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Correlations of renal parenchymal attenuations and CT severity scores on three consecutive CTs in COVID-19 patients

Ahmet Turan Kaya, Burcu Akman

Department of Radiology, Faculty of Medicine, Amasya University, Amasya, Turkey

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ABSTRACT

Aim: We aimed to investigate the correlation between the temporal changes of computed tomography severity score (CT-SS) and mean renal parenchymal attenuation (MRPA) values in consecutive chest computed topographies (CT).

Material and Method: This retrospective, single-center study included 65 (≥18 years) COVID-19 patients with positive RT-PCR tests. A radiologist calculated three consecutive chest CT-SSs and measured the MPRAs on CTs from the upper half of each kidney included in the cross-section. Paired samples test and Wilcoxon signed-rank test were used to evaluate the temporal changes of mean renal parenchymal attenuation (RPA) and median CT-SS values, in three consecutive CTs. Spearman's test was used to evaluate the correlation of each RPA and CT-SS value on three consecutive CTs.

Results: The study population included 65 patients with a mean age of 61.49±13.91 years. A total of 36/65 (55.4%) were male. We found a significant increase between the first and second CT-SS ($p<0.001$) values, and a significant decrease between the first and second RPA ($p<0.001$) values. There were statistically significant moderate negative linear correlations between MRPA values and consecutive CT-SSs in COVID-19 patients (correlation coefficient [r]1=-0.320, p=0.009; r2=-0.381, p=0.002; r3=-0.393, p=0.001).

Conclusion: The decrease in renal parenchymal attenuation in non-enhanced computed tomography is related to the severity of pneumonia in COVID-19 patients and may be an attention factor for acute kidney injury.

Keywords: COVID-19, Coronavirus, CT severity score, renal parenchymal attenuation

INTRODUCTION

Coronavirus disease 2019 (COVID-19) affects the pulmonary system or extrapulmonary systems in severe cases. The responsible microorganism is "Severe Acute Respiratory Syndrome Coronavirus 2" (SARS-CoV-2) (1). Many studies have reported that angiotensin-converting enzyme 2 (ACE2) is a functional receptor for SARS-CoV-2. Due to the dense presence of ACE2 receptors in the lungs, the lung is one of the most affected organs and can be seen in a wide clinical range from mild to severe (2). It is the intracellular entry receptor for SARS-CoV-2 of ACE2, which is also found in many organs such as the kidney, liver, and gallbladder outside the lung (3–5). The two most common kidney complications after COVID-19 are electrolyte imbalance with an incidence of 12.5%, and acute kidney injury (AKI) with an incidence of 11.0%, respectively. (6). In addition, the physiopathology in patients with elevated serum creatinine (SCr) levels after COVID-19 is unclear and the occurrence of AKI has been reported to be associated with poor prognosis (7–9). However, in a few studies, it has been reported that kidney damage may be due to cytokine storm, direct damage to the virus, hyperinflammatory immune response, and hypercoagulation (10–12).

On non-enhanced computed tomography (NECT) imaging of patients with AKI, there are thickening of the perirenal fascia, linear density increases due to inflammatory changes in the perinephric adipose tissue, and increases in fluid-related density (13,14). In NECT, due to fluid-related density changes, Hounsfield Units (HU) values are increased in low-density areas such as adipose tissue, while HU values are decreased in high-density areas such as parenchymal organs. In chest CT, the upper half of the renal parenchyma is included in the image, from which density measurements can be made.

CT severity scores (CT-SS) were developed to determine the pneumonia severity of patients on CT (15). CT-SS shows the severity of COVID-19 pneumonia, so it is a very

Corresponding Author: Ahmet Turan Kaya, hmttrnky.62@gmail.com
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important CT finding for the prognosis of patients. Total CT-SS was significantly higher in deceased COVID-19 patients than in convalescent patients, and in critical and severe patients compared to mild stages (16,17). A previous study suggests that renal parenchymal attenuation (RPA) measurement could be used as a quantitative method for COVID-19-associated kidney failure (13). In the literature, there are limited studies that measured CT density values in the renal parenchyma and compared these values with the severity of pneumonia (13,18). In these studies, CTs that were performed at the time of admission were used, and temporal changes of CT-SS and RPA values were not compared in follow-up CTs.

In this study, we investigated the correlation between severity scores (CT-SS) values and attenuation changes in the renal parenchyma in consecutive chest CTs.

MATERIAL AND METHOD

Our study is a retrospective, single-center study of 582 patients who applied to our hospital (February 2021 and February 2022). The study was carried out with the permission of Amasya University Faculty of Medicine Clinical Researches Ethics Committee (Date: 06.10.2022, Decision No: 96). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Study Population

Inclusion criteria: Patients older than 18 years of age and positive real-time reverse transcriptase-polymerase chain reaction (RT-PCR) test were included in the study.

Exclusion criteria: Pediatric patients, pregnant women, patients with negative RT-PCR tests, those with image artifacts that prevent evaluation on NECT, patients with contrast enhancement CT, incomplete clinical data and chest CT images, outpatients, with urolithiasis, and/or hydronephrosis, unilateral or bilateral atrophic kidney, chronic kidney disease (CKD) and acute pyelonephritis were excluded from the study.

We excluded a total of 517 patients according to our exclusion criteria. So finally, a total of 65 COVID-19 patients were included in the study (**Figure 1**).

Clinical and Laboratory Data

All patients' demographic information, comorbidities, the laboratory findings obtained within 1 day from the initial chest CT data were reviewed from the electronic medical records of our hospital.

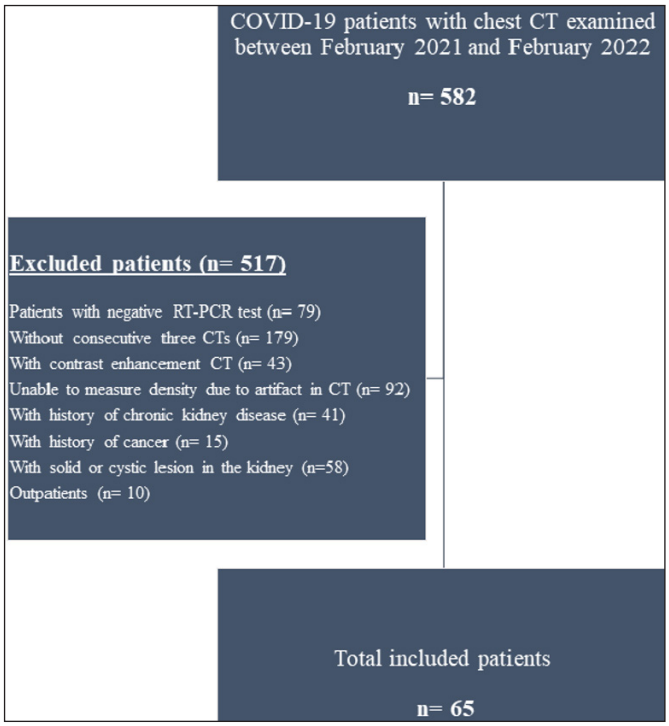

Figure 1. Flowchart for patient inclusion

Chest CT Image Acquisition

In all non-contrast chest CT scans, patients were instructed to hold their breath in the supine position. Axial images included areas from the beginning of the thorax to the middle part of the kidneys. Chest imaging was performed with a 128-slice CT scanner [(GE Healthcare Revolution EVO CT Milwaukee, WI)] using the routine protocols in our hospital.

Image Analysis

Chest CT images of the patients were retrospectively reviewed by a radiologist with 9 years of experience (XX), unaware of the patient's clinical data. CT severity scores (CT-SS) for COVID-19 pneumonia were calculated using a visual scoring system in CT images previously used in the literature (15). It was calculated as, 0 if there is no lung involvement; 1 if < 5% involvement; 2 if 5–25% involvement; 3 if 26–49%; 4 if 50-75% involvement; 5 if there is > 75% involvement. Total CT-SS is obtained by summing 5 lung lobe scores (score range: 0-25) (15) (**Figure 2a-c**).

The radiologist (XX) measured the renal parenchyma density on CT from the upper half of each kidney included in the cross-section. Renal parenchymal attenuation (RPA) values were measured by placing regions of interest (ROIs), each of approximately 0.5 cm^2, in three different areas of the parenchyma of each kidney. The average of 3 RPA values of each kidney was accepted as the RPA value of that kidney. The mean value of both kidneys [(Right RPA+Left RPA)/2] of each patient was used as the mean RPA (MRPA) value. This analysis was calculated on a total of three CTs of each patient, initially at admission and two at follow-up CTs (**Figure 2d-f**).

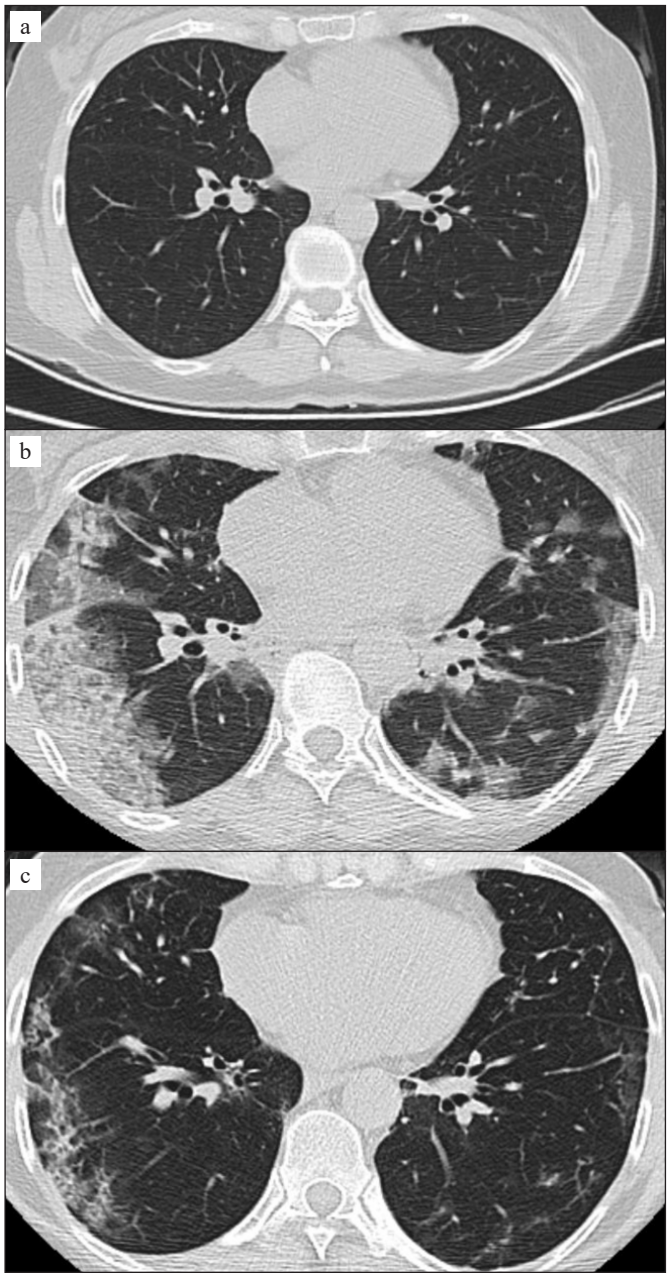

Figure 2 a-c. In three consecutive axial plane non-contrast CT images, **(a)** the first CT was normal, **(b)** the second CT showed peripherally located ground glass opacity, consolidation, and crazy paving pattern areas in both lungs. **(c)** On the third CT, the lesions appear to regress and linear band formations are observed [**(a)** CT-SS1=0; **(b)** CT-SS2=19; **(c)** CT-SS3=13].

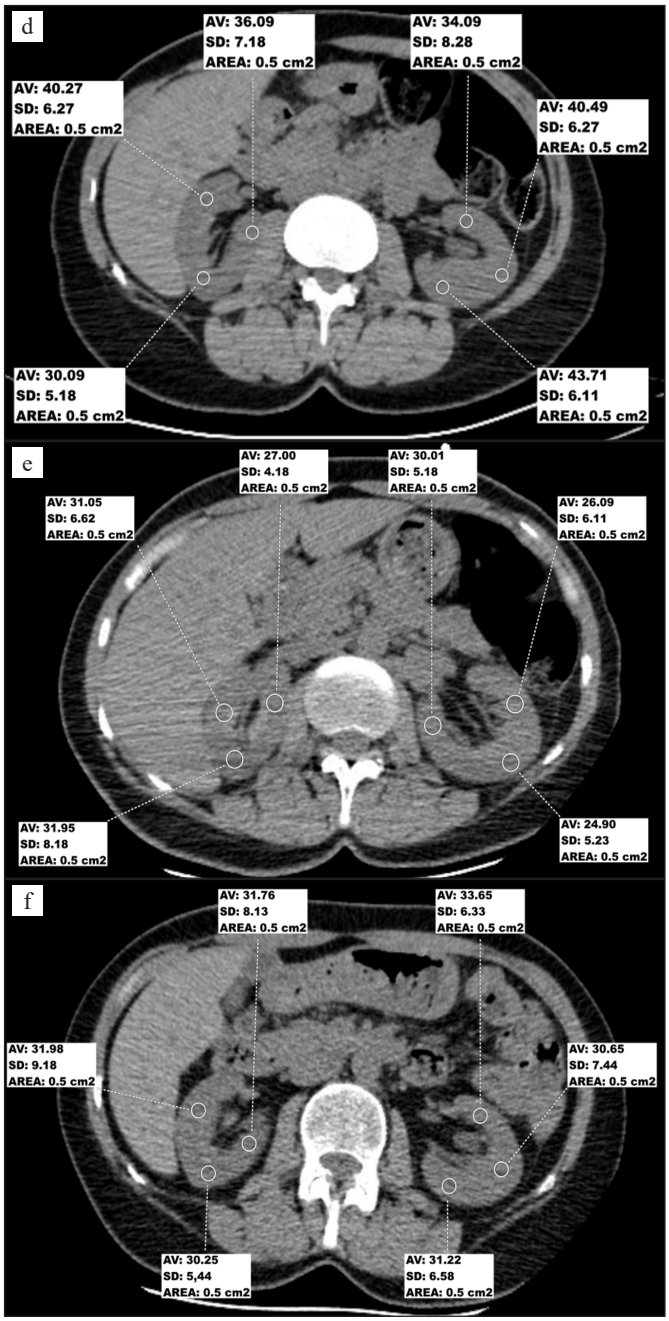

Fig 2 d-f. Renal parenchymal attenuation measurements are seen from slices passing through the kidney level on three consecutive axial plane non-contrast CT images [(a) mean RPA1=36.66 HU; (b) mean RPA 2=28.50 HU; (c) mean RPA 3=31.59 HU].

Statistical Analysis

We used SPSS Statistics for Windows, Version 22.0 (IBM Corp. Released 2017. Armonk, NY) for statistical analysis. The Kolmogorov-Smirnov test was used to examine the conformity of the variables to the normal distribution. CT-SS was considered the ordinal variable. In descriptive analyses, frequency and percentage were used for categorical variables; mean and standard deviation were used for continuous variables. Paired samples test and Wilcoxon signed-rank test (*) were used to evaluate the temporal changes of mean RPA and median CT-SS (*) values, in three consecutive CTs. Spearman's test was used to evaluate the correlation of each MRPA and CT-SS value on three consecutive CTs. A $p<0.05$ value was considered a statistically significant result.

RESULTS

Demographic Features

The study population included 65 patients with a mean age of 61.49 ±13.91 years. A total of 36/65 (55.4%) were male. Of all patients, 11/65 (16.9%) patients were treated in the ICU and 6/65 (9.2%) died. The most common comorbidities of the study population were cardiovascular disease (40/65; 61.5%), and diabetes mellitus (DM) (21/65; 32.3%) (**Table 1**). The mean CT-

SS on CT at admission was 7.72 ± 7.42 (0-25) and the mean MRPA was 39.69±5.54 (27.34-59.21). Among the laboratory findings, the mean serum blood urea nitrogen (BUN) value was 35.23±18.41 (11.00-103.00) and the mean serum creatinine (Scr) value was 0.94±0.35 (0.48-2.52) (**Table 2**).

Table 1

		Frequency	Percent (%)
Gender	Female	29	44.6
	Male	36	55.4
Death or alive	Alive	59	90.8
	Death	6	9.2
ICU?	Non ICU	54	83.1
	ICU	11	16.9
Chronic pulmonary diseases	Absent	49	75.4
	Present	16	24.6
Cardiovascular disease	Absent	25	38.5
	Present	40	61.5
Diabetes mellitus	Absent	44	67.7
	Present	21	32.3
Neurological Diseases	Absent	61	93.8
	Present	4	6.2

Table 2

	Mean	Std. Deviation	Min	Max
Age	61.49	13.91	32	89
First CT-SS	7.72	7.42	0	25
Second CT-SS	14.97	7.48	0	25
Third CT-SS	14.38	8.10	0	25
First MRPA	39.69	5.54	27.34	59.21
Second MRPA	35.12	4.30	26.00	45.00
Third MRPA	35.20	5.54	23.00	51.95
First RRPA	39.88	5.95	27.82	61.92
Second RRPA	35.10	4.54	21.67	46.27
Third RRPA	35.00	6.07	23.00	51.56
First LRPA	39.50	5.88	25.51	56.49
Second LRPA	35.15	4.85	23.00	47.67
Third LRPA	35.40	6.08	23.00	56.61
WBC (3.39–8.86; 10^9/l)	7.87	7.92	3.19	63.34
Neutrophil count (1.65-4.97; 10^9/l)	5.93	8.55	1.76	69.00
Lymphocyte count (1.17-3.17; 10^9/l)	1.41	0.78	0.32	4.64
CRP (0-5; mg/L)	41.55	47.20	1.17	174.00
Ferritin (22-322; ug/L)	320.18	818.03	6.30	6300.60
ESR. (0-30; mm/H) 1. hour	48.58	26.28	7.00	112.00
Blood urea nitrogen (16.6-48.5; mg/dl)	35.23	18.41	11.00	103.00
Serum creatinine (SCr) (0.7-1.2; mg/dl)	0.94	0.35	0.48	2.52
Creatinine kinase. (0-190; U/l)	112.80	99.28	17.00	676.00
Sodium (136-145; mmol/l)	137.63	2.84	129.00	143.00
Potassium (3.5-5.1; mmol/l)	4.37	0.40	3.72	5.57

CT-SS: CT Severity Score; RRPA: Right renal parenchymal attenuation (HU); LRPA: Left renal parenchymal attenuation (HU); MRPA: Mean renal parenchymal attenuation [(RRPA+LRPA)/2]

Temporal Changes of Consecutive CT-SSs and RPAs

We compared the temporal changes of the values of CT-SSs and MRPAs in three consecutive CTs, respectively. While there was a significant increase between the first and second CT-SS (p<0.001) values, there was a statistically significant decrease between the first and second RPA (p<0.001) values (**Figure 3**) (**Table 3**).

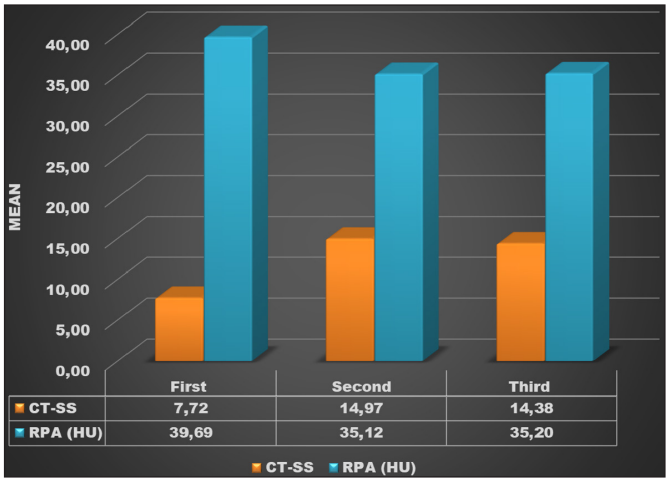

Figure 3. Bar chart showing the temporal changes of the mean CT-SS and RPA values in consecutive CTs.

Table 3

	Mean/Median	p value
CT-SS*		
Pair 1		<0.001
First CT	6.00	
Second CT	16.00	
Pair 2		0.566
Second CT	16.00	
Third CT	14.00	
RPA		
Pair 1		<0.001
First CT	39.69	
Second CT	35.12	
Pair 2		0.920
Second CT	35.12	
Third CT	35.20	

Pairwise comparisons were made using the Paired Samples t-test and Wilcoxon test (*). * Median values were used

Correlation Between RPA and CT-SS

We compared the correlations of CT-SS and MRPA values in three consecutive CTs, respectively. There were statistically significant moderate negative linear correlations between MRPA values and consecutive CT-SSs in COVID-19 patients (correlation coefficient [r]1=-0.320, p=0.009; r2=-0.381, p=0.002; r3=-0.393, p=0.001) (**Figure 4**).

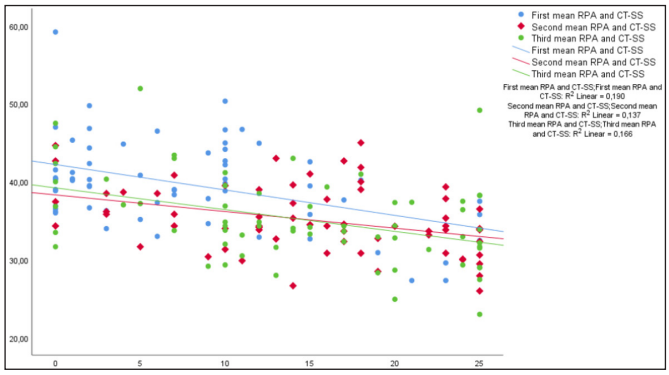

Figure 4. Scatterplot showing the correlation of the mean CT-SS and RPA values in consecutive CTs.

DISCUSSION

In our retrospective analysis, we investigated the temporal variation and correlation, between mean renal parenchymal attenuation (MRPA) and CT severity score (CT-SS). Our results showed that there was a significant negative correlation between MRPA and CT-SS in three consecutive CTs. While there was a significant increase between the first and second CT-SS, there was no significant increase between the second and third CT-SS. In addition, there was a significant decrease between the first and second MRPA, there was no significant decrease between the second and third CT-SS.

The most common kidney-related laboratory disorders after COVID-19 are hyperkalemia in blood analysis, proteinuria and hematuria due to AKI in urine analysis (6). ACE2 receptors, which are the entry gate of SARS-CoV-2 into the cell, are found in many organs in the body, but mostly in the ileum and kidneys (19,20). Since there are many ACE2 receptors in functional units of the kidney, the mechanism of damage by SARS-CoV-2 in this organ is not clear, but it has been suggested that many factors are effective (21). Many causes have been reported such as direct damage of the virus due to the intense content of ACE2 receptors in kidney cells, especially tubular and endothelial cells (22), disruption of the renin-angiotensin-aldosterone system (RAAS) (19), kidney damage due to treatment in severe patients, rhabdomyolysis associated with hyperventilation, renal hypoperfusion due to hypovolemia, abnormal coagulation and "cytokine storm" due to excessive inflammatory response (10,19,23). Prerenal factors cause AKI more frequently than renal factors in COVID-19 (24). Depending on these factors, RPA may decrease as a result of acute pyelonephritis, acute tubule damage, and swelling of endothelial cells due to an increase in the amount of intracellular fluid (10). The increased amount of fluid in the intracellular and extracellular areas of the renal parenchyma spreads to the extrarenal fatty tissue, resulting in hyperdense perinephric fat stranding on CT (10). Kunutsor et al. (6) reported the incidence of chronic kidney disease (CKD) before COVID-19 was 5.2% (2.8–8.1), while the incidence of AKI after COVID-19 was 11.0% (7.4–15.1) in their review. It has also been reported that pre-existing chronic kidney disease (CKD) is associated with poor prognosis in COVID-19, and the incidence of AKI increases after the disease (6,25,26). In our study, we eliminated patients with CKD that could contribute to changes in density because our main aim was to demonstrate the change in kidney parenchyma due to COVID-19 on CT. In addition, a decrease in RPA may occur in urinary obstruction, after the spontaneous passage of a stone, renal infection, inflammation, renal vascular disease, and renal trauma (27). Therefore, we excluded patients with urinary stones or hydronephrosis and underlying renal failure and pyelonephritis in our study.

Consistent with our study, Huang et al. (13) reported a statistically significant decrease in MRPA values compared to the control group after COVID-19. Huang et al. (13) compared the MRPA values of each COVID-19 patient with the control group in their study. Unlike this study, we investigated the mean values of RPA changes in consecutive CTs. We also included only inpatients to avoid heterogeneity of the patient population in our study. In our results, while there was a significant increase in CT-SS in the first and second CT, there was a statistically significant decrease in MRPAs. CT-SS and MRPA values in the first and second CTs of the patients showed a statistically significant negative correlation. As the severity of pneumonia increased and the patient's clinical worsened, kidneys were also affected and MRPA values decreased. There was no significant change in the second and third CT-SS values after appropriate treatment in the following period. As a result, no significant difference was found in the second and third MRPA measurements due to pneumonia and clinical stabilization of the patient. There was no significant change in the second and third CTs for both CT-SS and MRPA. In addition, MRPA values of consecutive CTs in COVID-19 showed a statistically significant negative linear correlation between CT-SS values (r1=-0.320, p=0.009; r2=-0.381, p=0.002; r3=-0.393, p=0.001). These findings suggest that RPA measurement and temporal variation may be a potential indicator for AKI associated with COVID-19 severity.

Differently, we found a negative correlation between MRPA and CT-SS values in three consecutive CTs. To our knowledge, this is the first study to evaluate temporal changes in CT-SSs and MRPAs in consecutive CTs in COVID-19 patients. We found that increasing CT-SS values caused a decrease in MRPAs.

The current study has several limitations. First, our study was a single-center retrospective analysis. Therefore, a multicenter prospective study is needed for more validation. Second, as the patients' non-contrast chest CTs were evaluated, the upper pole and middle parts of the kidneys were included in the images. It was more appropriate for the entire kidney to be included in the evaluation area. But in our study, chest CTs of COVID-19 patients were scanned retrospectively.

CONCLUSION

The decrease in renal parenchymal attenuation (RPA) in NECT is related to the severity of pneumonia in COVID-19 patients and may be an attention factor for acute kidney injury. Therefore, when evaluating chest CT scans of COVID-19 patients, examination of the renal parenchyma and adjacent fatty tissue for RPA may provide useful information about COVID-19-related kidney damage.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Amasya University Faculty of Medicine Clinical Researches Ethics Committee (Date: 06.10.2022, Decision No: 96).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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