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COVID-19 and risk of long-term mortality in COPD: a nationwide population-based cohort study

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ABSTRACT

Background Chronic obstructive pulmonary disease (COPD) is a risk factor for severe COVID-19. However, mortality after COVID-19 recovery in this population remains unclear.

Methods We retrospectively enrolled individuals with COPD from the Korean National Health Insurance database. We compared the mortality rate in individuals with COPD who recovered from COVID-19 between 8 October 2020 and 31 December 2021 (COVID-19 cohort, n=2499) with that in 1:1 propensity score-matched controls (n=2499). The study population was followed until either death or 30 September 2022, whichever came first.

Results The COVID-19 cohort had a 4.8% mortality rate vs 2.7% in matched controls during a median follow-up of 319 days (IQR, 293–422 days), including 14 days of recovery time. The COVID-19 cohort had a higher risk of death than matched controls (adjusted HR (aHR)=1.81, 95% CI=1.35 to 2.45). The risk of mortality was notably higher in individuals with severe COVID-19 (aHR=5.05, 95% CI=3.65 to 6.97), especially during the first 180 days of recovery (highest during the first 30 days (aHR=20.25, 95% CI=7.79 to 52.64)). Non-severe COVID-19 does not increase the risk of mortality compared with controls (aHR=0.85, 95% CI=0.57 to 1.28).

Conclusion Individuals with COPD recovering from COVID-19 showed an increased risk of long-term mortality, particularly within the first 180 days post-recovery, especially those who experienced severe COVID-19.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Previous studies indicate that individuals with chronic obstructive pulmonary disease (COPD) are more susceptible to severe COVID-19 and exhibit higher mortality risk compared with those without COPD. Still, long-term outcomes after recovery from COVID-19 have been less clearly defined in this population.

WHAT THIS STUDY ADDS

⇒ Individuals with COPD who recover from COVID-19 exhibit a significantly higher long-term mortality risk compared with matched controls who did not experience COVID-19. Notably, the risk is markedly elevated in severe COVID-19 cases, especially within the first 180 days post-recovery, with the highest risk observed in the initial 30 days.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The findings of this study underscore the necessity for active surveillance and tailored post-recovery care for individuals with COPD who have experienced COVID-19, particularly in severe COVID-19 cases.

INTRODUCTION

The emergence of coronavirus disease 2019 (COVID-19) in late 2019 sparked a global pandemic, resulting in a significant loss of human lives.[1] A tremendous global effort, including COVID-19 vaccination, has mitigated its severity, and we are now entering an endemic phase.[2 3] However, most countries are still at risk of a local or global outbreak of COVID-19, in which individuals with underlying health conditions could encounter short-term as well as long-term poor prognoses.[4]

Of individuals living with respiratory comorbidities, those with chronic obstructive pulmonary disease (COPD) are considered to be at a higher risk of experiencing COVID-19.[5–7] In addition to increased susceptibility to COVID-19, the short-term prognosis of individuals with COPD, such as mortality, was worse compared with those without COPD.[6 8–10] Considering that increased respiratory symptom burden from COVID-19 could last even after recovery from COVID-19,[11] post-COVID-19 status could lead to poor long-term outcomes in individuals with COPD.[12] However, since most previous studies focused on outcomes during the acute infectious phase of COVID-19,[6 8–10] limited information is available regarding the long-term effect of COVID-19 on COPD.[13] In addition, given that the severity of COVID-19 is associated with long-term outcomes in the general population,[14] understanding the impact of COVID-19 severity on the long-term mortality

in COPD would be very informative. However, available data on this issue are limited.

Therefore, we aimed to investigate the association between COVID-19 and long-term mortality risk in individuals with COPD who recovered from COVID-19, focusing on COVID-19 severity.

METHODS

Study population

We performed a retrospective cohort study using the dataset derived from claims data from the Korean National Health Insurance Service (NHIS). The NHIS is a government-managed universal insurance provider for nearly 97% of the Korean population, accounting for approximately 50 million individuals.[15] The NHIS database has been widely adopted in epidemiological research associated with COVID-19 and post-COVID-19 complications.[16–18]

The inclusion criteria were individuals with COPD who experienced COVID-19 between 8 October 2020 and 31 December 2021, or their 1:1 propensity score (PS)-matched controls. The exclusion criteria were as follows: (1) individuals with no available health screening examination data between 1 January 2019 and 31 December 2020, (2) individuals diagnosed with COPD after the index date (recovery date from COVID-19) and (3) death before the index date. The index date was the recovery date in the COVID-19 cohort and the matched date for controls. The recovery date from COVID-19 was defined as follows: (1) 14 days after COVID-19 diagnosis for individuals who were not admitted, (2) 14 days after COVID-19 diagnosis for individuals who were admitted but discharged within 14 days and (3) discharge date for individuals who were hospitalised for more than 14 days after COVID-19 diagnosis. Discharge to long-term care facilities was also regarded as recovery.

COPD was defined as at least two prescriptions for COPD medications and the 10th International Classification of Disease (ICD-10) diagnosis code of J43.1, J43.2, J43.8, J43.9 or J44. COPD medications were defined as follows: (1) long-acting muscarinic antagonists (LAMA), (2) long-acting beta-2 agonists (LABA), (3) inhaled corticosteroids combined with LABA (ICS+LABA), (4) LABA combined with LAMA (LABA+LAMA), (5) ICS combined with LABA and LAMA (ICS+LABA+LAMA), (6) short-acting muscarinic antagonists, (7) short-acting beta-2 agonists, (8) phosphodiesterase-4 inhibitors, (9) systemic bronchodilators or (10) theophylline.[19–22]

As shown in figure 1, we enrolled 75 485 individuals with COPD from 1 January 2015 to 7 October 2020. Of 75 485 individuals, we excluded 34 460 with missing values on health screening examination data between 2019 and 2020 and included 41 025 individuals with COPD. Among them, 2627 were diagnosed with COVID-19 (COVID-19 cohort), and 38 398 were not diagnosed with COVID-19 (control cohort). Among the COVID-19 cohort, we excluded 128 individuals who died before the index date, resulting in 2499 individuals.

We conducted 1:1 PS matching between the COVID-19 cohort and matched controls. As a result, 2499 COVID-19 cases (COVID-19 cohort) were matched to control cases (matched controls). We used the standard mean difference (SMD) to assess the balance between the two groups, with an SMD >0.1 indicating an imbalance.

Patients and public involvement

Patients and the public were not involved in the design, conduct, reporting or dissemination of this study.

Exposure: COVID-19

Diagnosis of COVID-19 was established based on a positive result obtained from real-time reverse transcription-PCR testing of nasal or pharyngeal swabs in individuals with a history of COVID-19 defined by the ICD-10 code (U07.1).[17 18 23 24] During the pandemic, the Korean government encouraged citizens to undergo COVID-19 tests and provided health insurance to all Koreans with COVID-19 (NHIS-2022-1-623).[17 18 23 24] The NHIS SARS-CoV-2 database includes medical data for all individuals tested for SARS-CoV-2.

To assess the impact of COVID-19 severity on long-term mortality risk, we categorised COVID-19 into non-severe and severe cases. Severe COVID-19 cases were defined as those requiring oxygen therapy, intensive care unit (ICU) admission, mechanical ventilation or extracorporeal membrane oxygenation during hospitalisation due to COVID-19.[16 17 23 24]

Outcome: long-term mortality

The primary outcome was long-term mortality after recovery from COVID-19. The study population was followed from the index date until either death or the last follow-up date (30 September 2022), whichever came first. Mortality data were individually linked from Statistics Korea using unique personal identification numbers, as reporting all deaths to Statistics Korea is mandated by law.[21 25 26]

Covariates

We collected basic demographics (age, sex, residential location and income status), anthropometric (body mass index, BMI) and lifestyle information (smoking status and alcohol consumption). BMI was classified into five groups as recommended for the Asian population: normal (18.5–22.9 kg/m^2), low (<18.5 kg/m^2), overweight (23.0–24.9 kg/m^2), obese (25–29.9 kg/m^2) and highly obese (≥30 kg/m^2).

Income status was categorised into three groups: highest 30% (high income), lowest 30% (low income) and remaining subjects (middle income). Those receiving support from the medical aid programme were considered part of the low-income group. The residential

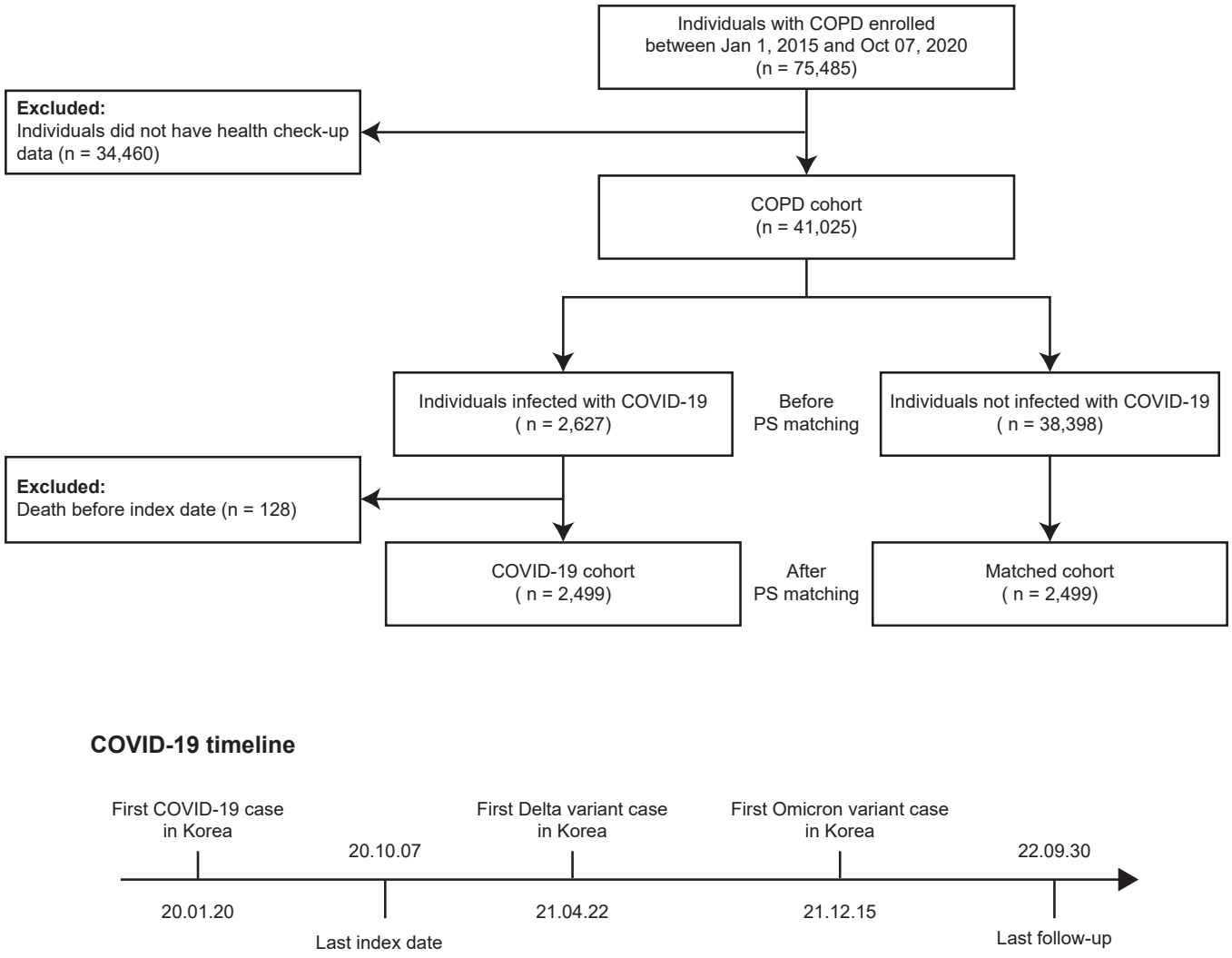


Figure 1 Flow chart of the study population. COPD, chronic obstructive pulmonary disease; PS, propensity score.

area was divided into metropolitan cities, middle-sized and small-sized cities and rural areas.

Regarding personal health-related habits, smoking status and alcohol consumption were determined through self-reported questionnaires and categorised as follows: never smoker or ever smoker for smoking status; none, 1–2 times a week, 3–4 times a week or nearly daily for alcohol consumption. The following criteria define regular physical activity: (1) more than 30 min of moderate physical activity on at least 5 days per week or (2) more than 20 min of vigorous physical activity on at least 3 days per week.[27–29]

Previous history of severe exacerbation of COPD was defined as an emergency room visit or hospitalisation and the use of systemic steroids for COPD (ICD-10 codes J43.1, J43.2, J43.8, J43.9 or J44) within 1 year before enrolment.[19 21 22 29 30] Asthma was defined using ICD-10 codes J45–J46 and the use of asthma-related medication (oral corticosteroids, bronchodilators with and without inhaled corticosteroids, leukotriene receptor antagonists and xanthine derivatives).[17 21 23] Other comorbidities were defined using ICD-10 codes: hypertension (I10–13 and I15), diabetes mellitus (E10–14), dyslipidaemia (E78) and chronic kidney disease (CKD) (N18).[31–40]

Statistical analysis

PS matching was conducted using a greedy nearest-neighbour algorithm with a 1:1 ratio. The control group was recruited using 1:1 PS matching based on age, sex, BMI, regular physical activity, smoking status, alcohol consumption, economic status, residential area, the number of severe exacerbations in the previous year and comorbidities (hypertension, diabetes, dyslipidaemia, CKD and asthma). When the outcome was stratified by COVID-19 severity, baseline characteristics differed (online supplemental table S1); however, further matching was not feasible due to the limited number of severe COVID-19 cases.

Data were expressed as numbers with percentages for categorical variables and mean±SD or median (IQR) for continuous variables, as appropriate. We used the χ^2 test for categorical variables and t-tests for continuous variables for group comparisons. The mortality rate was

calculated by dividing the deaths by the total follow-up duration (10 000 person-years). We compared the mortality between the COVID-19 cohort and matched controls using cumulative incidence curves and assessed statistical differences using a log-rank test. Cox proportional hazards regression analysis was used to assess the risk of mortality. To minimise the possible effects of covariates on mortality even after PS matching, including the difference between non-severe COVID-19 and severe COVID-19 cases, we conducted additional adjustments for all the variables used in the matching process. To evaluate the impact of the time interval after recovery from COVID-19, we categorised follow-up duration into <30 days, 30–90 days, 90–180 days and ≥180 days. A two-sided p<0.05 indicates statistical significance. Statistical analyses were conducted using SAS V.9.4 (SAS Institute) and R V.4.0.3 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Baseline characteristics

Table 1 presents the baseline characteristics of the study participants in the final analytical cohort. There were no significant differences in baseline characteristics between the COVID-19 cohorts and matched controls, with all SMD <0.1.

Incidence rate and risk of mortality

During a median follow-up of 319 days (IQR 293–422 days), including a median 14 days of recovery time after COVID-19, 120 (4.8%) of 2499 individuals in the COVID-19 cohort and 67 (2.7%) individuals in the matched controls died during follow-up (p<0.01). This difference was also evident in the cumulative incidence rate plot for death (figure 2A, log-rank p<0.01). As shown in table 2, the risk of death was significantly higher in individuals in the COVID-19 cohort than in the matched controls (adjusted HR (aHR)=1.81, 95% CI=1.35 to 2.45).

When the COVID-19 cohort was subdivided into severe and non-severe subgroups, the risk of mortality in the COVID-19 cohort was notably higher in the severe group compared with controls (aHR=5.05, 95% CI=3.65 to 6.97), while no increased risk of mortality was observed in individuals with non-severe COVID-19 (aHR=0.85, 95% CI=0.57 to 1.28). Cumulative incidence plots showed similar results (figure 2B, log-rank p<0.01).

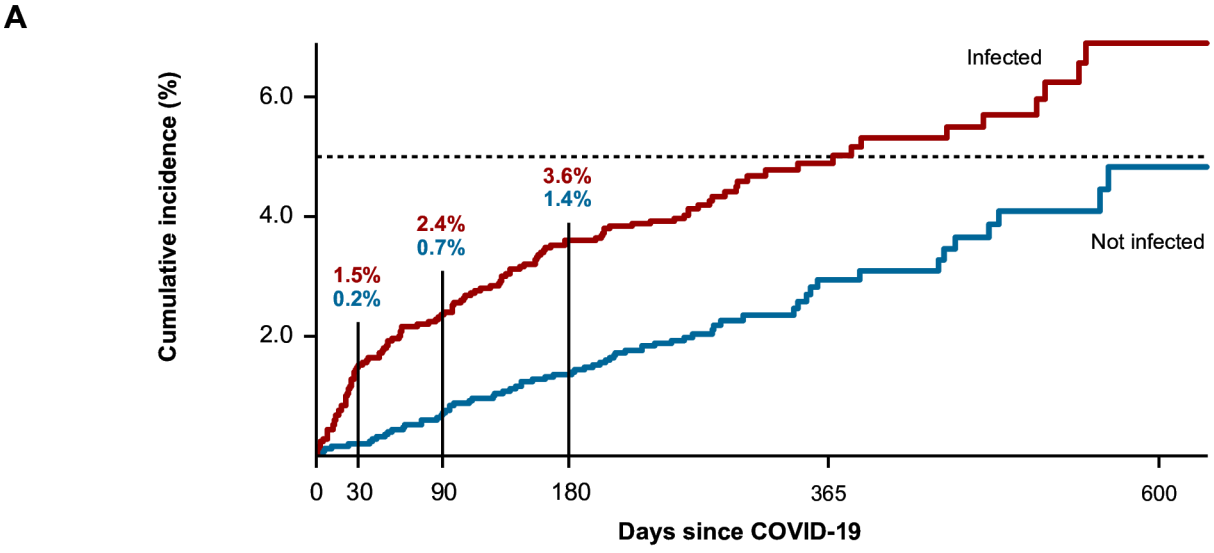
Risk of mortality according to time interval from the index date

As shown in table 3, when analysed by time interval from index date (recovery date from COVID-19), the risk of mortality in the COVID-19 cohort versus matched controls was significantly higher within 30 days (aHR=7.49, 95% CI=2.95 to 19.06) and 90–180 days (aHR=2.07, 95% CI=1.13 to 3.80) from the index date.

Table 1 Baseline characteristics of the study population

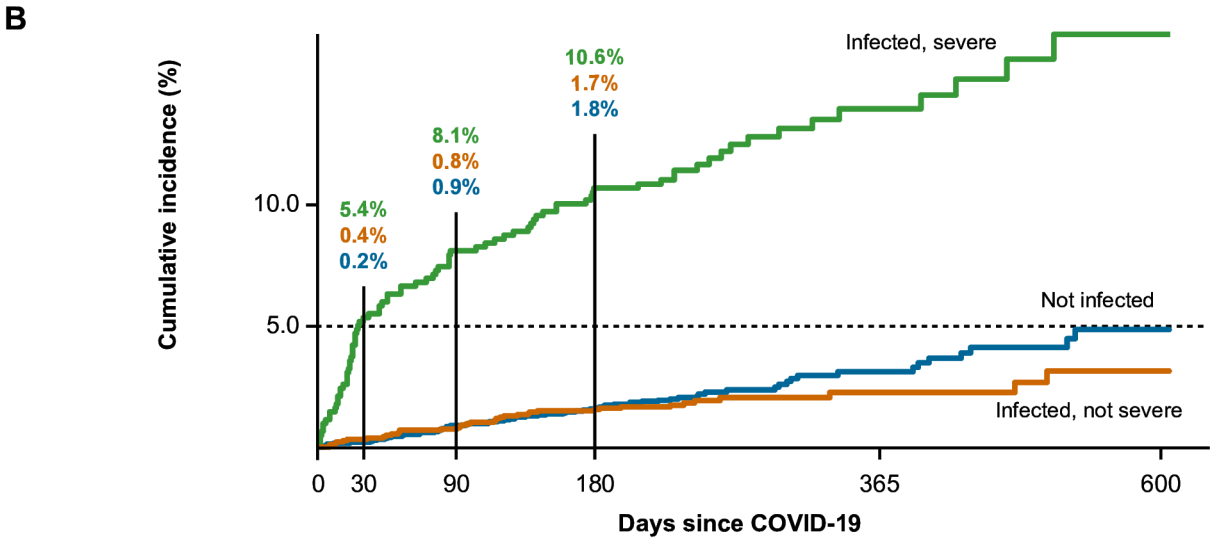
	Matched controls (n=2499)	COVID-19 cohort (n=2499)	SMD
Age, years, mean (SD)	68.3 (11.5)	68.5 (11.4)	0.02
Age, years			0.04
20–49	177 (7.1)	167 (6.7)	
50–59	245 (9.8)	257 (10.3)	
60–69	827 (33.1)	802 (32.1)	
70–79	890 (35.6)	893 (35.7)	
≥80	360 (14.4)	380 (15.2)	
Sex, male	1668 (66.7)	1671 (66.9)	<0.01
BMI, kg/m^2, mean (SD)	24.6 (3.8)	24.5 (3.6)	0.03
BMI			0.05
Low (<18.5 kg/m^2)	119 (4.8)	99 (4.0)	
Normal (18.5–22.9 kg/m^2)	704 (28.2)	733 (29.3)	
Overweight (23.0–24.9 kg/m^2)	580 (23.2)	593 (23.7)	
Obese (25.0–29.9 kg/m^2)	911 (36.5)	905 (36.2)	
Highly obese (≥30 kg/m^2)	185 (7.4)	169 (6.8)	
Regular physical activity			<0.01
No	1824 (73.0)	1821 (72.9)	
Yes	675 (27.0)	678 (27.1)	
Smoking status			0.05
Never smoker	1263 (50.5)	1273 (50.9)	
Ever smoker	1236 (49.5)	1226 (49.1)	
Alcohol consumption			0.03
None	1763 (70.5)	1754 (70.2)	
1–2 times	425 (17.0)	435 (17.4)	
3–4 times	194 (7.8)	182 (7.3)	
Almost every day	117 (4.7)	128 (5.1)	
Economic status			0.02
Low	596 (23.8)	616 (24.6)	
Middle	1086 (43.5)	1065 (42.6)	
High	817 (32.7)	818 (32.7)	
Residential area			0.05
Metropolitan cities	1795 (71.8)	1787 (71.5)	
Mid-size and small cities	526 (21.0)	502 (20.1)	
Rural areas	178 (7.1)	210 (8.4)	
Number of severe exacerbations in the previous year			0.02
None	2194 (87.8)	2182 (87.3)	
≥1	305 (12.2)	317 (12.7)	
Comorbidities			
Hypertension	1080 (43.2)	1093 (43.7)	0.01
Diabetes mellitus	598 (23.9)	638 (25.5)	0.04
Chronic kidney disease	97 (3.9)	82 (3.3)	0.03
Asthma	1056 (42.3)	1026 (41.1)	0.02
Dyslipidaemia	435 (17.4)	443 (17.7)	<0.01

Data are shown in mean (SD) or number (%), as appropriate.
BMI, body mass index; SMD, standard mean difference.



No. at Risk

Not infected	2499	2461	595	159
Infected	2499	2408	593	165



No. at Risk

Not infected	2499	2461	595	159
Infected, severe	620	557	183	49
Infected, not severe	1879	1851	410	116

Figure 2 (A) Cumulative incidence of death in the COVID-19 cohort versus matched controls. (B) Cumulative incidence of death in the COVID-19 cohort versus matched controls according to COVID-19 severity.

When the COVID-19 cohort was subdivided according to COVID-19 severity across all time intervals, the non-severe COVID-19 group did not have an increased risk of mortality compared with controls. In contrast, the risk of mortality was substantially higher in the severe COVID-19 group compared with controls within 180 days from the index date. The risk of mortality gradually decreased as the time interval from index date increased (aHR for <30 days after index date=20.25, 95% CI=7.79 to 52.64; aHR for 30–90 days from index date=3.68, 95% CI=1.69 to 8.02; aHR for 90–180 days from index date=3.33, 95% CI=1.64 to 6.76).

Table 2 Long-term mortality risk in the COVID-19 cohort versus matched controls

	N	Number of deaths	Mortality rate (per 10 000 population)	Unadjusted HR (95% CI)	Adjusted HR (95% CI)
Matched controls	2499	67	270.831	Ref.	Ref.
COVID-19 cohort					
Overall	2499	120	491.822	1.81 (1.35 to 2.45)	1.81 (1.34 to 2.44)
Non-severe	1879	38	207.410	0.76 (0.51 to 1.13)	0.85 (0.57 to 1.28)
Severe	620	82	1349.146	5.05 (3.65 to 6.97)	3.73 (2.68 to 5.20)

Data are shown as number or ratio (95% CI), as appropriate.
In the adjustment, age, sex, body mass index, regular physical activity, smoking status, alcohol consumption, economic status, residential area, number of severe exacerbations in the previous year, and comorbidities (hypertension, diabetes, dyslipidaemia, chronic kidney disease, and asthma) were included.

DISCUSSION

This study evaluated the risk of long-term mortality in individuals with COPD who recovered from COVID-19 compared with those who did not experience COVID-19. The notable findings from our nationwide dataset are as follows. First, the long-term mortality rate in individuals with COPD after COVID-19 was 4.8% during the study period, which was about twofold higher compared with individuals with COPD who did not experience COVID-19. Second, the more severe COVID-19 was, the greater the increase in mortality risk in individuals with COPD. Third, the effect of COVID-19 on mortality was especially pronounced in the severe COVID-19 group within 180 days of recovery from COVID-19, showing the highest mortality risk – about 20-fold increased risk – within 30 days of recovery.

It is well known that COVID-19-related deaths occur in a considerable proportion of subjects even after the resolution of acute phase infection and inflammation and are more significant in individuals with COPD. A previous meta-analysis of 42 studies of more than 420 000 individuals hospitalised due to COVID-19 showed that individuals with COPD showed an increased risk of in-hospital mortality (pooled HR=1.71) compared with those without COPD.[41] Extending the short-term mortality results, studies showed that the presence of COPD or asthma was associated with increased odds of 1-year mortality in patients who were hospitalised or admitted to the ICU due to COVID-19.[42 43] However, since these studies evaluated hospitalised patients, the impact of COVID-19 on long-term mortality in individuals with non-severe COVID-19 remains unclear. In addition, those studies evaluated COPD as one of the comorbidities.

From this view, our study has the advantage of focusing on COPD populations using a nationwide COPD cohort. In addition, we matched various confounding factors between the COVID-19 cohort and controls to objectively evaluate our study aims. Another advantage is the consideration of COVID-19 severity and recovery time. These comprehensive analyses provide deeper insights: the mortality risk was markedly higher during the first 30 days after recovery from COVID-19, particularly in severe COVID-19 cases.

Several viral infections can lead to acute exacerbations of COPD (AECOPD), and a COVID-19 infection might also represent a subtype of AECOPD. While COVID-19 may share some components with COPD, key differences exist between the two conditions. First, COVID-19 has specific treatments, including antiviral and immunosuppressive agents (eg, anti-interleukin-6 receptor antibody or Janus kinase inhibitors inhibitors).[44 45] Second, distinct characteristics of COVID-19, such as bilateral pneumonia and

Table 3 Long-term mortality risk between the COVID-19 cohort and matched controls according to time interval following recovery date from COVID-19

	Adjusted HR (95% CI)			
	<30 days	30–90 days	90–180 days	≥180 days
Matched controls	Ref.	Ref.	Ref.	Ref.
COVID-19 cohort				
Overall	7.49 (2.95 to 19.06)	1.55 (0.77 to 3.10)	2.07 (1.13 to 3.80)	0.93 (0.57 to 1.53)
Non-severe	1.73 (0.53 to 5.69)	0.72 (0.29 to 1.81)	1.47 (0.72 to 2.99)	0.50 (0.24 to 1.01)
Severe	20.25 (7.79 to 52.64)	3.68 (1.69 to 8.02)	3.33 (1.64 to 6.76)	1.64 (0.93 to 2.89)

Data are shown as number or ratio (95% CI), as appropriate.
In the adjustment, age, sex, body mass index, regular physical activity, smoking status, alcohol consumption, economic status, residential area, number of severe exacerbations in the previous year, and comorbidities (hypertension, diabetes, dyslipidaemia, chronic kidney disease and asthma) were included.

acute respiratory distress syndrome, differ from typical AECOPD presentations.[46 47] Supporting this distinction, the recent COPD guidelines provide a specific section for COVID-19, separate from the AECOPD section.

It is unclear whether the clinical course after COVID-19 recovery resembles that of AECOPD. Distinguishing these clinical entities is challenging due to overlapping treatment strategies, such as steroid use.[13 48] In this context, it is informative to compare outcomes with previous studies evaluating long-term outcomes after AECOPD. Since prior studies were conducted on hospitalised patients, the 1-year mortality rate following AECOPD was generally over 10%, reaching up to 40%, which is higher than in our study (4.8%) that included mild COVID-19 cases treated in outpatient settings.[49–52] However, even when limited to severe COVID-19 cases, the mortality rate remained relatively lower (13.2%) than previous reports for AECOPD. This suggests that post-hospitalization courses may differ between COVID-19 and AECOPD. In terms of time intervals, a similar trend of high mortality risk within 30 days was observed for both AECOPD and COVID-19, though the magnitude of this risk was lower for COVID-19.

Individuals with COPD are considered a high-risk group for severe clinical outcomes following COVID-19.[53] However, no guidelines outline a post-COVID-19 management strategy tailored explicitly to individuals with COPD.[13 54] In our study, individuals with COPD showed a significantly higher long-term mortality rate when they experienced COVID-19. This highlights the urgent need to address effective management strategies for individuals with COPD even after recovery from COVID-19. Notably, the risk of death was significantly higher within 180 days after recovery from severe COVID-19. Close monitoring during this time after the acute phase of COVID-19 may be imperative for these populations, especially those who experienced severe COVID-19.

With COVID-19 evolving into an endemic disease, there is a growing emphasis on the necessity of annual booster vaccination.[55] Individuals with COPD seem to have an increased short-term and long-term mortality risk following COVID-19; therefore, those with COPD should be strongly encouraged to be vaccinated against COVID-19. In summary, a comprehensive and tailored approach to managing COPD before and after COVID-19 is essential for reducing mortality risks and ensuring the well-being of individuals with COPD.

We must acknowledge some limitations in our study. First, selection bias may be present, as we enrolled individuals who underwent health screening examinations based on claim data; healthier individuals are more likely to participate in these screenings than those who are less healthy. Additionally, the results may reflect primary care practices, including possible bias in COPD diagnosis, as suggested by the high prevalence of never-smokers and comorbid asthma.[56] Second, this study was conducted during the pandemic when strict discrimination policies were in place. Consequently, the results may differ during an endemic period. Third, this study could not extend beyond 2021 due to the unavailability of data, leaving us without information on viral types and preventing evaluation of this issue. Since the virulence of the omicron variant is weaker than that of previous types of COVID-19, overall mortality might be lower in those infected with the omicron variant.[57] Fourth, certain potential confounders, such as home oxygen therapy, types of inhaler medications and lung function, were not included in the analysis, as these data were not provided. Individuals on home oxygen therapy could be classified as severe COVID-19 cases, even if their COVID-19 severity was mild. Fifth, although we made additional adjustments for covariates in the stratified analyses, certain aspects of severe COVID-19 compared with non-severe COVID-19, such as immunocompromised states, may exist but could not be assessed. Finally, this study was conducted in a single Asian country, and caution is needed when generalising our results.

In conclusion, COVID-19 is associated with an increased long-term mortality risk in individuals with COPD who recover from COVID-19. The risk was significantly higher within 180 days after recovery from COVID-19 in individuals who experienced severe COVID-19.

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Contributors JSK and J-YM are the guarantors of the manuscript and take responsibility for the content of the manuscript, including the data and analysis. HL, SHK, CYJ, J-EC, YK, KHM, KHY, JSK and J-YM contributed to the conception of the study and were involved in the data collection. J-YM and HL contributed to the design of the study. HL and SHK were involved in the interpretation of the data. CYJ and JSK were involved in the statistical analyses. HL and SHK were major contributors to the manuscript. J-EC, YK, KHM and KHY were contributors in reviewing the manuscript. All authors read and approved the final manuscript.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval The study protocol was approved by the Institutional Review Board of Hanyang University Hospital (No. HYUH 2023-11-049). The requirement for informed consent was waived because all patient records were anonymised before use.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data may be obtained from a third party and are not publicly available. The data that support the findings of this study are available from the Korea NHIS but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are, however, available from the authors on reasonable request and with permission of the Korea NHIS.

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