










CT visual quantitative evaluation of hypertensive patients with coronavirus disease (COVID-19): Potential influence of angiotensin converting enzyme inhibitors / angiotensin receptor blockers on severity of lung involvement

Cesur Samanci ^a, Bengu Saylan ^b, Gokce Gulsen ^c, Yuksel Akkaya ^d, Melike Yesildal ^e, Sinem Akkaya Isik ^f, and Fethi Emre Ustabasioglu ^g

^aDepartment of Radiology, MD Radiology Associate Professor Istanbul University-Cerrahpaşa Cerrahpaşa Faculty of Medicine; ^bDepartment of Pulmonary Medicine, MD Pulmonary Medicine Specialist Haydarpaşa Sultan Abdülhamidhan Training and Research Hospital, Turkey; ^cDepartment of Radiology, MD Radiology Specialist Haseki Training and Research Hospital, Turkey; ^dDepartment of Microbiology and Clinical Microbiology, MD Microbiology and Clinical Microbiology Specialist Haydarpaşa Sultan Abdülhamidhan Training and Research Hospital, Turkey; ^eDepartment of Radiology, MD Radiology Assistant, Haydarpaşa Sultan Abdülhamidhan Training and Research Hospital, Turkey; ^fDepartment of Infectious Diseases, MD Haydarpaşa Sultan Abdülhamidhan Training and Research Hospital, Turkey; ^gDepartment of Radiology, MD Radiology Assistant Professor Trakya University Medical Faculty, Turkey

ABSTRACT

Objective: There is not enough data on the effect of angiotensin-converting enzyme inhibitors (ACEIs)/angiotensin receptor blockers (ARBs) on lung involvement in patients with COVID-19 pneumonia and hypertension (HT). Our aim was to compare the lung involvement of the HT patients hospitalized for COVID-19 using ACEIs/ARBs with the patients taking other anti-HT medications.

Methods: Patients who have a diagnosis of HT among the patients treated for laboratory-confirmed COVID-19 between 31 March 2020 and 28 May 2020 were included in the study. One hundred and twenty-four patients were divided into two as ACEIs/ARBs group (n = 75) and non-ACEIs/ARBs group (n = 49) according to the anti-HT drug used. The chest CT involvement areas of these two groups were evaluated quantitatively by two observers including all lobes, and total severity score (TSS) was calculated. These TSS values were compared between drug groups and clinical groups

Results: In clinical classification; there were 4 (3.2%) asymptomatic, 5 (4.0%) mild type, 92 (74.1%) common type, 14 (11.3%) severe type, 9 (7.3%) critical type patients. ACEI/ARB group's TSS (mean±SD, 7.74 ± 3.54) was statistically higher than other anti-HT medication group (mean±SD, 4.40 ± 1.89) ($p < .001$). Likewise, severe-critical clinical type's TSS (mean±SD, 9.17 ± 3.44) was statistically higher than common type (mean±SD, 5.76 ± 3.07) ($p < .001$). Excellent agreement was established between the two blinded observers in the TSS measurements.

Conclusions: Quantitative evaluation of CT and TSS score can give an idea about the clinical classification of the patient. TSS is higher in ACEI/ARB group than non-ACEIs/ARBs group.

ARTICLE HISTORY

Received 10 December 2020
Revised 31 December 2020
Accepted 9 January 2021

KEYWORDS

Coronavirus disease; covid-19; computed tomography; pneumonia

Introduction

Coronavirus disease (COVID-19) is a rapidly spreading epidemic infection worldwide caused by a new coronavirus (SARS-CoV-2) in Wuhan Province, China (1–3). Like other types of coronaviral pneumonia, COVID-19 can cause acute respiratory distress syndrome, even death in critical cases. Therefore, early diagnosis of the disease is very important in these patients (4,5). Computed tomography (CT) is the primary imaging tool for the diagnosis of patients suspected of COVID-19 (6). CT a

llows us to track changes in the lung parenchyma during the course of the disease, as well as diagnose the patients with negative reverse transcriptase polymerase chain reaction (RT-PCR) testing (7,8). Also, CT images can give an idea about the severity of the disease (9).

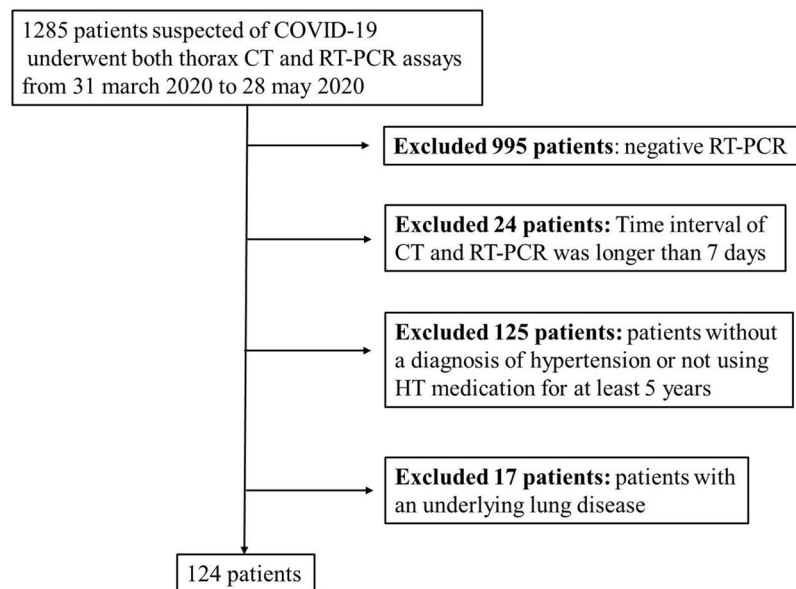
It has been shown that SARS-CoV-2 uses angiotensin-converting enzyme (ACE) 2 receptor to enter the cell and ACE 2 increases significantly in those who use ACE inhibitor

(ACEIs)/angiotensin receptor blocker (ARBs) (10,11). It was also recently shown that patients with HT had more than 3 times the mortality rate of all other patients hospitalized with COVID-19 (12). CT total severity scores (TSS) of patients using ACEIs/ARBs with the patients who are taking other anti-HT medications were compared in this study. Also the relationship between TSS and clinical category in the same patient group was investigated.

Methods

Patient population

The local ethics committee of our institution approved our retrospective study. In our single-center study 124 consecutive patients who have a diagnosis of HT among the patients treated for laboratory-confirmed COVID-19 between 31 March 2020 and 28 May 2020 were included (Figure 1). All patients were positive for COVID-19 in PCR tests obtained by nasopharyngeal



RT-PCR= reverse transcription polymerase chain reaction.

Figure 1. Flow chart of this study. RT-PCR = reverse transcription-polymerase chain reaction.

swab, or oropharyngeal swab. Patients without a diagnosis of HT or not using HT medication for at least 5 years were excluded. There were two groups; first group ($n = 75$) was using ACEIs or ARBs (renin-angiotensin system inhibitors) with or without additional anti HT medication (calcium-channel blockers ($n = 34$), β receptor blockers ($n = 25$)) second group ($n = 49$) was using other anti-HT medications (calcium-channel blockers $n = 26$, β receptor blockers $n = 23$) (Non-ACEIs/ARBs group).

CT acquisition and visual quantitative evaluation

All patients were imaged in supine position, on a 320 detector CT (Aquilion-ONE, Toshiba Medical Systems, Otawara, Japan.). All images were obtained in standard dose protocol with a 5 mm slice thickness in lung window setting. All images were evaluated independently from each other by two observers with 8 and 9 years of thoracic imaging experience (XX and YY) who did not know the patient's clinical and laboratory data. For CT visual quantitative evaluation; observers calculated the "total severity score (TSS)" which was previously described by Chung et al. (13). The degree of involvement of each of the five lung lobes was evaluated and classified as none (0%), minimal (1–25%), mild (26–50%), moderate (51–75%), or severe (76–100%). None, minimal, mild, moderate and severe corresponded to a lobe score of 0, 1, 2, 3 and 4, respectively. TSS was achieved by summing these five lobe scores (range of possible scores: 0–20).

Clinical assessment

All patients were evaluated in terms of smoking, diabetes mellitus (DM), fever, cough, sputum, dyspnea, sore throat, hemoptysis, muscle pain, abdominal pain, headache, diare and contact history (Tables 1 and table 5). Based on their

clinical severity patients were classified into 4 groups. These groups were structured according to the Diagnosis and Treatment Plan of COVID-19 issued by National Health Commission (7th ed.) (9,14) (1). Mild type: mild symptoms and no pneumonia findings in chest CT (2); common type: fever, respiratory tract and other symptoms with pneumonia findings in chest CT (3); severe type: respiratory distress, respiratory rate ≥ 30 times/min; in resting state, oxygen saturation $\leq 93\%$; $\text{PaO}_2/\text{FiO}_2 \leq 300$ MMHG (4); critical type: respiratory failure requiring mechanical ventilation, shock and other organ failure requiring intensive care unit monitoring and treatment.

Statistical analysis

Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) software (version 16, SPSS, Inc, Chicago, IL). Quantitative data were expressed as mean \pm standard deviation and categorical data as frequencies/percentages. Baseline data were evaluated using the Kolmogorov–Smirnov test, which showed that the data were normally distributed. Statistical significance was accepted at a P value of less than 0.05. Comparison of the distribution of pulmonary lobe involvement in different clinical categories was calculated by chi-square test. Also clinical scores were compared in different anti-HT medication groups by chi-square test. TSSs between these anti-HT medication groups and between clinical groups were compared by Student-T test. Also Student's T test was used to assess the difference in the number of lobes affected between clinical groups. The TSS score that maximizes the accuracy for the prediction of severe-critical clinical type was established on the receiver operating characteristic (ROC) curve. We performed logistic regression analysis to compare severity scores of COVID-19 pneumonia on CT examinations between the

Table 1. Patient Characteristics.

Sex	n (%)
Men	64 (51.6)
Women	60 (48.4)
Age (years)	
Mean	63.46
Standard Deviation	11.10
Range	39–94
Medication	
ACEi/ARB	75 (60.5)
Other	49 (39.5)
Smoking history	
Never smoker	94 (75.8)
Current smoker	9 (7.3)
Former smoker	21 (16.9)
Exposure History	
No known contacts	67 (54.0)
Traveling abroad	4 (3.2)
Contact with a known infected person	53 (42.7)
Fever	
37.3–38°C	39 (31.5)
38.1–39°C	37 (29.8)
> 39°C	7 (5.6)
None	41 (33.1)
Symptoms	
Cough	70 (56.5)
Sputum	4 (3.2)
Dyspnea	40 (32.3)
Sore Throat	12 (9.7)
Hemoptysis	0 (0)
Muscle pain	51 (41.1)
Abdominal pain	4 (3.2)
Headache	7 (5.6)
Diare	6 (4.8)
Clinical Groups	
0 asymptomatic	4 (3.2)
1 (mild) symptoms + imaging (-)	5 (4.0)
2 (common) symptoms + imaging (+)	92 (74.1)
3 (severe) respiratory distress, res rate > 30, sat < 93, paO2/fiO2 < 300	14 (11.3)
4 (critical) intubation, shock, organ failure	9 (7.3)

ACEi/ARBs group and Non-ACEi/ARBs group, for adjustment of confounding factors (Table 6). Interobserver agreement in the CT visual quantitative analysis (TSS) was calculated using intraclass correlation coefficients (ICCs) from a one-way random effects model analysis of variance, with the subject as the random effect. A 95% confidence interval (CI) was constructed for each ICC. An ICC greater than 0.80 indicated excellent agreement. Correlations between variables on patients were evaluated by Pearson's correlation coefficient value.

Results

Patients with negative PCR test, patients with a PCR and CT interval more than 7 days and patients with an underlying lung disease (chronic obstructive pulmonary disease, etc.) or without HT were excluded from the study. After these patients were excluded, 124 patients (mean age, 63.4 ± 11.1 years; 48.4% (60/124) women) were analyzed. Figure 1 shows the flow chart of our study. Five of 124 patients had no CT findings, but had clinical findings and PCR was positive. Findings on chest CT are summarized in Table 2. Main clinical symptoms of COVID-19 patients were fever (66.9%), cough (56.5%), muscle pain (41.1%) and dyspnea (32.3%) (Table 1). In clinical classification; there were 4 (3.2%) asymptomatic, 5 (4.0%) mild type, 92 (74.1%) common type, 14 (11.3%) severe type, 9 (7.3%) critical type

Table 2. Findings on Thorax CT.

Number of Lobes Affected	n (%)
0	5 (4.0)
1	8 (6.5)
2	7 (5.6)
3	9 (7.3)
4	12 (9.7)
5	83 (66.9)
More than 2 lobes affected	104 (83.8)
Bilateral lung disease	13 (10.5)
Frequency of Lobe involvement	
Right upper lobe	98 (79.0)
Right middle lobe	100 (80.6)
Right lower lobe	109 (87.9)
Left upper lobe	101 (81.5)
Left lower lobe	103 (83.7)
Other Findings	
Fibrotic lesion	7 (5.6)
Centrilobular nodules	5 (4.0)
P.effusion	15 (12.1)
Thoracic LAP(short axis>10 mm)	4 (3.2)
Underlying lung disease	0 (0)
Air bronchogram	22 (17.7)
Interlobular septa	29 (23.4)
Cavity	0 (0)
Distribution	
No finding on thorax CT	5 (4.0)
Peripheral	110 (88.7)
Peribronovascular	9 (7.3)
Density	
No finding on thorax CT	5 (4.0)
Ground glass opacity	75 (60.4)
Mixed ground glass opacity	44 (35.5)
Consolidation	0 (0)
total lung severity score	
Mean ± SD	6.42 ± 3.41
Range	39–16

Thoracic LAP; thoracic lymphadenopathy

patients. Clinical types were compared in different anti-HT medication groups. Compared with the others, ACEi/ARB group had a higher incidence of being severe-critical clinical type and higher incidence for the need of intensive care hospitalization ($p < .05$). There was no significant difference between ACEi/ARB group and other anti-HT medication groups in terms of sex, smoking history, DM, pleural effusion, thoracic lymphadenopathy, unilateral or bilateral involvement, fever, cough or other symptoms. In distribution of pulmonary lobe involvement; compared with the others, ACEi/ARB group had a higher incidence of right upper lobe, right middle lobe, left upper and lower lobe involvement ($p = .001$; $p = .021$, $p = .010$, $p = .021$, respectively), however, there was no significant difference in right lower lobe involvement ($p = .166$). ACEi/ARBs group's TSS (mean±SD, 7.74 ± 3.54) was statistically higher than other anti-HT medication group (mean±SD, 4.40 ± 1.89) ($p < .001$) (Table 3). Likewise, severe-critical clinical type's TSS (mean±SD, 9.17 ± 3.44) was statistically higher than common type (mean±SD, 5.76 ± 3.07) ($p < .001$). Figures 2 and figure 3 show chest CTs of two patients using ACEi/ARBs and non ACEi/ARBs, respectively. Interobserver variability results are shown in Table 4. Excellent agreement was found between the two blinded observers in TSS measurements. In our study, TSS for diagnosing severe-critical clinical type with maximum accuracy was 6.5 (AUC 0.774; 95% CI 0.670–0.878), with a sensitivity and specificity of 69.6% and 66.7%, respectively. Figure 4 shows the ROC curve drawn based on TSS values.

Table 3. Mean CT total severity scores (TSS) for patients using angiotensin converting enzyme inhibitors (ACEIs)/angiotensin receptor blockers (ARBs) and the patients taking other anti-HT medications.

	ACEIs/ARBs (n = 75)	other anti-HT medications (n = 49)	P value
TSS (mean \pm SD)	7.74 \pm 3.54	4.40 \pm 1.89	<0.001*

TSS CT total severity score

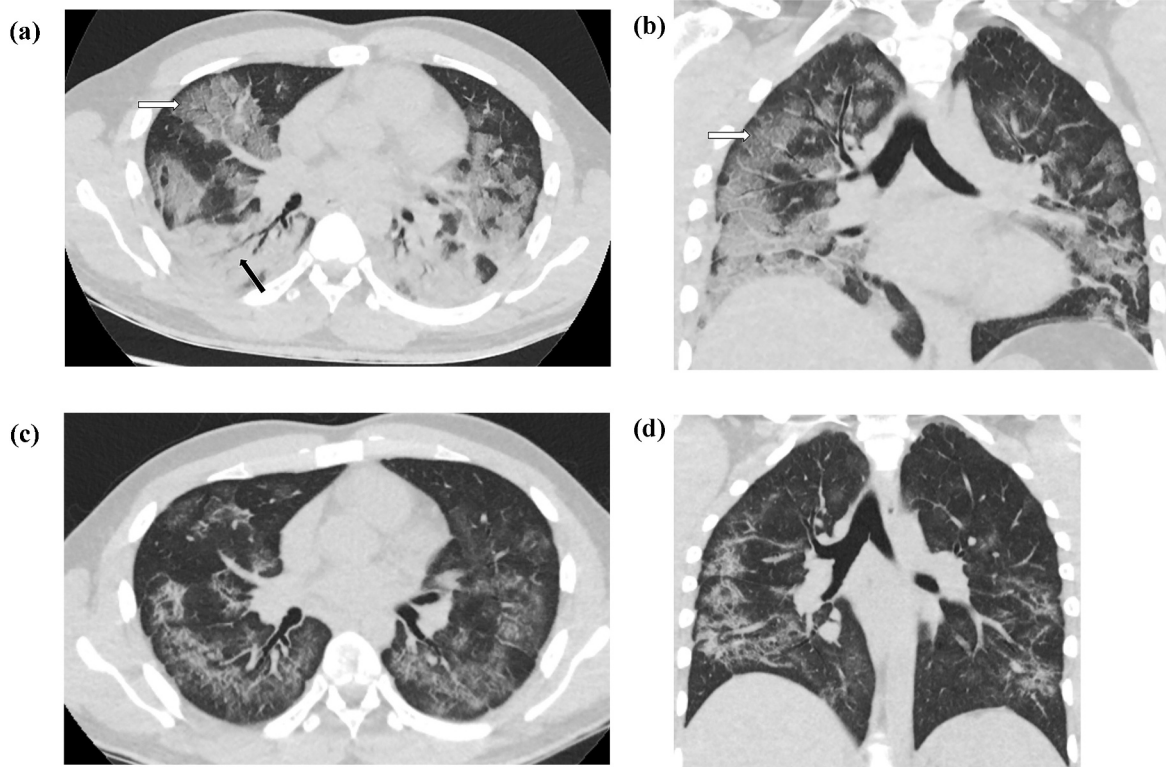
*Statistical comparison between groups with Student's *t*-test

Figure 2. A 44-year-old male patient with a history of traveling to Italy 3 weeks ago applied to our hospital with complaints of 39 degrees of fever, dyspnea and cough. Patient has respiratory distress; respiratory rate was 32/min, saturation was 78% in room air, 91% under 4 lt/min nasal oxygen. He has lymphopenia, his CRP was high, and his leukocyte was within normal limits. He was using ramipril (ACE-inhibitor) because of hypertension and he was not a smoker. In the initial CT examination of the patient (**a, b**) central and peripherally distributed ground glass opacities more prominent in the lower lobes, consolidations with air bronchograms (**black arrow**), and a crazy paving pattern (**white arrow**) in the bilateral upper lobes were observed. TSS score was calculated as 16. In clinical classification; he was severe type. Ten days later in the follow-up chest CT (**c, d**) significant regression in infiltrations were observed.

Discussion

Radiologists are interpreting more chest CTs than ever in this COVID-19 pandemic which affects the whole world. A recent study has shown that coronavirus that causes this pandemic uses the ACE 2 receptor to enter the cell (15). Moreover, upon understanding that ACEIs/ARBs upregulate ACE 2 receptors (16–18), COVID-19 patients using these anti-HT drugs began to be examined more closely (12).

Chung et al. (13) characterized the key CT findings of COVID-19 infection and described TSS for degree of involvement in chest CT. In our study, it was shown that in patients with HT hospitalized due to COVID-19, TSS in the group using ACEIs/ARBs was higher than patients using other anti-HT drugs. It was also shown that ACEI/ARB group had a higher incidence of being severe-critical clinical type and higher incidence for the need of intensive care hospitalization. Li et al. (12) explored the association between ACEIs/ARBs and disease severity and death rates in HT patients admitted to hospital for COVID-19 pneumonia. They showed that ACEIs/

ARBs in those patients are not significantly associated with COVID-19 severity, death rates or clinical outcomes.

Zhang et al. (19) evaluated the relationship between these ACEIs/ARBs and mortality in hypertensive COVID-19 patients. They also showed that the use of ACEIs/ARBs did not increase mortality. Such results provide clinical evidence that supports recent recommendations by several international societies to continue ACEIs/ARBs in COVID-19 patients (20) In contrast to the studies mentioned above, we found TSS higher in patients with HT who used ACEIs/ARBs than those who did not. On the other hand, the same societies do not recommend starting ACEI/ARBs if patients with COVID-19 pneumonia do not have diseases such as HT, heart failure, and DM (21). ACEIs/ARBs increase the expression of ACE2 receptors, which are the entrance gate of the coronavirus to the cell, so it can be thought to increase the severity of the infection. However, in animal studies, ACE2 has been shown to regulate RAS negatively and act as a balance against ACE function (11,22). COVID-19 infection has been shown to significantly decrease ACE2 expression; thus, renin-angiotensin system

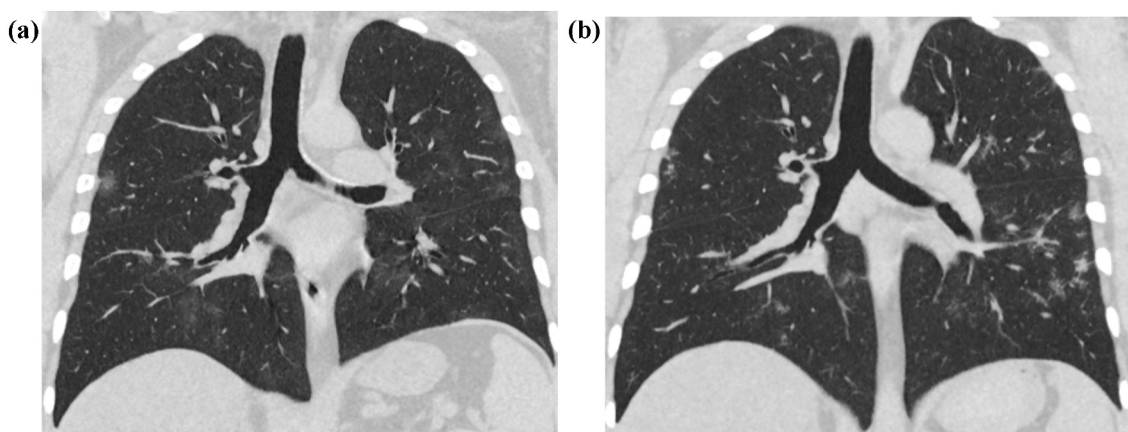


Figure 3. A 57-year-old male patient living with his daughter who is working as a nurse in a pandemic hospital applied to our hospital with 38.1 degrees of fever, widespread muscle pain and cough. Patient was using amlodipine (Ca channel blocker) due to hypertension and he is a former smoker. In the initial CT (a); peripherally located ground glass opacities were observed in all lobes, dominantly in the lower lobes. TSS score was calculated as 7. He was common type in clinical classification. In the follow up chest CT (b), which was taken 5 days later, it is observed that the density of ground glass opacities increased and became consolidated.

Table 4. Interobserver variability for CT total severity scores (TSS) measurements.

	Observer 1	Observer 2	ICC
	(mean \pm SD)	(mean \pm SD)	intraclass correlation coefficient
TSS values (n = 124)	6.42 \pm 3.41	6.45 \pm 3.54	0.974 (0.964–0.982)

TSS: CT total severity score; ICC: Intraclass Correlation Coefficients; SD: standard deviation

Table 5. Clinical parameters of our patient population.

	ACEIs/ARBs	Non-ACEIs/ARBs	p Value
	(n = 75)	(n = 49)	
Clinical factors			
Age (years, mean SD)	63.89 \pm 10.92	62.82 \pm 11.74	.810
Gender, n (female %)	32 (42.6%)	28 (57.1%)	.142*
Angina pectoris, n (%)	2 (2%)	31 (63.2%)	.000*
CVD (Angina, stent, MI, AF, Arrhythmia etc, n (%))	11 (14.6%)	35 (71.4%)	.000*
Chronic renal failure, n (%)	6 (8%)	6 (12.2%)	.434*
Diabetes Mellitus, n (%)	24 (32%)	19 (38.7%)	.438*
Total severity score (mean +SD)	7.43 \pm 3.79	4.22 \pm 2.05	.000
Body mass index	26.43 \pm 4.16	25.83 \pm 3.76	.406
Systolic blood pressure (mmHg)	133.84 \pm 18.66	140.35 \pm 18.9	.062
Diastolic blood pressure (mmHg)	5.36 \pm 0.58	83.41 \pm 13.13	.010
Glucose (mg / dl)	119.01 \pm 50.5	112.78 \pm 41.07	.472
Urea (mg / dl)	45.65 \pm 27.18	39.12 \pm 21.02	.157
Creatinine (mg / dl)	1.42 \pm 1.26	1.13 \pm 0.54	.130
ALT (U / L)	49.17 \pm 92.7	28.92 \pm 17.7	.134
AST (U / L)	81.80 \pm 392	29.02 \pm 17.4	.350
CRP (mg / L)	66.07 \pm 62.7	54.50 \pm 61.5	.314
HB (g / dL)	12.9 \pm 1.76	13.12 \pm 1.39	.450
LYM (10^3 / mm ³)	1.41 \pm 0.78	1.69 \pm 1.04	.085
NEU (10^3 / mm ³)	4.73 \pm 2.25	5.61 \pm 4.2	.137

Statistically significant p values ($p < 0.05$) are shown in bold. *Chi-square test, others are Student T test

cascade is markedly activated (23). As a result, loss of ACE2 in mice resists COVID-19 infection, but also results in severe vascular permeability, pulmonary edema, neutrophil accumulation and pulmonary dysfunction (19,24).

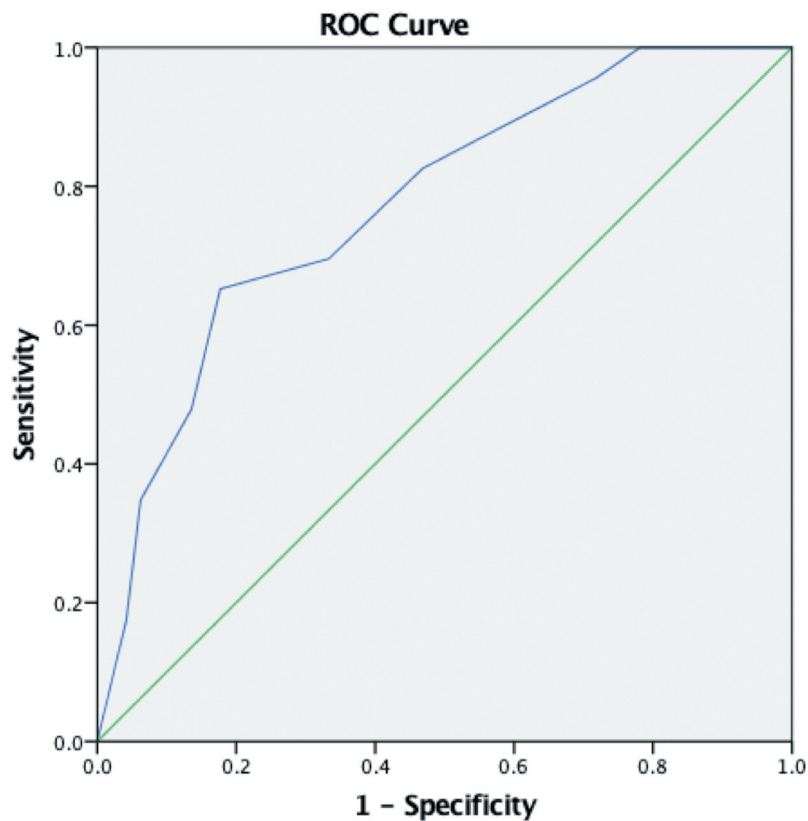
In our study, CT findings of patients with COVID-19 consisted of mostly ground-glass opacities and mixed ground-glass appearances, similar to previous studies (25,26). In a study (9) evaluating the relationship between TSS and clinical classification, TSS of severe-critical clinical type was found higher than common clinical type like our results. In the same study, the rate of mild type COVID-19 patients without CT findings was

relatively high (30.8%), whereas this rate was quite low in our study (4%). The reason for this was probably the mean age of the patients in our study was significantly higher than them (mean \pm SD, 63.4 \pm 11.1 and 44.6 \pm 17.9, respectively), and our entire study population consisted of patients with HT. According to our study, when there is suspicion of COVID-19, since the rate of negative chest CT is very low in patients with HT, CT can also be used as a screening method. HT itself is a disease that worsens the clinic for COVID-19. When patients with HT are infected with COVID-19, mortality is 3 times higher than those without HT (12). While calculating

Table 6. Logistic Regression analysis to predict high TSS score.

Variable	ACEIs/ARBs			Non-ACEIs/ARBs		
	Odds ratio	95% Confidence Interval	P value	Odds ratio	95% Confidence Interval	P value
Gender	1.029	0.375–2.826	0.956	0.497	0.024–10.51	0.654
Smoking	0.873	0.442–1.723	0.650	0.427	0.049–3.693	0.439
Diabetes Mellitus	0.904	0.321–2.550	0.613	1.160	0.172–47.935	0.463
KVH	2.186	0.500–9.562	0.299	1.853	0.109–31.55	0.670
CKD	3.698	0.392–34.924	0.254	.000	.000	0.999
Yaş	1.006	0.942–1.074	0.865	1.072	0.955–1.203	0.240
BMI	0.991	0.835–1.176	0.916	1.189	0.912–1.551	0.200
Sistolik	0.957	0.914–1.003	0.067	0.988	0.911–1.073	0.776
Variable	ACEIs/ARBs			Non-ACEIs/ARBs		
Variable	Odds ratio	95% Confidence Interval	P value	Odds ratio	95% Confidence Interval	P value
Gender	1.029	0.375–2.826	0.956	0.497	0.024–10.51	0.654
Smoking	0.873	0.442–1.723	0.650	0.427	0.049–3.693	0.439
Diabetes Mellitus	0.904	0.321–2.550	0.613	1.160	0.172–47.935	0.463
KVH	2.186	0.500–9.562	0.299	1.853	0.109–31.55	0.670
CKD	3.698	0.392–34.924	0.254	.000	.000	0.999
Yaş	1.006	0.942–1.074	0.865	1.072	0.955–1.203	0.240
BMI	0.991	0.835–1.176	0.916	1.189	0.912–1.551	0.200
Sistolik	0.957	0.914–1.003	0.067	0.988	0.911–1.073	0.776
Diyastolik	1.086	1000–1.179	0.050	1.058	0.934–1.200	0.375
GLUKOZ (mg/dl)	1.001	0.988–1.014	0.896	1.010	0.982–1.039	0.483
ÜRE (mg/dl)	0.982	0.950–1.015	0.280	0.954	0.847–1.034	0.975
Kreatinin (mg/dl)	2.012	0.677–5.982	0.209	0.389	0.024–6.431	0.509
ALT (U/L)	1.008	0.988–1.028	0.432	1.071	0.985–1.166	0.109
AST (U/L)	0.998	0.989–1.006	0.576	0.998	0.916–1.086	0.955
CRP (mg/L)	1.018	1002–1.034	0.025	1.033	1.006–1.061	0.015
HB (g/dL)	0.778	0.525–1.153	0.210	2.301	0.663–7.985	0.189
LYM (10 ³ /mm ³)	0.384	0.140–1.049	0.062	1.428	0.310–6.590	0.648
NEU (10 ³ /mm ³)	1.117	0.768–1.625	0.564	0.493	0.191–1.275	0.145

Statistically significant p values ($p < 0.05$) are shown in bold



Diagonal segments are produced by ties.

Figure 4. ROC curve for severe-critical clinical type diagnosis based on TSS values.

TSS, agreement between observers was excellent as in another study (9), which shows that the TSS scoring system is highly reproducible.

There were some limitations in our study. Since our study was based on radiological evaluation rather than molecular level analyzes, clinical and laboratory examinations, we compared patients radiologically over TSS values. Factors such as underlying diseases, pleural effusion, advanced age may not increase TSS, but it may worsen the patient's clinic. We wrote the article in a hurry to quickly contribute to the literature in the COVID-19 epidemic. We could not evaluate chest radiographs. We did not compare subgroups such as beta blockers, calcium channel blockers in the non-ACEIs/ARBs group because the number of patients in these groups was low and this was not the main point of our study. Similarly, the differences between ACEIs and ARBs themselves may be the subject of more extensive further studies.

Conclusion

Although the lung areas affected in the group using ACEIs/ARBs are more than non-ACEIs/ARBs group, an inference such as discontinuation of the use of these drugs or the use of other drugs may only be a result of large clinical trials. Randomized controlled studies with larger patient groups are needed to demonstrate the effect of ACEIs/ARBs on the clinic in patients with HT and COVID-19.

Acknowledgments

None.

Disclosure statement

Authors declare that they have no conflict of interest.

Funding

The authors have no funding to report.

Financial disclosure

The authors have no relevant financial interest in this article

ORCID

Cesur Samanci  <http://orcid.org/0000-0003-2389-3035>
 Bengu Saylan  <http://orcid.org/0000-0002-5922-0847>
 Gokce Gulsen  <http://orcid.org/0000-0002-2480-4527>
 Yuksel Akkaya  <http://orcid.org/0000-0002-3167-8055>
 Melike Yesildal  <http://orcid.org/0000-0003-4341-6076>
 Sinem Akkaya Isik  <http://orcid.org/0000-0001-9941-2993>
 Fethi Emre Ustabasioglu  <http://orcid.org/0000-0002-0340-4487>

References

- Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, Ren R, Leung KSM, Lau EHY, Wong JY, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *New England Journal of Medicine*. 2020; Jan 29 382:13-1199-207. [10.1056/NEJMoa2001316](https://doi.org/10.1056/NEJMoa2001316)
- Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, Qiu Y, Wang J, Liu Y, Wei Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *The Lancet*. 2020;395(10223):507-13. doi:[10.1016/S0140-6736\(20\)30211-7](https://doi.org/10.1016/S0140-6736(20)30211-7).
- Wu F, Zhao S, Yu B, Chen YM, Wang W, Song ZG, Hu Y, Tao ZW, Tian JH, Pei YY, et al. A new coronavirus associated with human respiratory disease in China. *Nature*. 2020. doi:[10.1038/s41586-020-2008-3](https://doi.org/10.1038/s41586-020-2008-3).
- Rubin GD, Ryerson CJ, Haramati LB, Sverzellati N, Kanne JP, Raouf S, Schluger NW, Volpi A, Yim JJ, Martin IB, et al. The role of chest imaging in patient management during the COVID-19 pandemic: a multinational consensus statement from the Fleischner Society. *Chest*. 2020; 158(1), 106-116.
- Choi H, Qi X, Yoon SH, Park SJ, Lee KH, Kim JY, Lee YK, Ko H, Kim KH, Park CM, et al. Extension of coronavirus disease 2019 (COVID-19) on chest CT and implications for chest radiograph interpretation. *Radiology. Cardiothoracic Imaging*. 2020;2(2):p. e200107.
- Joob B, Wiwanitkit V, Findings CCT. and Clinical Conditions of Coronavirus Disease (COVID-19). *AJR Am J Roentgenol*. 2020 Apr 1
- Huang P, Liu T, Huang L, Liu H, Lei M, Xu W, Hu X, Chen J, Liu B. Use of chest CT in combination with negative RT-PCR assay for the 2019 novel coronavirus but high clinical suspicion. *Radiology*. 2020;295(1):22-23.
- Xie X, Zhong Z, Zhao W, Zheng C, Wang F, Liu J. Chest CT for typical 2019-nCoV pneumonia: relationship to negative RT-PCR testing. *Radiology*. 2020 Feb 12.
- Li K, Fang Y, Li W, Pan C, Qin P, Zhong Y, Liu X, Huang M, Liao Y, Li S. CT image visual quantitative evaluation and clinical classification of coronavirus disease (COVID-19). *Eur Radiol* 2020 25 Mar;1. 30(8): 4407-4416.
- Klimas J, Olvedy M, Ochodnicka-Mackovicova K, Kruzliak P, Cacanyiova S, Kristek F, Krenek P, Ochodnický P. Perinataly administered losartan augments renal ACE 2 expression but not cardiac or renal Mas receptor in spontaneously hypertensive rats. *J Cell Mol Med*. 2015;19(8):1965-74. doi:[10.1111/jcmm.12573](https://doi.org/10.1111/jcmm.12573).
- Ferrario CM, Jessup J, Chappell MC, Averill DB, Brosnihan KB, Tallant EA, Diz DI, Gallagher PE. Effect of angiotensin-converting enzyme inhibition and angiotensin II receptor blockers on cardiac angiotensin-converting enzyme 2. *Circulation*. 2005;111(20):2605-10.
- Li J, Wang X, Chen J, Zhang H, Deng A. Association of renin-angiotensin system inhibitors with severity or risk of death in patients with hypertension hospitalized for coronavirus disease 2019 (COVID-19) infection in Wuhan. *China JAMA Cardiology*. 2020; Apr 23 57: 825. [10.1001/jamacardio.2020.1624](https://doi.org/10.1001/jamacardio.2020.1624)
- Chung M, Bernheim A, Mei X, Zhang N, Huang M, Zeng X, Cui J, Xu W, Yang Y, Fayad ZA, et al. CT Imaging Features of 2019 Novel Coronavirus (2019-nCoV). *Radiology*. 2020;295(1):202-07. doi:[10.1148/radiol.2020200230](https://doi.org/10.1148/radiol.2020200230).
- General Office of National Health Committee. Notice on the issuance of a program for the diagnosis and treatment of novel coronavirus (2019-nCoV) infected pneumonia (trial revised fifth edition). Accessed 3 Mar (2020)
- Hoffmann M, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, Erichsen S, Schiergens TS, Herrler G, Wu N-H, Nitsche A, et al. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. *Cell*. 2020;181(2):271-280.e8. doi:[10.1016/j.cell.2020.02.052](https://doi.org/10.1016/j.cell.2020.02.052).
- Ferrario CMFJ, Jessup J, Chappell MC, Averill DB, Brosnihan KB, Tallant EA, Diz DI, Gallagher PE. Effect of Angiotensin-Converting Enzyme Inhibition and Angiotensin II Receptor Blockers on Cardiac Angiotensin-Converting Enzyme 2. *Circulation*. 2005;111(20): 2605-10.
- Karram T, Abbasi A, Keidar S, Golomb E, Hochberg I, Winaver J, Hoffman A, Abassi Z. Effects of spironolactone and eprosartan on cardiac remodeling and angiotensin-converting enzyme isoforms in rats with experimental heart failure. *Am J Physiol Heart Circ Physiol*. 2005;289(4):H1351-1358. doi:[10.1152/ajpheart.01186.2004](https://doi.org/10.1152/ajpheart.01186.2004).

18. Ishiyama Y, Gallagher PE, Averill DB, Tallant EA, Brosnihan KB, Ferrario CM. Upregulation of angiotensin-converting enzyme 2 after myocardial infarction by blockade of angiotensin II receptors. *Hypertension*. 2004;43(5):970–76. doi:10.1161/01.HYP.0000124667.34652.1a.
19. Zhang P, Zhu L, Cai J, Lei F, Qin JJ, Xie J, Liu YM, Zhao YC, Huang X, Lin L, et al. Association of inpatient use of angiotensin converting enzyme inhibitors and angiotensin II receptor blockers with mortality among patients with hypertension hospitalized with COVID-19.
20. American Heart Association (AHA), Heart Failure Society of America (HFSA) and American College of Cardiology (ACC). Patients taking ACE-i and ARBs who contract COVID-19 should continue treatment, unless otherwise advised by their physician. 2020. 21. International Society of Hypertension. A statement from the International Society of Hypertension on COVID-19. (2020)
21. Bavishi C, Maddox TM, Messerli FH. Coronavirus disease. 2019. (COVID-19) infection and renin angiotensin system blockers. *JAMA cardiology* (2020) Apr 3. 5(7): 745-747.
22. Igase M, Kohara K, Nagai T, Miki T, Ferrario CM. Increased expression of angiotensin converting enzyme 2 in conjunction with reduction of neointima by angiotensin II type 1 receptor blockade. *Hypertens Res*. 2020;5(3):553–59. 10.1291/hypres.31.553CrossrefMedlineGoogle Scholar. doi:10.1291/hypres.31.553.
23. Kuba K, Imai Y, Penninger JM. 2006; Angiotensin-converting enzyme 2 in lung diseases. *Curr Opin Pharmacol*. 6(3):271–76. doi:10.1016/j.coph.2006.03.001
24. Imai Y, Kuba K, Rao S, Huan Y, Guo F, Guan B, Yang P, Sarao R, Wada T, Leong-Poi H, et al. Angiotensin-converting enzyme 2 protects from severe acute lung failure. *Nature*. 2005;436(7047):112–16. doi:10.1038/nature03712.
25. Lei J, Li J, Li X, Qi X. CT Imaging of the 2019 Novel Coronavirus (2019-nCoV) Pneumonia. *Radiology*. 2020 Apr;295(1):18–18. doi:10.1148/radiol.2020200236.
26. Fang Y, Zhang H, Xu Y, Xie J, Pang P, Ji W. CT Manifestations of Two Cases of 2019 Novel Coronavirus (2019-nCoV) Pneumonia. *Radiology*. 2020;295(1):208–09. <https://doi.org/10.1148/radiol.2020200280>. doi:10.1148/radiol.2020200280.