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COVID-19 severity in hospitalized patients with asthma: A matched cohort study

Lacey B. Robinson, MD[a,b,c], Xiaoqing Fu, MS[b], Ingrid V. Bassett, MD, MPH[c,d,e], Virginia A. Triant, MD, MPH[c,d,f,g], Andrea S. Foulkes, PhD[f,g,h], Yuqing Zhang, DSc[a,b,c], Carlos A. Camargo, Jr, MD, DrPH[a,b,c,i], and Kimberly G. Blumenthal, MD, MSc[a,b,c]

Clinical Implications

- In this matched cohort study conducted in Boston, asthma was not a risk factor for worse outcomes from coronavirus disease 2019 (COVID-19) infection. Further understanding the association between asthma and COVID-19 is critical in guiding patient care as the pandemic continues.

Coronavirus disease 2019 (COVID-19), caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is a global health crisis. The United States (US) became an epicenter for COVID-19, reporting the highest of number cases and deaths in the world.[1] In the spring of 2020, Massachusetts experienced a significant epidemic.

Viral respiratory infections are known to be more severe in patients with asthma.[2] Whether asthma is associated with worse COVID-19 outcomes is unclear, but of clinical importance to approximately 20 million adult US asthma patients.[3] We sought to understand the relation of asthma to COVID-19 severity in a registry of hospitalized patients from Massachusetts General Hospital (MGH).

We performed a matched cohort study using data from the MGH COVID-19 Data Registry for confirmed SARS-CoV-2 infected patients hospitalized at MGH.[4] The registry included 866 COVID-19 inpatients (hospitalized March 8, 2020, to April 27, 2020) and was created using both manual chart review and coded data extraction from the electronic health record in the Mass General Brigham Enterprise Data Warehouse. Trained chart reviewers extracted demographics, comorbid conditions, intensive care unit (ICU) admission, clinical complications, and death.

We identified adult ($\geq$18 years of age) registry patients with a positive SARS-CoV-2 polymerase chain reaction test and diagnosis of asthma by chart review, with chart verification by a board-certified allergist/immunologist (LBR). For each COVID-19 asthma inpatient, we identified up to 5 COVID-19 non-asthma inpatient comparators matched on age (within 5 years), sex, and date of positive SARS-CoV-2 test (within 7 days). For patients with multiple test dates, the earliest date was used. We excluded patients with other chronic lung disease (eg, chronic obstructive pulmonary disease [COPD], cystic fibrosis, interstitial lung disease) from both asthma and comparator cohorts. The primary outcomes considered were ICU admission, mechanical ventilation, and death.

Person-days of follow-up for each patient were computed as the amount of time from the date of the hospitalization to the date of the ICU (or mechanical ventilation, or death) or discharge from hospital. We examined the relation of asthma to COVID-19 outcomes using multivariable-adjusted Cox-proportional hazards models; for the outcomes of ICU admission and mechanical ventilation, models accounted for the competing risk of death. Multivariable models included covariates selected *a priori*. Statistical analyses were completed using SAS (version 9.4; SAS Institute, Inc., Cary, NC), with a 2-tailed $P < .05$ considered statistically significant.

We matched 80 asthma inpatients with COVID-19 to 323 comparators (Table I). Inpatients with asthma were similar to their comparators for matching variables (age, sex), as well as race/ethnicity, smoking status, and comorbid conditions. Asthma patients had a higher mean body mass index than their non-asthma comparators (32.9 kg/m^2 vs 30.7 kg/m^2, respectively). Asthma patients had documentation of using short-acting beta-agonist (89%), inhaled corticosteroid with long-acting beta-agonist (26%), inhaled corticosteroid (25%), montelukast (13%), and long-acting antimuscarinic antagonists (6%); none were on biologics.

There were 19 (24%) asthma patients and 108 (33%) comparators who required ICU admission. In the fully adjusted model, the risk of ICU admission was lower among asthma patients than comparators (adjusted hazard ratio [aHR]: 0.52, 95% confidence interval [CI]: 0.30-0.90) (Table II). Mechanical ventilation was used in 12 (15%) asthma patients and 91 (28%) of comparators. In the fully adjusted model, the risk of mechanical ventilation was lower among asthma patients than comparators (aHR: 0.42, 95% CI: 0.21-0.81). Death occurred in 7 (9%) asthma patients and 38 (12%) comparators. In the fully adjusted model, risk of death did not differ between groups (aHR: 0.64, 95% CI: 0.24-1.68). The 7 asthma deaths occurred in patients aged 57 to 88 years, 6 (86%) were male, and all had at least 2 other substantial comorbid conditions, with 4 (57%) having dementia/cognitive impairment that guided prior asthma treatment and code status.

In this matched cohort study of MGH inpatients with COVID-19, we identified that asthma patients were less likely to require ICU admission and mechanical ventilation but were not at increased risk for death.

Given that asthma exacerbations are triggered by viral respiratory infections and that asthma patients have a higher risk of severe illness from other respiratory viruses,[2] asthma was considered a COVID-19 risk factor by the Centers for Disease Control and Prevention.[5] Although current research specifically assessing asthma and COVID-19 remains limited, recent reports suggest that asthma is not overrepresented among severe COVID-19 cases and may not be associated with an increased risk of hospitalization or death.[6-9] However, most of these studies included other pulmonary conditions (eg, COPD) with asthma cases. Although patients with concomitant asthma-COPD may have a higher risk of severe outcomes, this risk appears to be driven by COPD.[5,9] In this study, we uniquely used a strict diagnosis of asthma and excluded patients with additional

TABLE I. Clinical characteristics of COVID-19 patients with and without asthma

Characteristic	Asthma (n = 80)	No asthma* (n = 323)	*P* value†
Age (y), mean (SD)	57 (17)	59 (16)	—
Age group			—
<26	1 (1)	3 (1)	
26-35	7 (8)	19 (6)	
36-45	12 (15)	44 (14)	
46-55	17 (21)	65 (20)	
56-65	18 (23)	87 (27)	
66-75	12 (15)	52 (16)	
76-85	7 (9)	33 (10)	
86-95	6 (8)	20 (6)	
Female	43 (54)	169 (52)	—
Race/ethnicity			.92
Non-Hispanic white	28 (35)	115 (36)	
Non-Hispanic black	10 (13)	35 (11)	
Hispanic	34 (43)	133 (41)	
Other	8 (10)	40 (12)	
Body mass index (kg/m^2), mean (SD)	32.9 (7.7)	30.7 (6.7)	.02
Body mass index category			.05
<18.5	4 (5)	34 (11)	
18.5-24.9	7 (9)	52 (16)	
25-29.9	22 (28)	88 (27)	
30-34.9	25 (31)	87 (27)	
35-39.9	9 (11)	39 (12)	
>40	13 (16)	23 (7)	
Smoking status			.81
Former	22 (28)	86 (27)	
Current	3 (4)	17 (5)	
Never	51 (64)	196 (61)	
Unknown	4 (5)	24 (7)	
Diabetes, type I	0 (0)	1 (<1)	>.99
Diabetes, type II	27 (34)	104 (32)	.79
Hypertension	38 (48)	160 (50)	.74
Coronary artery disease or myocardial infarction	11 (14)	39 (12)	.68
Congestive heart failure	3 (4)	25 (8)	.21
Renal disease	9 (11)	53 (16)	.25
Liver disease	9 (11)	32 (10)	.72
Cancer	8 (10)	45 (14)	.35
Rheumatic or autoimmune	5 (6)	40 (12)	.12
Organ transplantation	0 (0)	9 (3)	.21
HIV	0 (0)	6 (2)	.60
Immunodeficiency	0 (0)	2 (<1)	>.99

Data are represented by mean (SD) or number (percentage) unless otherwise indicated.
COVID-19, Coronavirus disease 2019; *SD*, standard deviation; *SARS-CoV-2*, severe acute respiratory syndrome coronavirus 2.
*Age, sex, and date of SARS-CoV-2 diagnosis matched comparators.
†Compared using a 2-sample *t*-test, Mann-Whitney *U* test, or Fisher-exact test, as appropriate.

chronic pulmonary diseases, thus isolating the association of asthma and risk of worse outcomes among hospitalized COVID-19 patients. With our reduced misclassification of asthma, our findings do not suggest that asthma increases risk of severe outcomes in COVID-19.

The factors that underlie our findings of reduced risk of ICU admission and mechanical ventilation among patients with asthma are not currently known.[8] Our findings may be explained by immune alterations associated with asthma and allergy, including decreased expression of ACE2—the receptor required for SARS-CoV-2 entry into human cells.[9] Future studies should explore the differences in risk associated with asthma phenotypes including allergic and nonallergic asthma.

Because all patients in our study were hospitalized for COVID-19, we are unable to estimate the total population effect of asthma on the risk of severe outcomes from COVID-19. Our study may be affected by collider bias because we restricted the study population to patients with COVID-19. Prospective population-based cohort studies that include patients with and without asthma are required to further understand these associations. We did not consider different COVID-19 treatments; however, all patients were cared for at MGH with the same

TABLE II. Clinical outcomes of COVID-19 patients with asthma and without asthma

Outcomes	Asthma (n = 80)	No asthma (n = 323)*
Intensive care unit admission		
No. of events	19 (24)	108 (33)
Rate of event per 1000 person-days	3.43 (1.89, 4.98)	5.66 (4.59, 6.73)
Matched unadjusted hazard ratio (95% CI)†	0.64 (0.40, 1.02)	1.00 (reference)
Partially adjusted hazard ratio (95% CI)‡	0.53 (0.31, 0.90)	1.00
Fully adjusted hazard ratio (95% CI)§	0.52 (0.30, 0.90)	1.00
Mechanical ventilation		
No. of events	12 (15)	95 (28)
Rate of event per 1000 person-days	1.96 (0.85, 3.07)	4.67 (3.73, 5.61)
Matched unadjusted hazard ratio (95% CI)†	0.52 (0.29, 0.94)	1.00 (reference)
Partially adjusted hazard ratio (95% CI)‡	0.42 (0.22, 0.80)	1.00
Fully adjusted hazard ratio (95% CI)§	0.42 (0.21, 0.81)	1.00
Death		
No. of events	7 (9)	38 (12)
Rate of event per 1000 person-days	1.02 (0.26, 1.77)	1.40 (0.95, 1.84)
Matched unadjusted hazard ratio (95% CI)†	0.70 (0.32, 1.52)	1.00 (reference)
Partially adjusted hazard ratio (95% CI)‡	0.78 (0.32, 1.92)	1.00
Fully adjusted hazard ratio (95% CI)§	0.64 (0.24, 1.68)	1.00

CI, Confidence interval; *COVID-19*, coronavirus disease 2019; *SARS-CoV-2*, severe acute respiratory syndrome coronavirus 2.
*Age, sex, and date of SARS-CoV-2 diagnosis matched comparators.
†Matched on age, sex, and date of SARS-CoV-2 test.
‡Matched on age, sex, and date of SARS-CoV-2 test and adjusted for race/ethnicity, body mass index, and smoking status.
§Matched on age, sex, and date of SARS-CoV-2 test and adjusted for race/ethnicity, body mass index, smoking status, and comorbid conditions (diabetes type II, coronary artery disease or myocardial infarction, liver disease, and rheumatic or autoimmune disease).

treatment protocols and there was no approved treatment at the time of this study.

In summary, among patients hospitalized for COVID-19, asthma was not associated with an increased risk of ICU admission, mechanical ventilation, or death compared with inpatient comparators matched by age, sex, and date of positive SARS-CoV-2 test.

Acknowledgments

We would like to acknowledge all members of the MGH COVID-19 registry for their work on the development and data management for the registry. We thank Christian M. Mancini for his research assistance.

L. B. Robinson, Y. Zhang, C. A. Camargo, and K. G. Blumenthal were involved in the study conception or design. L. B. Robinson, I. V. Bassett, V. A. Triant, and A. S. Foulkes acquired the data; X. Fu, A. S. Foulkes, and Y. Zhang analyzed the data. Lacey B. Robinson, Xiaoqing Fu, Y. Zhang, and K. G. Blumenthal drafted the initial report. All authors critically revised the manuscript and involved in the final approval of the manuscript version to be published.

The authors agree that they are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

[a]Division of Rheumatology, Allergy, and Immunology, Massachusetts General Hospital, Boston, Mass
[b]Clinical Epidemiology Program, Mongan Institute, Department of Medicine, Massachusetts General Hospital, Boston, Mass
[c]Harvard Medical School, Boston, Mass
[d]Division of Infectious Disease, Massachusetts General Hospital, Boston, Mass
[e]Medical Practice Evaluation Center, Mongan Institute, Department of Medicine, Massachusetts General Hospital, Boston, Mass
[f]Division of General Internal Medicine, Massachusetts General Hospital, Boston, Mass
[g]Mongan Institute, Massachusetts General Hospital, Boston, Mass
[h]Biostatistics Center, Massachusetts General Hospital, Boston, Mass
[i]Emergency Medicine Network, Department of Emergency Medicine, Massachusetts General Hospital, Boston, Mass

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. L. B. Robinson was supported by the National Institutes of Health (NIH) T32 HL116275. I. V. Bassett is supported by the NIH K24AI141036 and the Weissman Family MGH Scholar Award. V. A. Triant is supported by NIH R01HL132786 and NIH R01AG062393. C. A. Camargo is supported, in part, by grant R01AI127507 from the NIH. K. G. Blumenthal is supported by NIH K01AI125631, the American Academy of Allergy Asthma and Immunology Foundation (AAAAI), and the MGH Claflin Distinguished Scholars Award. The MGH COVID patient registry is supported by the MGH Division of Clinical Research. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH, AAAAI Foundation, nor the MGH.

Conflicts of interest: The authors declare that they have no relevant conflicts of interest.

Received for publication September 15, 2020; revised October 11, 2020; accepted for publication October 12, 2020.

Available online October 22, 2020.

Corresponding author: Lacey B. Robinson, MD, Massachusetts General Hospital, 55 Fruit Street, Bulfinch 165, Boston, MA 02114. E-mail: lbrobinson@mgh.harvard.edu.

2213-2198

https://doi.org/10.1016/j.jaip.2020.10.021

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