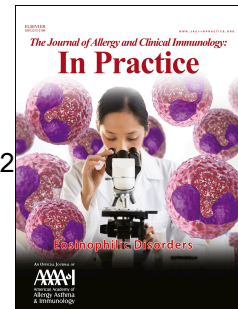


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Asthma and COPD are not risk factors for ICU stay and death in case of SARS-CoV-2 infection

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Asthma and COPD are not risk factors for ICU stay and death in case of SARS-CoV-2 infection

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Abstract**Background.**

Asthmatics and COPD patients have more severe outcomes with viral infections than people without obstructive disease.

Objective. To evaluate if obstructive diseases are risk factors for ICU stay and death due to COVID19.

Methods. We collected data from the electronic medical record from 596 adult patients hospitalized in University hospital of Liege between 18th of March and 17th of April 2020 for SARS-CoV2 infection. We classified patients in three groups according to the underlying respiratory disease, present prior to COVID19 pandemics.

Results. Among patients requiring hospitalization for COVID19, asthma and COPD accounted for 9.6% and 7.7% respectively. The proportions of asthmatics, COPD and patients without obstructive airway disease hospitalized in ICU were 17.5%, 19.6% and 14% respectively. One third of COPD patients died during hospitalization while only 7.0% of asthmatics and 13.6% of patients without airway obstruction died due to SARS-CoV2. The multivariate analysis showed that asthma, COPD, ICS treatment and OCS treatment were not independent risk factors for ICU admission or death. Male gender (OR:1.9; 95%CI: 1.1 to 3.2) and obesity (OR:8.5; 95%CI: 5.1 to 14.1) were predictors of ICU admission while male gender (OR1.9; 95%CI: 1.1-3.2), older age (OR:1.9; 95%CI: 1.6-2.3), cardiopathy (OR: 1.8; 95%CI: 1.1-3.1) and immunosuppressive diseases (OR: 3.6; 95%CI: 1.5-8.4) were independent predictors of death.

Conclusion. Asthma and COPD are not risk factors for ICU admission and death related to SARS-CoV2 infection.

Highlights**What is already known about this topic?**

Asthmatics and COPD patients are at risk of more severe outcomes with common cold virus infections. Prior studies have suggested that allergic diseases, asthma and COPD may not be risk factors for SARS-CoV-2 infection.

What does this article add to our knowledge?

The strength of this study is the characterization of obstructive disease according to lung function testing. In our study, asthma, COPD, treatment with ICS or OCS were not risk factors for admission to the ICU or mortality.

How does this study impact current management guidelines?

Our results confirm the recommendations that patients with obstructive airway disease should not decrease the dose of ICS during SARS-CoV2 infection. Asthma and COPD treatments should be pursued and adapted to ensure optimal control of the lung disease throughout the pandemic, potentially reducing the risk of severe COVID19 disease.

KEY WORDS: asthma – COPD – risk factors – ICU – death – COVID19 – SARS-CoV2 – viral infection – severe asthma

Abbreviations list**BMI:** body mass index**CK:** creatinine kinase**COPD** : chronic obstructive pulmonary disease**COVID19:** disease due to the novel coronavirus discovered in late 2019 in Wuhan, China later renamed SARS-CoV2.**CRF:** chronic renal failure**CRP:** C-reactive protein**FEV₁:** Forced Expiratory Volume in one second**FVC:** forced vital capacity**GFR:** glomerular filtration rate**GOR:** gastro-esophageal reflux**H5N1:** Hemagglutinin Type 5 and Neuraminidase type 1, Influenza A virus**H7N9:** Hemagglutinin Type 7 and Neuraminidase type 9, Influenza A virus**ICS:** inhaled corticosteroids**ICU:** intensive care unit**IQR:** interquartile range**LDH:** lactate dehydrogenase**OCS:** oral corticosteroids**ORF:** Open Reading Frame**PC20:** methacholine concentration provoking a 20% fall in FEV₁**PCR:** polymerase chain reaction**SARS-CoV2:** severe acute respiratory syndrome coronavirus 2**SD:** standard deviation**SpO₂:** ambient air oxygen saturation

Introduction

Asthmatics and chronic obstructive pulmonary disease (COPD) patients are at risk of more severe outcomes with common cold virus infections than are people without obstructive lung disease (1,2). This seems to be partly due to a deficient and delayed innate anti-viral immune response in these patients. SARS-CoV-2 is a new virus that appeared in China end of 2019 and is responsible for COVID19 disease. At the beginning of the COVID19 pandemic, respiratory physicians were worried about the vulnerability of patients exhibiting chronic obstructive airway disease in case of SARS-CoV-2 infection. It seemed inevitable that patients with airway obstruction were at risk of severe COVID19. In the first publications from Wuhan in China (3), the prevalence of patients with obstructive diseases in patients with COVID19 was surprisingly lower than that reported in the general population. The authors concluded that allergic diseases, asthma and COPD were not risk factors for SARS-CoV-2 infection. However, they found that older age, high number of comorbidities and more prominent laboratory abnormalities were associated with severity of disease. It was suggested that chronic pulmonary disease was under diagnosed in the first studies or that there was a possible protective effect of inhaled corticosteroids (ICS) (4).

Some authors hypothesize that type 2 inflammation may suppress anti-viral immunity in the lung (5) and may increase susceptibility to severe COVID19. Suppressing type-2 inflammation with the use of topical steroids might thus restore local antiviral immunity.

Moreover it has been shown that poor asthma control was a risk factor for greater virus-induced exacerbations severity (6). Like H5N1 and H7N9 (7), SARS-CoV2 is responsible for severe lymphopenia. SARS-CoV2 infected patients also presented with eosinopenia, extensive highly hypoxemic interstitial pneumonia, in the most severe cases diffuse lung tissue damage, a cytokine storm leading to acute respiratory distress syndrome requiring intensive care unit stay and mechanical ventilation.

International guidelines currently recommend the use of the same maintenance medication during the pandemic, including a regular treatment with ICS in asthmatics

(8–10) or in COPD patients (11) who are frequent exacerbators with Forced Expiratory Volume in one second (FEV₁) lower than 50%. Corticosteroids are immunosuppressive drugs and could be deleterious during viral infection. Dong et al however previously confirmed the safety of ICS use in COPD patients (12).

In our study, we collected data from patients who were hospitalized due to COVID19 and classified them according to their lung status either in a non-obstructive group or in an asthma or COPD group. The aim of the study was to determine if patients with asthma or COPD are at risk of experiencing an intensive care unit admission and death as compared to non-obstructive patients.

Methods

We collected data from the electronic medical record from 596 adult patients who were hospitalized in University hospital of Liege between 18th of March and 17th of April 2020 for COVID19.

Demographic characteristics, maintenance treatments and comorbidities at baseline were extracted. Subjects were characterized as atopic if they had at least one positive specific IgE test (0.35 kU/l; Phadia, Groot-Bijgaarden, Belgium) for at least one common aeroallergen (cat, dog, house dust mites, grass pollen, tree pollen and a mixture of molds). Chronic renal failure was defined as a permanent reduction in glomerular filtration rate $<60\text{ml/min/1.73m}^2$. Cardiopathy involved ischemic cardiomyopathy, hypertensive cardiomyopathy, chronic heart failure, cardiomegaly, cardiac hypertrophy and congestive heart failure. Emphysema and bronchiectasis were defined based on Chest CT according to current guidelines (13,14) and according to lung function testing for emphysema. Immunosuppressive diseases recorded among hospitalized patients were grafts, history of splenectomy and HIV infection.

We classified patients in three groups according to the underlying respiratory disease that was present prior to COVID19. The diagnosis was done by a pulmonologist according to lung function tests, bronchodilation test and PC20 if necessary as previously described (15,16). We distinguished one group with asthmatics, a second group with patients suffering from COPD and a third group, which included all patients without a history of obstructive pulmonary disease. The latest lung function tests performed over the last three years were reported in patients with asthma and COPD. Symptoms at admission such as dyspnea, chest pain, rhinorrhea, pharyngeal pain, nonproductive and productive cough, diarrhea, headache, myalgia, fever, nausea and vomiting were extracted. Ambient air oxygen saturation (SpO₂) was measured and blood sampling was taken at hospital admission while Chest CT Scanner was performed.

We reported the number of cycles of PCR COVID19 (Gene E and gene ORF1ab) at baseline. We used a real-time RT-PCR test intended for the qualitative detection of nucleic acids from SARS-CoV-2 in collected nasopharyngeal swab samples (Cobas® SARS-CoV-2 assay for use on the Cobas® 6800/8800 Systems). We detected

specific nucleic acid sequences from the non-structural Open Reading Frame (ORF 1a/b) in the genome of the SARS-CoV-2 virus in the FAM channel and the conserved sequences in the structural envelope (E) gene to provide a high degree of robustness.

A “COVID working group” constituted in the University Hospital of Liege at the beginning of the pandemic decided to treat all hospitalized patients tested positive to COVID19 with hydroxychloroquine for 5 days (400mg on day 1 and 200mg from day 2 to day 5) and doxycycline 200mg per day for 5 days but this was not part of a clinical trial.

Statistical analysis

The results were expressed as mean $\pm$ standard deviation (SD) for continuous variables; median (interquartile range, IQR) was preferred for skewed distributions. For categorical variables, the number of observations and percentages are given in each category. For continuous variables, comparisons between different subgroups were performed with ANOVA method, or using Kruskal–Wallis tests for skewed distributions. Chi-square test for contingency table was used for categorical variables. Variables associated to ICU admission and death were identified by binary logistic regression. For each variable, results were presented as odd ratios (OR), their 95% Confidence intervals (95%CI), and p-values of simple logistic regression models and of logistic regression models adjusted for age and gender. Multiple regression models were built for each outcome (ICU stay and death) including age, gender, asthma, COPD and the other comorbidities with $p < 0.10$ in the models adjusted for age and gender. Since atopy is highly correlated with asthma, this variable was not included in the multiple model predicting ICU stay. Final multiple models obtained by stepwise selection (with age, gender, asthma and COPD forced to be included) were presented in the results. In all the regression models, skewed continuous variables were log-transformed or expressed as ordered qualitative variables.

A p value < 0.05 was considered as statistically significant. Missing values were not replaced. Statistical analysis was done using SAS (version 9.4) software.

Results

Demographic characteristics

Among the 596 patients requiring hospitalization for COVID19, asthma and COPD accounted for 9.6% (N=57) and 7.7% (N=46) respectively. Not surprisingly, asthmatic patients were more often atopic than COPD and non-obstructive ones (table 1). COPD patients were older, more often current or ex-smokers with higher rates of emphysema. Regarding comorbidities, COPD patients had more often hypertension, gastro-esophageal reflux, cardiopathy, chronic renal failure, and a cancer history. Patients with chronic airway obstructive diseases were more often treated with anxiolytics before admission. Seventy percent of asthmatics were treated with ICS and half of them received high doses of ICS ($\geq 1000\mu\text{g}$ beclomethasone equivalent per day). One third of COPD patients were treated with ICS with 19% of them receiving high doses and 44% moderate doses of ICS. 3% of asthma and 2% of COPD patients received chronic OCS with a median dose of 4mg per day while 4% of the non-obstructive patients were treated with chronic OCS with a median dose of 16mg/day.

Symptoms at admission and SARS-COV2 PCR.

Fever, headache, nonproductive cough and myalgia were the most common symptoms at admission (table 2). COPD patients had less headache than asthmatics and non-obstructive patients. Other symptoms were similar between the subgroups. The number of cycles of positive PCR for COVID19 Gene E and Gene ORF1ab were similar between the groups (table 3).

Risk factors for Intensive care unit stay

The proportions of asthmatics (N=10/57), COPD (N=9/46) and patients without obstructive airway disease (N=69/493) hospitalized in ICU were 17.5%, 19.6% and 14% respectively (table 4).

We searched for risk factors of being hospitalized in the ICU for the whole population (table 5). The regression analysis showed that male gender and older age increased the risk of intensive care unit stay. Independently from age and gender, atopy, obesity, diabetes, high baseline CRP, D-dimers and fibrinogen levels were associated with a risk of intensive care unit stay (table 5). Moreover, higher white blood cell and neutrophil counts, lower blood eosinophil and lymphocyte counts,

lower glomerular filtration rate, higher creatinine and urea levels, lower concentration of albumin and higher procalcitonin, LDH and CK levels were associated with a higher risk of intensive care unit stay independently of age or gender.

The multivariate analysis confirmed that male gender and obesity were risk factors for hospitalization in the intensive care unit (table 5). Men had 1.9 times (95%CI :1.1 to 3.2) more risk of ICU stay, obesity increased 8.5 times (95%CI: 5.1 to 14.1) the risk of ICU stay. Interestingly, neither having asthma nor COPD nor ICS or OCS treatment were significant risk factors for ICU admission.

Risk factors for death due to COVID

One third of COPD patients hospitalized for SARS-CoV2 infection died during hospitalization (34.8%, N=16/46), while only 7.0% of asthmatics (N=4/57) and 13.6% (N=67/493) of patients without obstructive airway disease died due to COVID19 (table 4). The regression analysis revealed that male gender and older age increased the risk of death and that, independently of age and gender, cardiopathy, diabetes, immunosuppressive disease, obesity, and chronic renal failure were predictors of death in hospitalized patients (table 6). Higher baseline CRP level increased the risk of death. Level of LDH was higher and value of albumin was lower at admission to the hospital in patients who died from SARS-CoV2 infection. Patients dying from COVID19 had also significantly lower number of cycles of PCR gene E and ORF1ab suggesting a higher viral load (Fig 1). Moreover, higher levels of white blood cells, neutrophils, urea, pro-calcitonin and CK and lower levels of eosinophils, monocytes, red blood cells, hemoglobin and total proteins were predictors of death.

The multivariate analysis confirmed that male gender, older age, cardiopathy, and immunosuppressive disease were predictors of death in patients hospitalized due to COVID19 infection. COPD was a predictor of death in the univariate but not in the age and gender adjusted models nor in the multivariate analysis, suggesting that this risk is probably linked to the higher rate of comorbidities recorded in this sub-population and to the older age of this subgroup. As for ICU admission, neither having asthma nor ICS or OCS treatment were significant risk factors for mortality.

DISCUSSION

Intensive care unit stay was necessary in one fifth of asthmatics and COPD patients hospitalized due to SARS-CoV2 infection. Predictors of hospitalization in the ICU were gender and obesity. The presence of high baseline CRP levels increased the risk of ICU admission. Asthma, COPD, ICS treatment, and chronic OCS requirement were not identified as significant risk factors for ICU admission or mortality. The multivariate analysis showed that male gender, older age, cardiopathy and immunosuppressive disease were independent predictors of death in patients hospitalized for SARS-CoV2 infection.

In the previous reports on COVID19, the prevalence of asthma in patients with SARS-CoV2 infection was surprisingly low (3,17). However, most of the first reports combined asthmatics and COPD patients in a « chronic obstructive respiratory diseases » group and it has been suggested that chronic pulmonary diseases were under diagnosed in the first studies (18). The proportion of asthmatics and COPD patients hospitalized in CHU of Liege due to COVID19 is similar to the one reported by Richardson et al (19) and close to the percentage of patients suffering from these diseases in the general population (20,21). This suggests that asthma and COPD are not risk factors for hospitalization due to SARS-CoV2 infection. One hypothesis is that asthmatics and COPD patients were more compliant to their treatment (22) and respected social distancing during the pandemic because they were afraid of having severe pulmonary infection. A protective role of inhalation therapy by ICS has also been proposed as a possible explanation. Moreover, Peters *et al.* found that there were no significant differences in gene expression of angiotensin converting enzyme 2 (ACE2) in sputum between asthma and healthy subjects, suggesting that asthma subjects might not be at increased risk of COVID19 (4). However, we have to recognize that hospitalized asthmatics in our series are not representative of the general population of asthmatics seen in our hospital (15) since the mean post-bronchodilation FEV₁/FVC ratio was below 70%, thereby indicating fixed airway obstruction. It would therefore suggest that fixed airway obstruction in asthma may be a risk factor to be hospitalized. However among the 226 severe asthmatics treated with anti-IgE, anti-IL5 and anti-IL5R in the Asthma Clinic of CHU of Liege,

only 4 presented a SARS-CoV2 infection and none of them were admitted to the hospital due to COVID19 (unpublished data).

We found that one fifth of asthmatic and COPD patients who were hospitalized due to COVID19 required a stay in the ICU. Previous studies have suggested that patients suffering from airway obstructive disease had a deficient and delayed innate anti-viral immune response (1,2). In a meta-analysis, Lippi et al (23) reported that COPD was associated with severe coronavirus disease with an odds ratio of 5.69. In another study, the prevalence of COPD patients was higher in the non-survivors (24). This paper has however been retracted. In our population, COPD was a predictor of death during hospitalization in the univariate but not in the multivariate analysis suggesting that this risk is probably linked to the higher rate of comorbidities recorded in this sub-population and to the older age of this subgroup. Cardiopathy is indeed frequently associated with COPD and has emerged as a key comorbidity to predict death following COVID19.

In our study, we confirm that older age and high number of comorbidities are associated with more severe infections (3). Male gender and the presence of obesity were indeed predictors of ICU stay while male gender, older age, cardiopathy, and immunosuppressive disease were associated with death during hospitalization. Male gender and a history of diabetes mellitus have been found to be associated with an elevated ACE2, a receptor for SARS-CoV-2 to enter host target cells (4). In the report of Xiaochen et al, patients with older age and hypertension were significantly associated with severe COVID19 on admission (17). Mehra et al found that underlying cardiovascular disease was associated with increased risk of in-hospital death among patients hospitalized with COVID19 (25). We also found that high baseline CRP levels at hospital admission were predictors of ICU stay or death. We found higher fibrinogen and D-dimers levels in patients who stayed in the ICU. This is not surprising as a high incidence of thromboembolic events has been reported in such patients and this suggests an important role of SARS-Cov2-induced endothelial activation (26).

We did not find a higher risk of severe infections in patients treated with ICS or OCS. It has been previously shown that type-2 inflammation may suppress anti-viral immunity in the lung (5) and may increase susceptibility to severe COVID19. Our

group also previously found that allergic asthma was characterized by impaired spontaneous release of IFN-gamma that correlated with the magnitude of eosinophilic inflammation (27). Suppressing type-2 inflammation using local corticosteroids may thus restore antiviral immunity. Moreover, it has been recently suggested that ICS is dose-dependently associated with reduced ACE2 mRNA expression. This observation was however not confirmed in a study looking at bronchial brushes (28). This suggests that patients with obstructive airway disease should not decrease the dose of ICS during SARS-CoV2 infection as recommended by most of the current international guidelines (8–10). Asthma and COPD treatments should be pursued and adapted to ensure optimal control of the lung disease throughout the epidemic, thus potentially reducing the risk of severe COVID19 disease.

We also looked at intubation length according to airway status and did not find that asthma prolonged intubation as compared to non-obstructive patients. However, we found similar intubation length to the one reported by Mahdavinia et al (29) and a prolonged intubation in COPD patients.

Data related to smoking and risk of SARS-CoV-2 infection have been somewhat contradictory despite the fact that association between smoking and an increased risk of respiratory diseases is clear. Recent publications suggested that smoking upregulates ACE2 receptor, which could increase the susceptibility to the infection (30). The proportion of current smokers in our patients hospitalized for COVID19 was lower than that in the general population in Belgium. In addition, smoking was not a risk factor for ICU stay or death in our study. It might be that smoking is protective against COVID19 by damaging cells who are entrance gate to the virus such as pneumocytes type 2 expressing ACE2.

CONCLUSION

Asthma and COPD are not risk factors for ICU stay and death due to SARS-CoV2 infection. Independent predictors of hospitalization in the ICU were male gender and obesity. Male gender, older age, cardiopathy, and immunosuppressive disease were independent predictors of death due to COVID19.

REFERENCES

1. Hewitt R, Farne H, Ritchie A, Luke E, Johnston SL, Mallia P. The role of viral infections in exacerbations of chronic obstructive pulmonary disease and asthma. *Therapeutic Advances in Respiratory Disease*. 2016. 10(2):158-74.
2. Makris S, Johnston S. Recent advances in understanding rhinovirus immunity. *F1000Research*. 2018; 7:F1000 Faculty Rev-1537.
3. Zhang J jin, Dong X, Cao Y yuan, Yuan Y dong, Yang Y bin, Yan Y qin, et al. Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. *Allergy* 2020; doi:10.1111/all.14238.
4. Peters MC, Sajuthi S, Deford P, Christenson S, Rios CL, Montgomery MT, et al. COVID-19 Related Genes in Sputum Cells in Asthma: Relationship to Demographic Features and Corticosteroids. *Am J Respir Crit Care Med*. 2020; doi:10.1164/rccm.202003-08210C
5. Contoli M, Ito K, Padovani A, Poletti D, Marku B, Edwards MR, et al. Th2 cytokines impair innate immune responses to rhinovirus in respiratory epithelial cells. *Allergy Eur J Allergy Clin Immunol*. 2015; 70(8):910-20.
6. Jackson DJ, Trujillo-Torralbo MB, Del-Rosario J, Bartlett NW, Edwards MR, Mallia P, et al. The influence of asthma control on the severity of virus-induced asthma exacerbations. *J Allergy Clin Immunol*. 2015; 136(2):497-500.
7. Boonnak K, Vogel L, Feldmann F, Feldmann H, Legge KL, Subbarao K. Lymphopenia Associated with Highly Virulent H5N1 Virus Infection Due to Plasmacytoid Dendritic Cell–Mediated Apoptosis of T Cells. *J Immunol*. 2014; 192(12):5906-12.
8. COVID-19: GINA ANSWERS TO FREQUENTLY ASKED QUESTIONS ON ASTHMA MANAGEMENT. <https://ginasthma.org/covid-19-gina-answers-to-frequently-asked-questions-on-asthma-management/> Last reading June 29th 2020.
9. BTS guidelines. Advice for Healthcare Professionals Treating People with Asthma (adults) in relation to COVID-19 [Internet]. 2020 [cited 2020 Apr 3]. Available from: <https://www.brit-thoracic.org.uk/about-us/covid-19-information-for-the-respiratory-community/> Last reading June 29th 2020.
10. Guideline NICE. COVID-19 rapid guideline: severe asthma. <https://www.guidelines.co.uk/covid-19-rapid-guideline-severe-asthma/455275.article>. 03 April 2020.
11. Guidelines NICE. COVID-19 rapid guideline: community-based care of patients with chronic obstructive pulmonary disease. 2020. . <https://www.nice.org.uk/guidance/ng168>
12. Dong YH, Chang CH, Wu FLL, Shen LJ, Calverley PMA, Löfdahl CG, et al. Use of inhaled corticosteroids in patients with COPD and the risk of TB and influenza: A systematic review and meta-analysis of randomized controlled trials. *Chest*. 2014; 145(6):1286-1297.
13. Hill AT, Sullivan AL, Chalmers JD, De Soyza A, Stuart Elborn J, Andres Floto R, et al. British thoracic society guideline for bronchiectasis in adults. *Thorax*. 2019. 74:1-69.
14. Xie M, Wang W, Dou S, Cui L, Xiao W. Quantitative computed tomography measurements of emphysema for diagnosing asthma-chronic obstructive pulmonary disease overlap syndrome. *Int J COPD*. 2016; 11:953-961.
15. Schleich FN, Chevremont A, Paulus V, Henket M, Manise M, Seidel L, et al.

- Importance of concomitant local and systemic eosinophilia in uncontrolled asthma. *Eur Respir J*. 2014; 44:97-108.
16. Schleich F, Corhay JL, Louis R. Blood eosinophil count to predict bronchial eosinophilic inflammation in COPD. *European Respiratory Journal*. 2016. 47:1562-1564.
 17. Li X, Xu S, Yu M, Wang K, Tao Y, Zhou Y, et al. Risk factors for severity and mortality in adult COVID-19 inpatients in Wuhan. *J Allergy Clin Immunol*. 2020; DOI:10.1016/j.jaci.2020.04.006
 18. Chow N, Fleming-Dutra K, Gierke R, Hall A, Hughes M, Pilishvili T, et al. Preliminary estimates of the prevalence of selected underlying health conditions among patients with coronavirus disease 2019 - United States, February 12-March 28, 2020. *Morbidity and Mortality Weekly Report*. 2020. 69(13):382-386.
 19. Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW, et al. Presenting Characteristics, Comorbidities, and Outcomes among 5700 Patients Hospitalized with COVID-19 in the New York City Area. *JAMA - J Am Med Assoc*. 2020; 323(20):2052-2059.
 20. Kainu A, Pallasaho P, Piirilä P, Lindqvist A, Sovijärvi A, Pietinalho A. Increase in prevalence of physician-diagnosed asthma in Helsinki during the Finnish Asthma Programme: Improved recognition of asthma in primary care? A cross-sectional cohort study. *Prim Care Respir J*. 2013; 22(1):64-71.
 21. Ntritsos G, Franek J, Belbasis L, Christou MA, Markozannes G, Altman P, et al. Gender-specific estimates of COPD prevalence: A systematic review and meta-analysis. *International Journal of COPD*. 2018. 13:1507-1514.
 22. Kaye L, Theye B, Smeenk I, Gondalia R, Barrett MA, Stempel DA. Changes in medication adherence among patients with asthma and COPD during the COVID-19 pandemic. *J Allergy Clin Immunol Pract*. 2020; S2213-2198(20)30412-8.
 23. Lippi G, Henry BM. Chronic obstructive pulmonary disease is associated with severe coronavirus disease 2019 (COVID-19): COPD and COVID-19. *Respiratory Medicine*. 2020. 167. <https://doi.org/10.1016/j.rmed.2020.105941>
 24. Mehra MR, Desai SS, Ruschitzka F, Patel AN. Hydroxychloroquine or chloroquine with or without a macrolide for treatment of COVID-19: a multinational registry analysis. *Lancet*. 2020; [https://doi.org/10.1016/S0140-6736\(20\)31180-6](https://doi.org/10.1016/S0140-6736(20)31180-6)
 25. Mehra MR, Desai SS, Kuy S, Henry TD, Patel AN. Cardiovascular Disease, Drug Therapy, and Mortality in Covid-19. *N Engl J Med*. 2020; DOI: 10.1056/NEJMoa2007621
 26. Wichmann D, Sperhake J-P, Lütgehetmann M, Steurer S, Edler C, Heinemann A, et al. Autopsy Findings and Venous Thromboembolism in Patients With COVID-19: A Prospective Cohort Study FREE. *Ann Intern Med*. 2020; M20-2003. doi: 10.7326/M20-2003.
 27. Bettiol J, Bartsch P, Louis R, De Groote D, Gevaerts Y, Louis E, et al. Cytokine production from peripheral whole blood in atopic and nonatopic asthmatics: Relationship with blood and sputum eosinophilia and serum IgE levels. *Allergy Eur J Allergy Clin Immunol*. 2000; 55(12):1134-41.
 28. Bradding P, Richardson M, Hinks TSC, Howarth PH, Choy DF, Arron JR, et al. ACE2, TMPRSS2, and furin gene expression in the airways of people with asthma—implications for COVID-19. *J Allergy Clin Immunol*. 2020; S0091-6749(20)30730-2.

- 496
497 29. Mahdavinia M, Foster KJ, Jauregui E, Moore D, Adnan D, Andy-Nweye AB, et
498 al. Asthma prolongs intubation in COVID-19. J Allergy Clin Immunol Pract.
499 2020; S2213-2198(20)30476-1.
500 30. Brake SJ, Barnsley K, Lu W, McAlinden KD, Eapen MS, Sohal SS. Smoking
501 Upregulates Angiotensin-Converting Enzyme-2 Receptor: A Potential Adhesion
502 Site for Novel Coronavirus SARS-CoV-2 (Covid-19). J Clin Med. 2020;
503 9(3):841.
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507 **Figure Legend:**

508 Fig 1. Comparison of clinical parameters in patients who died during SARS-CoV2
509 infection as compared to patients who survived.

Table 1. Demographic, treatment and functional characteristics and comorbidities of patients hospitalized for SARS-CoV2 infection according to the presence or absence of asthma and COPD.

	No obstruction (N=493)		Asthma (N=57)		COPD (N=46)		
	N	Value	N	Value	N	Value	p-value
Female Gender	493	249 (50%)	57	32 (56%)	46	21 (46%)	0.56
Age (years)	493	58 ± 19	57	53 ± 18	46	74 ± 10	<0.0001
BMI (kg/m ²)	243	27.8 ± 5.8	32	28.6 ± 7.5	37	27.9 ± 5.4	0.80
Smoking status	411		57		46		<0.0001
Non smoker		268 (65%)		41 (72%)		3 (7%)	
Ex-smoker		102 (25%)		13 (23%)		37 (80%)	
Smoker		41 (10%)		3 (5%)		6 (13%)	
Anxiolytics	480	38 (8%)	56	2 (4%)	41	13 (32%)	<0.0001
Aspirin	480	96 (20%)	56	7 (12%)	41	20 (49%)	<0.0001
Azithromycin	485	0 (0%)	56	0 (0%)	42	3 (7%)	<0.0001
ICS	493	0 (0%)	57	40 (70%)	46	16 (35%)	<0.0001
Low dose		0		3		6	
Moderate dose		0		17		7	
High dose		0		20		3	
OCS (dose, mg)	493	20 (4%) (16 mg)	57	2 (3%) (4 mg)	46	1 (2%) (4 mg)	0.81
Post-BD FEV ₁ , % pred	0	-	57	88 (70-101)	46	64 (53-72)	<0.0001
Post-BD FEV ₁ /FVC (%)	0	-	57	69 (63-87)	46	58 (52-68)	0.0062
FVC, % pred	0	-	57	89 (80-99)	46	80 (68-92)	0.041
TLC, % pred	0	-	30	95 (88-106)	22	100 (93-112)	0.41
RV/TLC, % pred	0	-	27	37 (27-45)	18	53 (49-58)	0.0002
FRC, % pred	0	-	28	105 (91-134)	15	121 (104-147)	0.27
RV, % pred	0	-	29	96 (80-125)	20	120 (97-150)	0.066
DLCO, % pred	0	-	30	80 (68-87)	25	47 (32-64)	0.0003
KCO, % pred	0	-	29	91 (76-102)	24	72 (56-91)	0.023
sGaw, % pred	0	-	19	60 (42-72)	7	40 (34-66)	0.15
Atopy	484	105 (22%)	56	35 (62%)	46	14 (30%)	<0.0001
Emphysema	350	35 (10%)	56	7 (15%)	46	28 (61%)	<0.0001
Bronchiectasis	493	15 (3%)	56	4 (7%)	46	4 (9%)	0.067
Cardiopathy	493	88 (18%)	56	8 (14%)	46	20 (43%)	<0.0001
Diabetes	493	90 (18%)	56	11 (20%)	46	13 (28%)	0.26
History of cancer	493	53 (11%)	56	3 (5%)	46	14 (30%)	0.0007
Immunosuppressive disease	493	28 (6%)	57	0 (0%)	46	4 (9%)	0.11
Hypertension	493	198 (40%)	56	19 (34%)	46	29 (63%)	0.0053
Dyslipemia	493	109 (22%)	56	12 (21%)	46	16 (35%)	0.14
Obesity	493	89 (18%)	56	12 (21%)	46	14 (30%)	0.12
CRF	493	32 (7%)	56	2 (4%)	46	8 (17%)	0.012
GOR	479	65 (14%)	56	7 (12%)	41	16 (39%)	<0.0001

COPD: chronic obstructive pulmonary disease, BMI: body mass index, ICS: inhaled corticosteroids, OCS: oral corticosteroids, CRF: chronic renal failure, GOR: gastro-esophageal reflux, ICU: intensive care unit.

Values are n(%) and p-value chi-square test for contingency tables, or mean ± SD and p-value ANOVA, or median (IQR) and p-value Kruskal-Wallis test.

Table 2. Percentage of patients reporting symptoms at admission when hospitalized for SARS-CoV2 infection according to the presence or absence of asthma and COPD.

	No obstruction	Asthma	COPD	p-value
N	245	30	9	
Fever	163 (67%)	20 (67%)	6 (67%)	0.99
Headache	156 (64%)	21 (70%)	1 (11%)	0.0040
Nonproductive cough	150 (61%)	21 (70%)	4 (44%)	0.36
Myalgia	152 (62%)	17 (57%)	2 (22%)	0.052
Dyspnea	116 (47%)	15 (50%)	6 (67%)	0.51
Chest pain	78 (32%)	10 (33%)	2 (22%)	0.81
Diarrhea	74 (30%)	10 (33%)	2 (22%)	0.81
Nausea	74 (30%)	7 (23%)	0 (0%)	0.11
Rhinorrhea	54 (22%)	7 (23%)	0 (0%)	0.28
Pharyngeal pain	52 (21%)	6 (20%)	0 (0%)	0.30
Productive cough	50 (20%)	4 (13%)	3 (33%)	0.40
Vomiting	23 (9%)	1 (3%)	0 (0%)	0.35

Values are n(%) and p-value chi-square test for contingency tables.

Table 3. Blood tests and chest CT scan results at admission to the hospital.

	No obstruction (N=493)		Asthma (N=57)		COPD (N=46)		
	N	Med (IQR)	N	Med (IQR)	N	Med (IQR)	p-value
White blood cells, /mm ³	323	6370 (4650-8230)	31	6280 (5080-9830)	43	6080 (4620-9960)	0.83
Lymphocytes, /mm ³	322	890 (650-1250)	31	1060 (700-1370)	42	1000 (630-1280)	0.39
Neutrophils, /mm ³	322	4755 (3180-6580)	31	4520 (3200-7050)	42	4170 (2630-6670)	0.92
Eosinophils, /mm ³	322	10 (0-30)	31	10 (0-50)	42	10 (0-60)	0.42
Basophils, /mm ³	322	20 (10-30)	31	20 (10-30)	42	20 (10-30)	0.71
Monocytes, /mm ³	322	390 (250-560)	31	450 (300-630)	42	430 (240-820)	0.47
Platelets, /mm ³	323	197 (159-264)	30	194 (167-269)	43	179 (151-315)	0.92
Red blood cells, 10 ⁶ /mm ³	318	4.6 (4.1-4.9)	30	4.8 (4.3-5.3)	40	4.2 (3.8-4.7)	0.026
Hemoglobin, g/dL	323	13.5 (12.2-14.8)	30	14.0 (12.2-15.1)	43	12.6 (11.1-14.3)	0.078
GFR ml/min/1.73m ²	319	72 (51-90)	30	67 (49-89)	43	61 (46-82)	0.29
Creatinin, mg/dL	320	0.95 (0.76-1.3)	30	1.0 (0.69-1.4)	43	1.0 (0.75-1.5)	0.56
Urea, mg/dL	320	40 (29-59)	29	49 (27-64)	42	51 (32-74)	0.060
Albumin, g/L	290	38 (35-41)	29	40 (37-42)	36	37 (33-41)	0.14
Total proteins, g/L	300	69 (64-74)	30	70 (66-76)	37	67 (63-70)	0.12
Bicarbonates, mmol/l	280	24 (22-26)	27	25 (22-26)	34	26 (22-29)	0.040
CRP, mg/l	323	76 (28-152)	31	60 (10-117)	43	55 (15-111)	0.11
D-dimers, µg/l	249	826 (486-1644)	24	582 (460-1140)	28	947 (494-1996)	0.29
Fibrinogen, g/l	290	5.1 (4.2-6.5)	25	4.9 (4.4-6.0)	33	4.3 (3.8-5.5)	0.018
Procalcitonin, µg/l	250	0.10 (0.05-0.24)	25	0.08 (0.02-0.45)	27	0.07 (0.04-0.40)	0.90
LDH, U/l	299	332 (250-446)	29	356 (266-503)	35	279 (216-383)	0.10
CK, U/l	292	134 (67-298)	27	115 (63-323)	32	106 (55-553)	0.88
PCR COVID Gene E positif	493	493 (100%)	57	56 (98.2%)	46	45 (97.8%)	
Number of cycles	241	27 (22-32)	31	29 (21-33)	25	24 (22-31)	0.71
PCR COVID ORF1ab positif	493	493 (100%)	57	56 (98.2%)	46	45 (97.8%)	
Number of cycles	240	27 (21-31)	31	28 (21-31)	25	24 (22-30)	0.77

GFR: glomerular filtration rate, CRP: C reactive protein, LDH: lactate dehydrogenase, CK: creatinine kinase, PCR: polymerase chain reaction, Number of cycles<19: very high positive, 19-25: high positive, 26-33: moderate positive, >33: low positive.

Values are Median (IQR) and p-values of Kruskal-Wallis test, or n(%).

Table 4. Deterioration and death rate of patients hospitalized for SARS-CoV2 infection according to the presence or absence of asthma and COPD.

	No obstruction	Asthma	COPD
N	493	57	46
ICU	69 (14.0%)	10 (17.5%)	9 (19.6%)
Mechanical ventilation days	12 (10-18)	12 (9-23)	17 (9-24)
Death	67 (13.6%)	4 (7.0%)	16 (34.8%)

Table 5. Factors associated with Intensive care unit stay due to SARS-CoV2 infection. Results of the logistic regression analysis.

	Simple logistic regression			Logistic regression adjusted for age and gender			Multiple logistic regression final model (N=595)	
	N	OR (95%CI)	p-value	N	OR (95%CI)	p-value	OR (95%CI)	p-value
Male gender	596	2.0 (1.2-3.2)	0.0041	-	-	-	1.9 (1.1-3.2)	0.013
Age (by 10 years)	596	1.2 (1.04-1.3)	0.0093	-	-	-	1.1 (0.96-1.3)	0.17
BMI (kg/m ²)	312	1.1 (1.1-1.2)	<0.0001	312	1.1 (1.1-1.2)	<0.0001	-	-
Smoker or ex-smoker	514	1.8 (1.1-2.9)	0.017	514	1.5 (0.90-2.5)	0.12	-	-
Atopy	586	2.1 (1.3-3.4)	0.0021	586	2.4 (1.5-3.9)	0.0005	-	-
Emphysema	452	0.72 (0.36-1.4)	0.34	452	0.66 (0.32-1.3)	0.24	-	-
Bronchiectasis	595	0.86 (0.25-3.0)	0.81	595	0.61 (0.17-2.1)	0.44	-	-
Cardiopathy	595	1.3 (0.73-2.2)	0.41	595	0.94 (0.53-1.7)	0.84	-	-
Diabetes	595	2.3 (1.4-3.8)	0.0013	595	2.1 (1.2-3.5)	0.0060	-	-
History of cancer	595	1.7 (0.91-3.1)	0.099	595	1.3 (0.69-2.5)	0.40	-	-
Immunosuppressive disease	596	0.82 (0.28-2.4)	0.71	596	0.73 (0.25-2.1)	0.57	-	-
Hypertension	595	1.9 (1.2-3.0)	0.0070	595	1.3 (0.98-2.7)	0.061	-	-
Dyslipemia	595	1.9 (1.2-3.2)	0.0083	595	1.6 (0.92-2.6)	0.10	-	-
Obesity	595	9.0 (4.5-15)	<0.0001	595	8.5 (5.1-14)	<0.0001	8.5 (5.1-14.1)	<0.0001
CRF	595	0.96 (0.39-2.3)	0.92	595	0.82 (0.33-2.0)	0.68	-	-
GOR	576	1.9 (1.04-3.4)	0.036	576	1.6 (0.85-2.9)	0.15	-	-
Asthma	596	1.3 (0.61-2.6)	0.53	596	1.4 (0.69-3.0)	0.33	1.4 (0.64-3.2)	0.39
COPD	596	1.4 (0.67-3.1)	0.34	596	1.1 (0.52-2.5)	0.74	0.94 (0.39-2.2)	0.89
Anxiolytics	577	1.4 (0.64-2.9)	0.41	577	1.1 (0.48-2.4)	0.86	-	-
Aspirin	577	2.4 (1.5-4.1)	0.0007	577	1.9 (1.1-3.5)	0.030	-	-
Azithromycin	583	13 (1.2-150)	0.035	583	13 (1.1-152)	0.041	-	-
ICS	596	1.9 (0.91-3.8)	0.088	596	1.8 (0.85-3.7)	0.13	-	-
OCS	596	2.1 (0.81-5.5)	0.13	596	2.1 (0.80-5.6)	0.13	-	-
Blood test at admission								
White blood cells, /mm ³ #	397	2.9 (1.7-4.8)	<0.0001	397	2.9 (1.7-4.8)	<0.0001	-	-
Lymphocytes, /mm ³ #	395	0.64 (0.41-0.99)	0.047	395	0.60 (0.38-0.96)	0.031	-	-
Neutrophils, /mm ³ #	395	2.9 (1.8-4.5)	<0.0001	395	2.9 (1.9-4.6)	<0.0001	-	-
Eosinophils, /mm ³ #	395	0.91 (0.87-0.96)	0.0001	395	0.91 (0.87-0.96)	0.0002	-	-
Basophils, /mm ³ #	395	0.99 (0.92-1.1)	0.70	395	0.99 (0.92-1.1)	0.77	-	-
Monocytes, /mm ³ #	395	1.02 (0.87-1.2)	0.83	395	1.02 (0.87-1.2)	0.80	-	-
Platelets, /mm ³ #	396	0.77 (0.46-1.3)	0.31	396	0.78 (0.46-1.3)	0.34	-	-
Red blood cells, 10 ⁶ /mm ³	388	1.4 (0.997-2.0)	0.052	388	1.3 (0.91-1.8)	0.46	-	-
Hemoglobin, g/dL	396	1.1 (1.02-1.3)	0.024	396	1.1 (0.99-1.3)	0.086	-	-
GFR ml/min/1.73m ²	392	0.99 (0.98-0.99)	0.0057	392	0.98 (0.97-0.99)	0.0001	-	-
Creatinin, mg/dL #	393	1.9 (1.2-3.1)	0.011	393	2.1 (1.3-3.6)	0.0042	-	-
Urea, mg/dL #	391	1.9 (1.2-2.9)	0.0027	391	2.7 (1.7-4.3)	<0.0001	-	-
Albumin, g/L	355	0.92 (0.88-0.97)	0.0022	355	0.90 (0.86-0.95)	0.0002	-	-
Total proteins, g/L	367	0.98 (0.95-1.01)	0.15	367	0.97 (0.94-1.001)	0.057	-	-
Bicarbonates, mmol/l	341	0.97 (0.91-1.04)	0.34	341	0.97 (0.91-1.04)	0.39	-	-
CRP, mg/l ###	397	2.1 (1.7-2.8)	<0.0001	397	2.2 (1.7-2.9)	<0.0001	-	-
D-dimers, µg/l #	301	1.6 (1.2-2.0)	0.0009	301	1.7 (1.3-2.3)	0.0002	-	-
Fibrinogen, g/l	348	1.5 (1.3-1.7)	<0.0001	348	1.4 (1.2-1.7)	<0.0001	-	-
Procalcitonin, µg/l #	302	1.6 (1.3-1.9)	<0.0001	302	1.8 (1.4-2.2)	<0.0001	-	-
LDH, U/l #	363	15 (7.4-30)	<0.0001	363	17 (8.1-34)	<0.0001	-	-
CK, U/l #	351	1.5 (1.2-1.9)	0.0003	351	1.5 (1.2-1.9)	0.0003	-	-

Log-transformed ; ## CRP: 0 if ≤25.6, 1 if >25.6 and ≤71.6, 2 if >71.6 and ≤148.7, 3 if >148.7 and ≤500.

COPD: chronic obstructive pulmonary disease, BMI: body mass index, ICS: inhaled corticosteroids, OCS: oral corticosteroids, CRF: chronic renal failure, GOR: gastro-esophageal reflux, ICU: intensive care unit.

Table 6. Factors associated with death during hospital admission due to SARS-CoV2 infection. Results of the logistic regression analysis.

	Simple logistic regression			Logistic regression adjusted for age and gender			Multiple logistic regression final model (N=595)	
	N	OR (95%CI)	p-value	N	OR (95%CI)	p-value	OR (95%CI)	p-value
Male gender	596	2.2 (1.4-3.5)	0.0013	-	-	-	1.9 (1.1-3.2)	0.016
Age (by 10 years)	596	1.9 (1.6-2.3)	<0.0001	-	-	-	1.9 (1.6-2.3)	<0.0001
BMI (kg/m ²)	312	1.0 (0.96-1.05)	0.98	312	1.0 (0.97-1.1)	0.47	-	-
Smoker or ex-smoker	514	2.3 (1.4-3.7)	0.0008	514	1.4 (0.81-2.3)	0.24	-	-
Atopy	586	1.03 (0.61-1.7)	0.91	586	1.2 (0.68-2.1)	0.53	-	-
Emphysema	452	1.7 (0.96-3.1)	0.068	452	1.3 (0.68-2.3)	0.46	-	-
Bronchiectasis	595	4.1 (1.47-9.7)	0.0016	595	1.9 (0.73-4.7)	0.20	-	-
Cardiopathy	595	3.6 (2.2-5.8)	<0.0001	595	1.9 (1.1-3.2)	0.018	1.8 (1.05-3.1)	0.033
Diabetes	595	2.3 (1.4-3.9)	0.0011	595	1.8 (1.1-3.1)	0.031	-	-
History of cancer	595	3.2 (1.8-5.7)	<0.0001	595	1.7 (0.94-3.2)	0.078	-	-
Immunosuppressive disease	596	3.4 (1.6-7.2)	0.0020	596	3.8 (1.6-8.6)	0.0017	3.6 (1.5-8.4)	0.0031
Hypertension	595	2.9 (1.8-4.6)	<0.0001	595	1.4 (0.80-2.3)	0.25	-	-
Dyslipemia	595	2.9 (1.8-4.6)	<0.0001	595	1.4 (0.86-2.4)	0.17	-	-
Obesity	595	2.0 (1.2-3.3)	0.0078	595	1.8 (1.1-3.2)	0.029	-	-
CRF	595	3.7 (1.9-7.3)	0.0002	595	2.5 (1.2-5.3)	0.014	-	-
GOR	576	1.8 (1.004-3.2)	0.048	576	0.86 (0.45-1.7)	0.66	-	-
Asthma	596	0.41 (0.15-1.2)	0.098	596	0.59 (0.20-1.8)	0.35	0.74 (0.24-2.3)	0.59
COPD	596	3.6 (1.9-6.9)	<0.0001	596	1.9 (0.95-3.8)	0.071	1.6 (0.80-3.3)	0.18
Anxiolytics	577	2.8 (1.4-5.3)	0.0020	577	1.1 (0.56-2.4)	0.70	-	-
Aspirin	577	3.2 (1.9-5.2)	<0.0001	577	0.97 (0.54-1.7)	0.93	-	-
Azithromycin	583	-	-	583	-	-	-	-
ICS	596	1.7 (0.79-3.4)	0.18	596	1.4 (0.62-3.0)	0.44	-	-
OCS	596	2.1 (0.82-5.6)	0.12	596	2.5 (0.88-7.2)	0.085	-	-
<i>Blood test at admission</i>								
White blood cells, /mm3 [#]	397	2.1 (1.3-3.4)	0.0041	397	2.1 (1.2-3.5)	0.0062	-	-
Lymphocytes, /mm3 [#]	395	0.60 (0.38-0.94)	0.027	395	0.74 (0.47-1.2)	0.20	-	-
Neutrophils, /mm3 [#]	395	2.1 (1.4-3.3)	0.0006	395	2.1 (1.3-3.4)	0.0013	-	-
Eosinophils, /mm3 [#]	395	0.95 (0.91-0.99)	0.028	395	0.94 (0.90-0.99)	0.024	-	-
Basophils, /mm3 [#]	395	0.94 (0.88-1.003)	0.060	395	0.94 (0.88-1.004)	0.067	-	-
Monocytes, /mm3 [#]	395	0.78 (0.65-0.93)	0.0060	395	0.74 (0.60-0.90)	0.0034	-	-
Platelets, /mm3 [#]	396	0.65 (0.39-1.1)	0.11	396	0.78 (0.45-1.3)	0.37	-	-
Red blood cells, 10 ⁶ /mm3	388	0.49 (0.35-0.68)	<0.0001	388	0.48 (0.34-0.70)	0.0001	-	-
Hemoglobin, g/dL	396	0.82 (0.73-0.92)	0.0008	396	0.81 (0.72-0.92)	0.0009	-	-
GFR ml/min/1.73m2	392	0.99 (0.98-1.000)	0.039	392	1.0 (0.99-1.008)	0.83	-	-
Creatinin, mg/dL [#]	393	1.8 (1.1-3.0)	0.017	393	1.3 (0.75-2.3)	0.34	-	-
Urea, mg/dL [#]	391	3.1 (2.0-4.9)	<0.0001	391	2.2 (1.3-3.6)	0.0026	-	-
Albumin, g/L	355	0.84 (0.79-0.89)	<0.0001	355	0.85 (0.80-0.90)	<0.0001	-	-
Total proteins, g/L	367	0.94 (0.91-0.97)	<0.0001	367	0.95 (0.92-0.98)	0.0018	-	-
Bicarbonates, mmol/l	341	0.95 (0.88-1.01)	0.12	341	0.95 (0.89-1.02)	0.19	-	-
CRP, mg/l ^{###}	397	1.9 (1.5-2.4)	<0.0001	397	1.9 (1.4-2.4)	<0.0001	-	-
D-dimers, µg/l [#]	301	1.6 (1.2-2.1)	0.0012	301	1.3 (0.97-1.8)	0.072	-	-
Fibrinogen, g/l	348	1.1 (0.92-1.3)	0.36	348	1.1 (0.94-1.3)	0.22	-	-
Procalcitonin, µg/l [#]	302	1.7 (1.3-2.0)	<0.0001	302	1.5 (1.2-1.9)	0.0002	-	-
LDH, U/l [#]	363	3.0 (1.7-5.2)	<0.0001	363	3.1 (1.7-5.6)	0.0002	-	-
CK, U/l [#]	351	1.4 (1.1-1.7)	0.0040	351	1.3 (1.02-1.7)	0.032	-	-

[#] Log-transformed ; ^{###} CRP: 0 if ≤25.6, 1 if >25.6 and ≤71.6, 2 if >71.6 and ≤148.7, 3 if >148.7 and ≤500.

COPD: chronic obstructive pulmonary disease, BMI: body mass index, ICS: inhaled corticosteroids, OCS: oral corticosteroids, CRF: chronic renal failure, GOR: gastro-esophageal reflux, ICU: intensive care unit.

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