19 patients with bronchiectasis showed more severe

clinical manifestations and poorer outcomes than those without bronchiectasis.

Author contributions

HC, HL, and SHK were responsible for the conception and design of the study. HC, HL, SKL, BY, SJC, YY, and SHK undertook the analysis and interpretation of the data. HC, HL, SKL, TSP, DWP, JYM, THK, JWS, and SHK drafted the manuscript. HC, HL, HJY, and SHK made a critical revision of the manuscript. All authors read and approved the final manuscript.

Availability of data and material

All data extracted in this study are included in this article.

Conflict of interest statement

The authors declare that there is no conflict of interest.

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Ethical approval and consent to participate

The institutional review board of our institution approved this study (application No. HYUH 2020-06-029). Since the NHIS database was constructed after anonymisation, the need for informed consent from the participants was waived.

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Supplemental material

The reviews of this paper are available via the supplemental material section.

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