Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Table 1
Characteristics of Patients With SARS-CoV-2

Characteristics	SARS-CoV-2	SARS-CoV-2 and asthma	
Total patients, n (%)	6310 (100)	577 (9.14)	
Mean age, y	59 ± 19	55 ± 20	MD: 4 ± 19 (CI: 2.3-5.6), $P < .001$[a]
Sex (woman), n (%)	3327 (59)	379 (66)	OR: 1.72 (CI: 1.4-2.0), $P < .001$[b]
Hospitalization, n (%)	2164 (34.2)	131 (22.7)	OR: 0.56 (CI: 0.46-0.59), $P < .001$[b]
Mortality, n (%)	250 (3.96)	21 (3.64)	OR: 1.00 (CI: 0.6-1.7), $P = .03$[b]
HBP, n (%)	3239 (51)	296 (51)	OR: 1.00 (CI: 0.8-1.1), $P = .98$[b]
Dyslipidemia, n (%)	2283 (36)	216 (37)	OR: 1.00 (CI: 0.8-1.2), $P = .54$[b]
DM, n (%)	1641 (26)	142 (25)	OR: 1.10 (CI: 0.7-1.3), $P = .46$[b]
Smoking, n (%)	873 (14)	103 (18)	OR: 1.35 (CI: 1.1-1.6), $P = .008$[b]

Abbreviations: CI, confidence interval; DM, diabetes mellitus; HBP, high blood pressure, MD, mean difference; OR: odds ratio; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.
[a]Student's *t* test.
[b]χ^2 test.

More studies are, therefore, needed to conclude whether asthma is a factor that increases the severity of the SARS-CoV-2 infection.

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Asthma is associated with increased risk of intubation but not hospitalization or death in coronavirus disease 2019

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Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has caused considerable morbidity and mortality. COVID-19 often presents with respiratory symptoms; however, the role of asthma in COVID-19 has not been well established. Although studies from China suggested that asthma was not a risk factor for severe COVID-19, other studies have revealed higher rates of asthma among hospitalized patients.[1,2] Therefore, the primary aim of this study was to assess the associations between asthma and hospitalization, intensive care unit (ICU) admission, or death among patients with COVID-19. Secondary objectives were to assess the associations between asthma and intubation, duration of intubation and hospitalization, and inflammatory markers in COVID-19.

This retrospective study was conducted at the George Washington University School of Medicine and Health Sciences in Washington, DC, and approved by its institutional review board. Patients were identified by an electronic medical record search of positive SARS-CoV-2 polymerase chain reaction test results between March and May 2020. Patients with underlying lung disease other than asthma were excluded. Demographics, clinical history, and laboratory markers (trough white blood cell, platelet, and lymphocyte counts; peak D-dimer, ferritin, C-reactive protein [CRP], lactate dehydrogenase [LDH], and interleukin-6 [IL-6] levels) were collected. Diagnosis of asthma was based on the *International Classification of Diseases, Tenth Revision* codes and verified by clinical history by a board-certified allergist.

A total of 787 patients with confirmed SARS-CoV-2 were identified. A total of 60 patients were excluded owing to unknown medical history or pulmonary disease other than asthma,

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Table 1
Clinical Characteristics

Characteristic	Overall, N = 727 (100%)	Non asthma, N = 622 (85.6%)	Asthma, N = 105 (14.4%)
Age, mean (SD)	49.46 (17.93)	49.95 (18.16)	46.61 (16.28)
BMI, mean (SD)	30.56 (8.14)	29.91 (7.57)	33.73 (9.92)
Allergic asthma	36 (4.9)	0 (0.0)	36 (34.3)
Race			
White	82 (11.3)	75 (12.0)	7 (6.7)
African American	380 (52.2)	315 (50.6)	65 (61.9)
Asian	31 (4.3)	29 (4.7)	2 (1.9)
Latino	70 (9.6)	61 (9.8)	9 (8.6)
Other or unknown	164 (22.6)	143 (23.0)	22 (21.0)
Risk factors			
CKD	63 (8.7)	58 (9.3)	5 (4.8)
Diabetes	165 (22.7)	145 (23.3)	20 (19.0)
CHF or CAD	27 (3.7)	26 (4.2)	1 (1.0)
HTN	278 (38.2)	243 (39.0)	35 (33.3)
Number of risk factors			
0	405 (55.7)	342 (54.9)	64 (61.0)
1	157 (21.6)	132 (21.2)	25 (23.8)
2	104 (14.3)	92 (14.8)	12 (11.4)
3	44 (6.0)	41 (6.6)	3 (2.9)
4	15 (2.1)	14 (2.2)	1 (1.0)
5	2 (0.3)	2 (0.3)	0 (0.0)
Outcomes			
Hospitalization with eventual discharge	274 (37.6)	235 (37.7)	39 (37.1)
ICU admission with eventual discharge	68 (9.3)	57 (9.1)	11 (10.5)
Death	61 (8.4)	51 (8.2)	10 (9.5)
Hospital length of stay	9.89 (9.14)	9.70 (8.91)	11.11 (10.46)
Intubation	44 (6.1)	33 (5.3)	11 (10.5)
Intubation length	11.14 (8.52)	11.32 (8.56)	10.44 (8.83)

Abbreviations: BMI, body mass index; CAD, coronary artery disease; CHF, congestive heart failure; CKD, chronic kidney disease; HTN, hypertension; ICU, intensive care unit.

resulting in 727 patients in the final analysis. We assessed whether asthma was associated with hospitalization using a multivariable logistic regression model, adjusting for age, body mass index, race, and a number of comorbidities (chronic kidney disease, coronary artery disease or congestive heart failure, diabetes, and hypertension). In addition, we assessed whether asthma was associated with outcome severity after hospitalization using an adjusted proportional odds model.[3] We used multivariate imputation by chained equations to generate 100 datasets with imputed values for 209 patients with missing body mass index measurements.[4] The imputation model included all levels of outcome severity and the covariates in our primary regression models.

We assessed whether intubation was associated with asthma using a Fisher's exact test, with exact confidence intervals.[5] Differences in mean duration of hospitalization and intubation were compared using 2-sided *t* tests. We used Wilcoxon ranked sum tests to assess the relationship between biomarkers and asthma. Statistical significance was summarized using nominal *P* values. All analyses were carried out using the R software, version 4.0.2 (The R Foundation, Vienna, Austria).[6]

Of the 727 patients, 274 (37.6%) were admitted to the hospital but did not require ICU-level care, 68 (9.3%) required ICU care but were discharged, and 61 (8.3%) died. A total of 105 patients (14.4%) had asthma. The proportion of patients with asthma treated as an outpatient vs those hospitalized were similar (14.6% vs 14.2%, respectively). Patient characteristics are summarized in Table 1.

Asthma was not significantly associated with hospitalization, ICU admission, or death. The adjusted odds of hospitalization among the patients with asthma was 1.4 times higher than those without asthma (95% confidence interval [CI], 0.82-2.4; $P = .22$). The adjusted odds of death vs either hospitalization or ICU admission or equivalently of death or ICU admission vs hospitalization was 1.3 times higher among patients with asthma (95% CI, 0.6-2.8; $P = .48$). Age, number of comorbidities, and race (non-White vs White; $P = .01$) were associated with increased odds of hospitalization.

The odds of intubation were 2-fold higher among patients with asthma than those without asthma (odds ratio, 2; 95% CI, 1-fold to 4-fold; $P = .047$). However, there was no significant difference in duration of intubation ($P = .44$) or hospitalization ($P = .44$). Asthma was associated with a higher platelet count (208 vs 191; $P = .046$). However, there was no association between asthma and leukopenia ($P = .43$), lymphopenia ($P = .26$), CRP ($P = .44$), D-dimer ($P = .36$), LDH ($P = .43$), ferritin ($P = .31$), or IL-6 ($P = .19$). Furthermore, we were unable to evaluate the association between biologic medications for asthma and COVID-19 outcomes, as only 1 patient with asthma was receiving a biologic (omalizumab) and did not require hospitalization.

This study assessed whether asthma was associated with COVID-19 severity with regard to outcomes and laboratory biomarkers. The proportion of patients with asthma and COVID-19 treated as an outpatient vs those hospitalized was similar. Our patients had a slightly higher prevalence of asthma than the overall prevalence of asthma in Washington, DC (14.4% vs 11%, respectively),[7] suggesting asthma may confer a slightly increased risk of contracting COVID-19. Even with the higher prevalence, asthma was not associated with hospitalization, ICU admission, or death. This is consistent with the study by Chhiba et al[8] that also did not find an association between asthma and risk of hospitalization.

In this study, patients with asthma were more likely to be intubated than those without asthma. This may reflect a lower threshold for intubating patients with asthma rather than more severe clinical disease. Mahdavinia et al[9] found a longer duration of intubation among patients with asthma, but our study revealed no association between asthma and duration of intubation or hospitalization.

Inflammatory markers, including leukopenia and lymphopenia, have been associated with severe COVID-19.[10] Chhiba et al[8] found that patients with asthma had significantly lower levels of ferritin, CRP, and LDH than those without asthma with COVID-19.[9] However, we did not find an association between asthma and laboratory parameters except for thrombocytopenia, which was likely not clinically significant.

Regarding study limitations, this was a retrospective study at a single medical center. We only had access to the electronic medical record from this center and were unable to identify the patients who may have been hospitalized at other institutions. Because this was a retrospective study, we are unable to make any causative associations.

In conclusion, there was no association between asthma and risk of hospitalization, ICU admission, or death among patients with COVID-19. Asthma was associated with increased odds of intubation, but not with duration of intubation or hospitalization. This study adds to the growing literature that patients with asthma may not be at a higher risk of severe outcomes with COVID-19.

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Delayed hypersensitivity reactions to edoxaban

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Edoxaban is the fourth approved direct oral anticoagulant (DOAC) that has been introduced in the European market (2015), after dabigatran (2008), rivaroxaban (2008), and apixaban (2011). Dabigatran is the only direct thrombin inhibitor, whereas apixaban, edoxaban, and rivaroxaban are factor-Xa inhibitors. In a few years, DOAC use has steadily increased in clinical practice for the prevention of stroke and systemic embolism in adult patients with nonvalvular atrial fibrillation (NVAF)[1] and for the treatment and prevention of recurrent deep vein thrombosis and pulmonary embolism.[2]

A better safety profile, ease of monitoring, and probable noninferior therapeutic effectiveness have led to increased use of DOACs in many countries. Although hemorrhage-related adverse reactions of DOACs have been well characterized, nonhemorrhage-related adverse effects have been reported, which considerably complicates management of these patients. Although drug hypersensitivity reactions (DHRs) are relatively uncommon, it is important to consider that clinicians may prefer to maintain patients on a different DOAC as opposed to switching to warfarin and may need guidance from an allergist on how to proceed. Several case reports of DHR to dabigatran, rivaroxaban, and apixaban[3] have been published, but to our knowledge, only a few cases of delayed hypersensitivity to edoxaban have been described in the literature thus far.[4,5] We report 3 cases of suspected DHR to edoxaban referred to our clinic in the previous 5 months.

To give consistency and collect all relevant available information, a standardized questionnaire developed by the European Network for Drug Allergy[6] was used as a guide and recommended algorithms for causality assessment, that is, the World Health Organization–Uppsala Monitoring Centre causality assessment system[7] and the Naranjo Adverse Drug Reaction Probability Scale[8] were applied.

A 70-year-old White man, with a medical history of cardiac amyloidosis and smoldering myeloma, was hospitalized for worsening dyspnea and fever. At admission, antibiotic therapy (clarithromycin) was started and edoxaban was prescribed for the treatment of newly diagnosed NVAF. The patient's home medications were continued (furosemide, atorvastatin, and tamsulosin). After 5 days, he developed a pruritic, maculopapular exanthema on the trunk and lower limbs. Routine laboratory test results were within normal ranges, including complete blood cell count, erythrocyte sedimentation rate, and serum beta 2 microglobulin, whereas the qualitative Bence-Jones protein test result was negative. Clarithromycin was stopped, edoxaban was replaced with fondaparinux, and systemic corticosteroids and antihistamines were given for 4 to 5 days with complete resolution of the skin lesions. Upon discharge, the patient was instructed to start anticoagulation therapy with warfarin in addition to all the other home medications and was referred for further allergy evaluation. After 1 month of discharge, the patient had completed a 7-day course of clarithromycin for a new upper airway infection without any adverse reaction. Furthermore, he lamented significant difficulty in maintaining therapeutic international normalized ratio values. Graded challenge test with rivaroxaban (drug indicated by cardiologist) was performed and well tolerated. The patient is still taking the drug.

A 73-year-old White woman with a suspected hypersensitivity to edoxaban was referred to our unit. Her past medical history included ischemic stroke in NVAF in 2016, acute myocardial

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