

# Continued In-Hospital Angiotensin-Converting Enzyme Inhibitor and Angiotensin II Receptor Blocker Use in Hypertensive COVID-19 Patients Is Associated With Positive Clinical Outcome

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**Background.** This study investigated continued and discontinued use of angiotensin-converting enzyme inhibitors (ACEi) or angiotensin II receptor blockers (ARB) during hospitalization of 614 hypertensive laboratory-confirmed COVID-19 patients.

**Methods.** Demographics, comorbidities, vital signs, laboratory data, and ACEi/ARB usage were analyzed. To account for confounders, patients were substratified by whether they developed hypotension and acute kidney injury (AKI) during the index hospitalization.

**Results.** Mortality (22% vs 17%,  $P > .05$ ) and intensive care unit (ICU) admission (26% vs 12%,  $P > .05$ ) rates were not significantly different between non-ACEi/ARB and ACEi/ARB groups. However, patients who continued ACEi/ARBs in the hospital had a markedly lower ICU admission rate (12% vs 26%;  $P = .001$ ; odds ratio [OR] = 0.347; 95% confidence interval [CI], .187–.643) and mortality rate (6% vs 28%;  $P = .001$ ; OR = 0.215; 95% CI, .101–.455) compared to patients who discontinued ACEi/ARB. The odds ratio for mortality remained significantly lower after accounting for development of hypotension or AKI.

**Conclusions.** These findings suggest that continued ACEi/ARB use in hypertensive COVID-19 patients yields better clinical outcomes.

**Keywords.** angiotensin-converting enzyme inhibitors; angiotensin II receptor blockers; troponin; hypotension; acute kidney injury.

Hypertension is a common comorbidity in patients with coronavirus disease 2019 (COVID-19) and has been associated with worse clinical outcomes [1–6]. Because the widely used antihypertensive medications angiotensin-converting enzyme inhibitors (ACEi) and angiotensin II receptor blockers (ARB) may upregulate ACE2 receptors [7–9], through which severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) enters the host cells [10], concerns have been raised as to whether their use may result in increased morbidity and mortality [4, 11–13]. On the other hand, ACE2 has also been shown to have vasodilatory, anti-inflammatory, and antifibrotic effects that could potentially alleviate disease severity [14–16].

Several clinical studies have reported that ACEi/ARB use in COVID-19 patients with hypertension does not worsen COVID-19 disease severity or mortality [16–22]. However, these studies have either focused on ACEi/ARB use prior to hospitalization or did not control for potential clinical interactions for which ACEi/ARB use might be discontinued, such as the development of hypotension or acute kidney injury (AKI). Despite limited data, a number of professional societies [23, 24] have released statements recommending that ACEi/ARBs should be continued in hypertensive COVID-19 patients [25, 26]. This is based, in part, on the belief that these agents serve a beneficial role in treating underlying cardiovascular disease and may preclude further clinical deterioration.

Stony Brook University Hospital, about 40 miles east of New York City, is the largest academic hospital in Suffolk County, serving a population of approximately 1.5 million people and with over 39 000 laboratory-confirmed COVID-19 patients at the time of this analysis. The goal of this study was to investigate the effects of in-hospital continuation and discontinuation of ACEi/ARBs on the clinical outcomes of hypertensive COVID-19 patients, controlling for newly developed hypotension or AKI during hospitalization.

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## METHODS

### Study Population and Data Collection

This retrospective single-center study from Stony Brook University Hospital was approved by the Human Subjects Committee with an exemption for informed consent and a Health Insurance Portability and Accountability Act (HIPAA) waiver. The Stony Brook University Hospital COVID-19 Persons Under Investigation Registry consisted of 6235 patients clinically suspected of COVID-19 infection from 7 February 2020 to 23 May 2020. Confirmation of COVID-19 infection was based on a positive real-time polymerase chain reaction test for SARS-CoV-2 on a nasopharyngeal swab specimen. Clinical data at hospital admission, including demographic information, chronic comorbidities present on admission, vital signs, laboratory blood tests, and outcomes, were extracted individually from the patients' electronic medical records. The primary outcome was in-hospital mortality and the secondary outcome was intensive care unit (ICU) admission.

Patients were divided into 2 groups; hypertensive patients: (1) that were not taking ACEi/ARBs at home (group A), and (2) taking ACEi/ARBs at home. The latter group was further divided into those who discontinued ACEi/ARBs during their hospital stay (group B), and those who continued ACEi/ARBs during their hospital stay (group C).

### Statistical Analysis

Frequencies and percentages for categorical variables between the ACEi/ARB groups were compared using  $\chi^2$  tests. Continuous variables, expressed as median (interquartile range [IQR]), were compared between groups using nonparametric Mann-Whitney *U* tests. Bonferroni correction for multiple comparisons was used where appropriate. Mortality and ICU admission rates were compared between group B (ACEi/ARB discontinued) and C (ACEi/ARB continued) with  $\chi^2$  tests (unadjusted without covariates) and with logistic regression (adjusted with covariates). Age, sex, and significantly different comorbidities between groups were included in logistic regression models as covariates for controlling confounding effects. Analyses were also stratified by hypotension and AKI status. *P* values < .05 were considered statistically significant. All statistical analyses were performed using SPSS version 26 (IBM Corporation).

## RESULTS

### Patient Selection

The Stony Brook University Hospital COVID-19 Persons Under Investigation Registry consisted of 6235 patients clinically suspected of COVID-19 infection who presented to the emergency department between 7 February and 23 May 2020, of which 2789 were confirmed to be COVID-19 positive (Figure 1). There were 875 patients in this cohort who had a history of hypertension. We excluded 211 patients who were discharged

directly from the emergency department, 5 who were transferred to other hospitals, and 45 whose discharge status was still unknown as of 23 May 2020. This yielded a final sample size of 614 hospitalized COVID-19 patients with a history of hypertension. Group A consisted of 279 hypertensive patients who did not take ACEi/ARBs prior to admission, of whom 224 did not require ICU care (ie, general admission) and 55 required ICU care at any point during hospitalization. There were 62 deaths in this group. Group B consisted of 171 hypertensive patients who discontinued their home medications, ACEi/ARBs, in the hospital, of whom 126 did not require ICU care and 45 required ICU care. There were 48 deaths in this group. Group C consisted of 164 hypertensive patients who continued their home medications, ACEi/ARBs, in the hospital, of whom 144 did not require ICU care and 20 required ICU care. There were 10 deaths in this group.

### Patient Demographics, Comorbidities, and Laboratory Tests

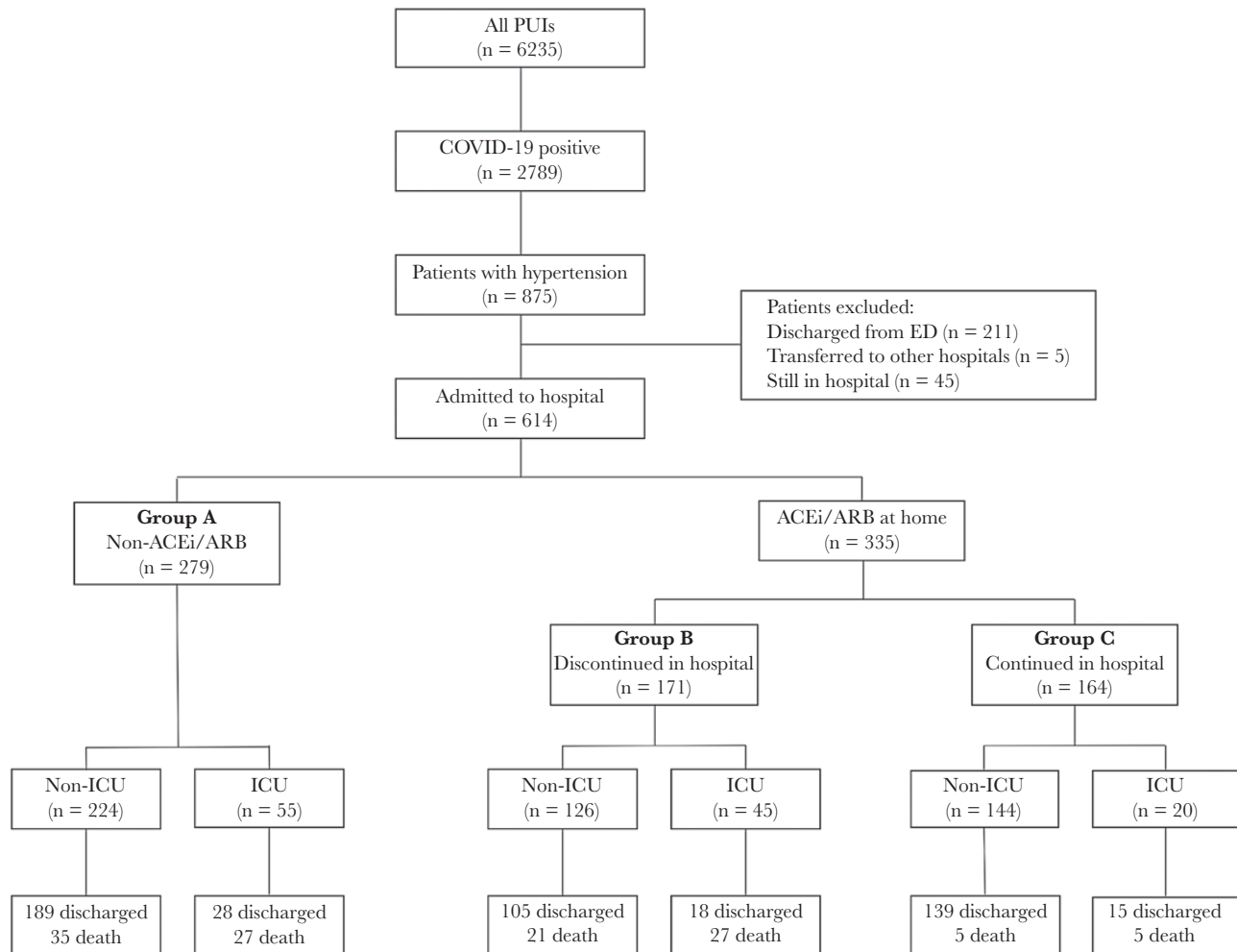
The median age of patients in the non-ACEi/ARB group was older than that of the ACEi/ARB group (73 years [IQR, 62–83] versus 68 years [IQR, 58–79], *P* = .004; Table 1). Sex and ethnicity were not significantly different between groups (*P* > .05). The prevalence of diabetes mellitus was higher in those in the ACEi/ARB group (*P* = .01) but lower in those with chronic kidney disease (CKD) at baseline (*P* = .001), whereas the prevalence of asthma, history of coronary heart disease, chronic obstructive pulmonary disease, and cancer were not significantly different between groups (*P* > .05). Note that the prevalence of CKD in our hypertensive COVID-19 patient cohort was higher than that for all COVID-19 patients in general [27] as expected.

Hematocrit (*P* = .003), sodium (*P* = .001), D-dimer (*P* = .003), and troponin (*P* = .005) levels were significantly different between the non-ACEi/ARB and ACEi/ARB groups after correction for multiple comparisons (Table 2). Elevated D-dimer and troponin levels have been previously associated with a more severe COVID-19 disease course [7, 18–20].

### Mortality

For hypertensive COVID-19–positive patients, the mortality was not statistically different between the non-ACEi/ARB and ACEi/ARB groups (unadjusted *P* = .127 without covariates, adjusted *P* = .336 with covariates; Figure 2A). By contrast, patients in the ACEi/ARB group who continued these medications in the hospital (group C) had a significantly lower mortality rate compared to those who discontinued ACEi/ARB in the hospital (group B) (unadjusted *P* = .001, adjusted *P* = .001; Figure 2B). The odds ratio was 0.215 (95% confidence interval, .101–.455).

The percentage of hospitalized patients who developed hypotension subsequent to the index hospitalization was higher in the discontinued ACEi/ARG group than the continued ACEi/ARG group (42.7%, 73/171 vs 15.69%, 26/164, respectively; *P* = .001). The percentage of hospitalized patients who



**Figure 1.** Flowchart of patient selection. Abbreviations: ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; ED, emergency department; ICU, intensive care unit; PUI, persons under investigation.

developed AKI subsequent to the index hospitalization was higher in the discontinued ACEi/ARB group than the continued ACEi/ARB group (59.1%, 101/171 vs 18.9%, 31/164, respectively;  $P = .001$ ).

Thus, mortality was stratified with respect to development of hypotension and AKI (Table 3). In patients that developed in-hospital hypotension, there was no significant difference in mortality between continuing or discontinuing ACEi/ARBs ( $P > .05$ ). In contrast, patients who did not develop hypotension and continued ACEi/ARBs had a significantly lower mortality rate than those who discontinued (unadjusted  $P = .001$ , adjusted  $P < .017$ ). Similarly, in patients who developed AKI, there was no significant difference in mortality between continuing or discontinuing ACEi/ARBs in the hospital (unadjusted  $P = .050$ , adjusted  $P = .117$ ). In patients who did not develop AKI, those who continued ACEi/ARBs had a significantly lower mortality rate than those who discontinued (unadjusted  $P = .001$ , adjusted  $P = .011$ ).

#### ICU Admission

The ICU admission rates were not significantly different between the non-ACEi/ARB and ACEi/ARB groups (unadjusted  $P = .923$ , adjusted  $P = .391$ ; Figure 3A). By contrast, the ICU admission rate was twice as high in the group that discontinued ACEi/ARBs compared to the group that continued (unadjusted  $P = .001$ , adjusted  $P = .001$ ; Figure 3B).

ICU admission was also stratified with respect to the development of hypotension or AKI (Table 4). In the hypotension and nonhypotension groups, there were no differences in ICU admission rates between continuation versus discontinuation of ACEi/ARBs in the hospital ( $P > .05$ ). Similarly, in the group that developed AKI, there was no difference in ICU admission rates between continuing or discontinuing ACEi/ARBs in the hospital ( $P > .05$ ). However, in patients who did not develop AKI, those who continued ACEi/ARBs had a significantly lower mortality rate than those who discontinued these agents (unadjusted  $P < .041$ , adjusted  $P = .043$ ).

**Table 1. Characteristics of Patients Who Did Not Receive ACEi/ARB (Group A) and Who Did Receive ACEi/ARB (Groups B and C)**

Demographics	Non-ACEi/ARB (Group A, n = 279)	ACEi/ARB (Groups B + C, n = 335)	P Value
Age, y, median (IQR)	73 (62–83)	68 (58–79)	<b>.004</b>
Hospital stay duration, d, median (IQR)	6 (3–11)	7 (4–12)	NS
<b>Sex</b>			
Female	130 (46.6)	146 (43.6)	NS
Male	149 (53.4)	189 (56.4)	
<b>Ethnicity</b>			
White	176 (63.1)	200 (59.7)	NS
African American	25 (9.0)	27 (8.1)	
Asian	9 (3.2)	13 (3.9)	
Native American	3 (1.1)	0 (0)	
Other	66 (23.6)	95 (28.4)	
<b>Comorbidities</b>			
Diabetes	98 (35.1)	152 (45.4)	<b>.010</b>
Asthma	11 (3.9)	22 (6.6)	NS
Coronary heart disease	66 (23.7)	82 (24.6)	NS
COPD	45 (16.1)	37 (11.0)	.065
Heart failure	44 (15.8)	38 (11.3)	NS
Cancer	39 (14.0)	32 (9.6)	.088
Chronic kidney disease	65 (23.4)	30 (9.0)	<b>.001</b>

Values are No. (%) except where indicated. Categorical comparison used  $\chi^2$  tests and continuous comparison used Mann-Whitney *U* tests. Significant values in which *P* < .05 are noted in bold.

Note that the prevalence of CKD in our hypertensive COVID-19 patient cohort was higher than that for all COVID-19 patients [27]. Although the non-ACEi/ARB group was older than the ACEi/ARB group, our statistical analysis included age as a covariate with logistic regression to ensure our primary finding was not due to age per se.

Abbreviations: ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; COPD, chronic obstructive pulmonary disease; IQR, interquartile range; NS, not significant.

## DISCUSSION

This study analyzed in-hospital ACEi/ARB use in hypertensive COVID-19 patients and the associated confounding variables that likely resulted in discontinuation of ACEi/ARB use. The major findings are: (1) hypertensive COVID-19 patients who continued ACEi/ARBs in the hospital had lower in-hospital mortality and ICU admission compared to those who discontinued ACEi/ARBs; (2) for in-hospital mortality, this conclusion remained true after controlling for confounders by excluding patients who developed hypotension or AKI for which ACEi/ARBs were withheld on clinical grounds; and (3) for ICU admission, this conclusion remained true after excluding patients who developed AKI. Overall, patients who were able to continue their ACEi/ARB had markedly lower mortality and ICU admission rates, suggesting that the ability to continue ACEi/ARB use is associated with improved clinical outcomes in hypertensive COVID-19–positive patients and ACEi/ARB may themselves be beneficial.

Although there were initial concerns regarding the safety of ACEi/ARB use in hypertensive COVID-19 patients, the majority of recent clinical studies found neutral effects of ACEi/ARB on

COVID-19 severity. In a propensity score-matched analysis of over 12 500 patients in a New York City health system, Reynolds et al reported that home-use of ACEi/ARBs conferred no significant increase in the likelihood of developing severe COVID-19 [18]. Yang et al conducted a retrospective case-control study in a single institution in Wuhan, China [19]. Similar to Reynolds et al, they reported no significant difference in mortality and disease severity in patients taking ACEi/ARBs, although they noted that patients taking ACEi/ARBs had lower levels of inflammatory markers such as C-reactive peptide and procalcitonin [19]. If these medications are indeed associated with lower inflammatory markers, they could conceivably play a role in mediating the dysregulated inflammatory response seen in severe COVID-19 infections. For the 2 aforementioned studies, it was unclear whether ACEi/ARB use was continued throughout the hospital course. Li et al accounted for inpatient use of ACEi/ARBs in COVID-19 patients, defining ACEi/ARB use as use of the medications at admission and continued throughout hospitalization [20]. They did not compare the outcomes of patients who continued versus discontinued medication use in the hospital. They concluded that the percentages of patients with hypertension taking ACEi/ARBs did not differ between those with severe and nonsevere infections nor did it differ between nonsurvivors and survivors [20]. Meng et al reported potentially positive outcomes in patients taking ACEi/ARBs [21]. In a small cohort of 51 hypertensive COVID-19 patients from Wuhan, China, they found that patients on ACEi/ARBs included fewer severe cases [21]. Zhang et al found similar positive associations [22]. They used propensity score matching for age, sex, symptoms, comorbidities, creatinine, and other variables. They reported that inpatient ACEi/ARB use was associated with lower mortality rates compared to non-ACEi/ARB users [22]. However, this study did not account for confounding clinical factors for which ACEi/ARBs may be discontinued, such as the development of AKI or hypotension during hospitalization.

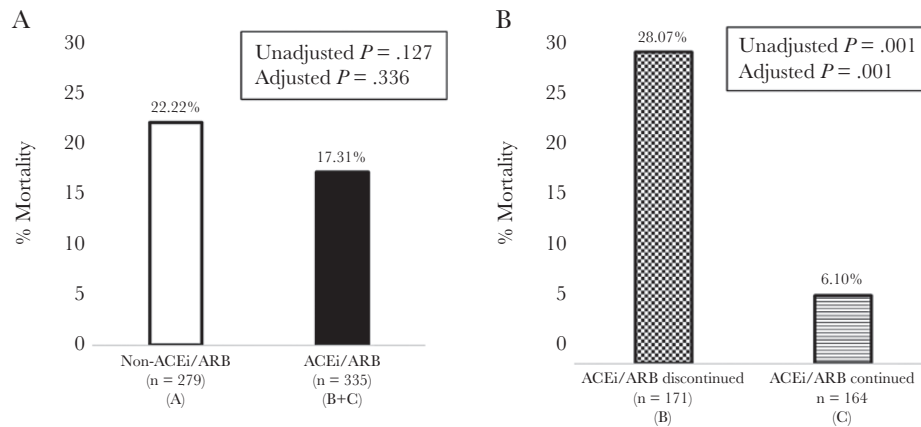
In contrast to most previous studies discussed above, we found that in-hospital continuation of ACEi/ARB use was associated with better outcomes compared to in-hospital discontinuation of ACEi/ARB use. Hypertensive SARS-CoV-2 patients not on ACEi/ARBs, compared with those taking ACEi/ARBs, did not show increased risk of development of hypotension or AKI. ACEi/ARBs were discontinued because of the development of hypotension or AKI. Patients who developed hypotension or AKI had a higher mortality rate. It is important to control for these 2 confounders. In the absence of hypotension or AKI, patients who continued ACEi/ARBs had lower mortality and ICU admission rates compared to those who discontinued them, further supporting that continued ACEi/ARB use may have beneficial effects. To our knowledge, this study reports the largest cohort of hospitalized hypertensive COVID-19 patients on ACEi/ARBs from a large academic hospital in the United States.

**Table 2. Clinical Variables of Patients Who Did Not Receive ACEi/ARB (Group A) and Who Did Receive ACEi/ARB (Groups B and C) at Admission**

Variable	Non-ACEi/ARB, Median (IQR) (Group A, n = 279)	ACEi/ARB, Median (IQR) (Groups B + C, n = 335)	P Value
Heart rate, beat/min	91 (79–107)	94 (80–106)	NS
Respiratory rate, /min	20 (18–24)	20 (18–24)	NS
O <sub>2</sub> saturation, %	95 (92–97)	94 (91–96)	NS
Fraction of inspired O <sub>2</sub> , %	50 (50–100)	50 (40–50)	.053
Arterial pressure of O <sub>2</sub> , mmHg	79 (62–103)	75 (61–99)	NS
Systolic blood pressure, mmHg	128 (115–149)	131 (113–148)	NS
Diastolic blood pressure, mmHg	74 (64–83)	74 (65–81)	NS
Mean arterial pressure, mmHg	91 (82–102)	92 (82–101)	NS
Temperature, °C	37.0 (36.7–37.6)	37.1 (36.8–37.7)	<b>.016</b>
<b>Hematology</b>			
Leukocytes, /μL	6.9 (4.9–9.2)	7.3(5.5–9.9)	NS
Lymphocytes, %	12.1 (7.8–17.6)	12.8 (7.5–18.9)	NS
Hematocrit, %	39.0 (33.9–43.4)	40.5(36.0–43.9)	<b>.003<sup>a</sup></b>
<b>Chemistry</b>			
Bicarbonate, mEq/L	23.5 (21.0–26.0)	23.0 (21.0–26.0)	NS
Creatinine, mg/dL	1.1 (0.9–1.8)	1.1 (0.8–1.5)	.086
Potassium, mEq/L	4.2 (3.9–4.6)	4.2 (3.8–4.6)	NS
Sodium, mEq/L	138 (135–140)	136 (133–139)	<b>.001<sup>a</sup></b>
pH	7.4 (7.3–7.5)	7.4 (7.3–7.5)	NS
<b>Inflammatory markers</b>			
Alanine aminotransferase, U/L	24.0 (15.0–41.0)	28.0 (16.0–42.0)	NS
Aspartate aminotransferase, U/L	37 (26–62)	38 (26–56)	NS
Brain natriuretic peptide, pg/mL	630 (143–3115)	451 (86–1517)	<b>.010</b>
C-reactive protein, mg/dL	7.5 (2.9–14.1)	7.0 (3.1–13.6)	NS
D-dimer, ng/mL	450 (268–911)	360 (220–700)	<b>.003<sup>a</sup></b>
Ferritin, ng/mL	691 (298–1358)	602 (302–1322)	NS
Lactate dehydrogenase, U/L	345 (260–461)	335 (257–439)	NS
Procalcitonin, ng/mL	0.2 (0.1–0.4)	0.2 (0.1–0.4)	NS
Troponin, ng/mL			
Median (IQR)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	<b>.005<sup>a</sup></b>
Mean (SD)	0.05 (0.162)	0.03 (0.155)	

Values are median (IQR) and statistical test employed Mann-Whitney *U* test. *P* values displayed are without Bonferroni correction. Significant values in which *P* < .05 are noted in bold. Abbreviations: ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; IQR, interquartile range; NS, not significant.

<sup>a</sup>After Bonferroni correction for multiple comparisons, hematocrit, plasma sodium, D-dimer, and troponin remained significantly different between group.



**Figure 2.** A, Mortality of non-ACEi/ARB (group A patients) and ACEi/ARB (group B + C patients). *P* = .127 using  $\chi^2$  test. *P* = .336 with adjustment for age, sex, history of chronic kidney disease, and diabetes using logistic regression (OR = 0.811; 95% CI, .529–1.243). B, Mortality of ACEi/ARB discontinued in the hospital (group B patients) and ACEi/ARB continued in the hospital (group C patients). *P* = .001 using  $\chi^2$  test. *P* = .001 with adjustment for age, sex, history of heart failure, chronic obstructive pulmonary disease, and asthma (OR = 0.215; 95% CI, .101–.455). Abbreviations: ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; CI, confidence interval; OR, odds ratio.



**Table 3. Mortality Rates in Patients who Continued ACEi/ARB Use During Hospitalization Versus Patients Who Discontinued ACEi/ARB Use During Hospitalization, Stratified by Hypotension and AKI**

Stratification	ACEi/ARB Discontinued, n/N (%) (Group B)	ACEi/ARB Continued, n/N (%) (Group C)	Unadjusted P Value <sup>a</sup>	Adjusted P Value <sup>b</sup>	Odds Ratio (95% CI) <sup>b</sup>
Without substratification (Figure 2B)	48/171 (28.07)	10/164 (6.09)	<b>.001</b>	<b>.001</b>	<b>0.215 (.101–.455)</b>
Hypotension	35/73 (47.94)	7/26 (26.92)	.063	.183	0.489 (.170–1.402)
Nonhypotension	13/98 (13.27)	3/138 (2.17)	<b>.001</b>	<b>.017</b>	<b>0.172 (.040–.730)</b>
AKI	35/101 (34.65)	5/31 (16.12)	.050	.117	0.423 (.144–1.242)
Non-AKI	13/70 (18.57)	5/133 (3.75)	<b>.001</b>	<b>.011</b>	<b>0.224 (.071–.708)</b>

Data are number of deaths/number of patients, n/N (%). Significant values in which  $P < .05$  are noted in bold.

Abbreviations: ACEi, angiotensin-converting enzyme inhibitor; AKI, acute kidney injury; ARB, angiotensin II receptor blocker; CI, confidence interval.

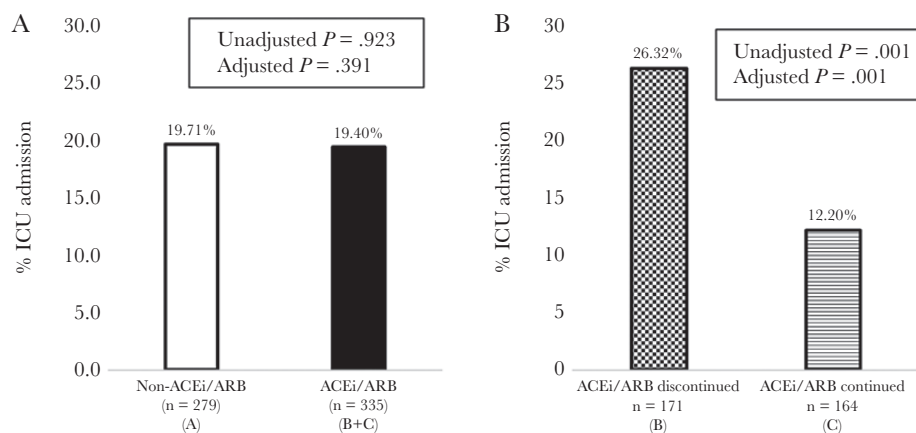
<sup>a</sup> $\chi^2$  tests.

<sup>b</sup>Logistic regression with adjustment for age, sex, history of heart failure, chronic obstructive pulmonary disease, and asthma (comorbidities that were significantly different between groups B and C).

The mechanisms by which ACEi and ARBs may exert their beneficial effects in hypertensive COVID-19 patients are unknown. The continuation of ACEi/ARBs during hospitalization may blunt the adverse effects of hypertension, a well-known risk factor for mortality in COVID-19 [26]. ACEi/ARBs have cardioprotective effects in postmyocardial infarction and heart failure patients by reducing myocardial wall stress [28, 29]. Additionally, ACEi/ARBs have been shown to reduce microvascular complications in patients with cardiac, cerebrovascular, and renal comorbidities [30, 31]. Experimentally, ACEis and ARBs have the ability to upregulate ACE2, which leads to the degradation of angiotensin II and the increased formation of angiotensin 1–7; the latter is thought to have beneficial

vasodilatory, anti-inflammatory, and antifibrotic effects [14]. It is also interesting to speculate that ACEi/ARBs may play a role in ameliorating the detrimental effects of the cytokine storm seen during the immune response to SARS-CoV-2 [32, 33], a state that has been linked to the proinflammatory effects of angiotensin II. Finally, ARBs have been shown to prevent aggravation of acute lung injury in mice infected with the closely related betacoronavirus SARS-CoV-1, suggesting a primary pulmonary protective role [34].

Finally, it is worth noting that the reasons for stopping ACEi/ARBs were undoubtedly complex with multiple documented and undocumented possibilities. In clinical practice, hypotension and AKI are the most frequent justifications for



**Figure 3.** A, ICU admission rates of non-ACEi/ARB (group A patients) and ACEi/ARB (group B + C patients).  $P = .923$  using  $\chi^2$  test.  $P = .391$  with adjustment for age, sex, history of chronic kidney disease, and diabetes using logistic regression (OR = 0.832; 95% CI, .547–1.266). B, ICU admission rates of ACEi/ARB discontinued in the hospital (group B patients) and ACEi/ARB continued in the hospital (group C patients).  $P = .001$  using  $\chi^2$  test.  $P = .001$  with adjustment for age, sex, history of heart failure, chronic obstructive pulmonary disease, and asthma (OR = 0.347; 95% CI, .187–.643). Abbreviations: ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; CI, confidence interval; ICU, intensive care unit; OR, odds ratio.

**Table 4. ICU Admission Rates in Patients Who Continued ACEi/ARB Use During Hospitalization Versus Patients Who Discontinued ACEi/ARB Use During Hospitalization, Stratified by Hypotension and AKI**

Stratification	ACEi/ARB Discontinued, n/N (%) (Group B)	ACEi/ARB Continued, n/N (%) (Group C)	Unadjusted P Value <sup>a</sup>	Adjusted P Value <sup>b</sup>	Odds Ratio (95% CI) <sup>b</sup>
Without substratification (Figure 3B)	45/171 (26.3)	20/164 (12.2)	<b>.001</b>	<b>.001</b>	<b>0.347 (.187–.643)</b>
Hypotension	38/73 (52.1)	8/26 (30.8)	.062	.057	0.349 (.118–1.033)
Nonhypotension	7/98 (7.1)	12/138 (8.7)	.666	.912	1.059 (.382–2.983)
AKI	31/101 (30.7)	7/31 (22.6)	.383	.149	0.474 (.171–1.308)
Non-AKI	14/70 (20)	13/133 (9.8)	<b>.041</b>	<b>.043</b>	<b>0.412 (.175–.971)</b>

Data are number of deaths/number of patients, n/N (%). Significant values in which  $P < .05$  are noted in bold.

Abbreviations: ACEi, angiotensin-converting enzyme inhibitor; AKI, acute kidney injury; ARB, angiotensin II receptor blocker; CI, confidence interval; ICU, intensive care unit.

<sup>a</sup> $\chi^2$  test.

<sup>b</sup>Logistic regression with adjustment for age, sex, history of heart failure, chronic obstructive pulmonary disease, and asthma (comorbidities that were significantly different between groups).

stopping ACEi/ARBs and there did not appear to be any indication that the current pandemic altered that paradigm. However, this is a retrospective study and the decision to continue or discontinue ACEi/ARB use was part of standard clinical care.

This study has several limitations. It was a retrospective single-center study. Laboratory values were not reassessed in patients who continued or discontinued ACEi/ARBs. Moreover, the difference between ACEi and ARB use could not be resolved due to the limited sample size. Although ACEis and ARBs have similar mechanisms of action, their effects may need to be studied separately. This study did not account for when ACEi/ARBs were discontinued for individual patients during their hospital stay. The current sample size did not allow for substratification based on how long the patients were on these medications before they were discontinued. Individual chart review indicated that hypotension and AKI were the main documented reasons for ACEi/ARB discontinuation. However, in some instances, justification could not be discerned. Moreover, early on in the pandemic, uncertainty existed as to whether ACEi/ARBs were harmful so individual practitioners may have reflexively held these medications without indicating their justification. This contribution is beyond the analysis of the present investigation.

## CONCLUSIONS

These findings not only confirm that ACEi/ARB use does not worsen clinical outcomes in COVID-19 patients with a history of hypertension, but also suggest that COVID-19 patients who are on ACEi/ARBs should continue these medications in the hospital as they may have beneficial effects, as long as these patients do not develop hypotension or AKI.

## Notes

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**Author contributions.** K. W. L., K.W.C., and J. V. carried out data collection, data analysis, literature research, writing/editing manuscript. W. H. and H. L. analyzed data. P. S. R., S. K. M., H. A. S., and A. J. S. discussed and edited the manuscript. T. Q. D. carried out conceptualization, discussion, editing manuscript, and supervision.

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