The association between the CT severity index and the pulmonary artery area in COVID-19 pneumonia

Acta Radiologica
2023, Vol. 64(7) 2238–2244

DOI: 10.1177/02841851211070491
journals.sagepub.com/home/acr
Sage

Gokhan Ongen[1], Gokhan Gokalp[1], Omer Fatih Nas[1], Rifat Ozpar[1] and Selman Candan[2]

Abstract

Background: The pulmonary artery area (PAA) is a valuable non-invasive method for the diagnosis of pulmonary hypertension.

Purpose: To compare the change in PAA in patients with COVID-19 with the computed tomography (CT) severity index using follow-up imaging.

Material and Methods: A total of 81 patients who were followed up and underwent CT assessment more than once at our hospital's pandemic department were evaluated retrospectively. Patients with progression were separated into three groups: progression ranging from mild-to-mild infiltration (Group A, CT severity index of 0–2); progression from mild to severe infiltration (Group B, CT severity index of 0-2 to 3–5); and progression from severe-to-severe infiltration (Group C, CT severity index of 3–5). The PAAs were calculated separately.

Results: The mean age was 56 ± 12 years. In terms of those patients showing progression in the CT images, the number of patients in Groups A, B, and C was 29, 40, and 12 in the right lung; 32, 45, and 4 in the left lung; 23, 45, and 13 on both lungs, respectively. There was no significant difference between the main, right, and left PAAs in Group A ($P > 0.05$). In Group B, there were significant increases in the areas of the main, right, and left PAAs ($P < 0.05$). There were also significant increases in the areas of the right and main pulmonary arteries in Group C ($P < 0.05$).

Conclusion: PAAs increase as disease involvement advances in cases with COVID-19 pneumonia, which is thought to be correlated with progression.

Keywords
COVID-19, pulmonary artery area, computed tomography severity index

Date received: 26 September 2021; accepted: 13 December 2021

Introduction

COVID-19 pneumonia is a pandemic viral infection that is transmitted between individuals by droplets and direct contact. It was first reported in the Wuhan district of China in December 2019, and by the end of January 2020, its effects had been felt globally (1–4).

Since the virus directly affects the respiratory tract and causes infection in the lungs, radiological modalities, primarily computed tomography (CT), play a significant role in diagnosis and follow-up. Bilateral peripheral and subpleural ground-glass views are frequently seen at the onset of the disease, but consolidations, inverted halo view, and crazy-paving pattern appearances are more frequently reported in advanced stages of the disease. Examples of common complications include acute respiratory distress syndrome (ARDS), acute cardiac injury, and secondary infection (5–10).

Respiratory tract diseases, infectious and non-infectious diseases that affect the lung parenchyma, may cause

[1]School of Medicine, Department of Radiology, Bursa Uludag University, Bursa, Turkey
[2]Ministry of Health, Department of Radiology, Kelkit State Hospital, Gumushane, Turkey

Corresponding author:
Gokhan Ongen, Department of Radiology, Bursa Uludag University Hospital, Bursa, Turkey.
Email: drgokhanongen@gmail.com

increased pulmonary artery diameter and hypertension, depending on the severity of involvement (11). Early diagnosis of pulmonary hypertension in the initial periods of the disease impacts the prognosis and may necessitate different treatment procedures (11,12). Pulmonary hypertension can be diagnosed non-invasively via echocardiography, CT, and magnetic resonance imaging (MRI). A pulmonary arterial diameter >29 mm has a sensitivity of 87% and specificity of 89% for pulmonary hypertension (13).

It was previously reported that deteriorations in the coagulation parameters and increased D-dimer levels were observed during the follow-up of cases with COVID-19 pneumonia (5). Moreover, ARDS, the most frequent cause of mortality in these cases, may also be associated with pulmonary arterial micro emboli and hypoxemia (14). Thus, the changes in the pulmonary artery measurements in the follow-up imaging of these patients have particular importance.

In patients with COVID-19 pneumonia showing the progression of chest CT findings, pulmonary artery areas may be affected due to the various reasons mentioned above. The aim of the present study was to retrospectively evaluate the association between the CT severity index based on the pulmonary involvement degree and the pulmonary artery area.

Material and Methods

Study population

A total of 102 patients were evaluated retrospectively, who were followed up and underwent CT assessment more than once at our hospital's pandemic department between the first reported COVID-19 case in our country, 11 March 2020, to 2 December 2020. The inclusion criteria in our study were as follows: a positive reverse transcriptase-polymerase chain reaction (RT-PCR) test for COVID-19 pneumonia; at least one initial and follow-up chest CT exam; and progression on subsequent CT images compared to the initial CT findings. A total of 21 patients with a secondary disorder, including chronic obstructive pulmonary disease, emphysema, lung cancer, heart failure, cardiomegaly in chest imaging, were excluded. In addition, the patients with frequent pulmonary findings of COVID-19 pneumonia but negative RT-PCR test results were excluded from the study. The study was completed with 81 patients. The RT-PCR tests were positive for all patients. The study was approved by the local ethical committee (2020-23/3). The investigation conforms to the principles outlined in the Declaration of Helsinki.

CT technique

The CT images of the patients were obtained with a 16-section device (Somatom; Siemens, Erlangen, Germany) with a slice thickness of 1.5 mm in multiplanar reformatted (MPR) images (120 kV, 110–540 mAs). To minimize motion artifacts, patients were instructed to hold their breath at full inspiration. The CT images were evaluated on the Picture Archiving Communication Systems (PACS) by a chest radiologist who had 15 years of experience (R1) and a specialist radiologist who had eight years of experience (R2). The CT findings were evaluated at two timelines (the initial CT and the last follow-up CT) and the CT severity index scores were calculated at each timeline. Two radiologists determined the final score with consensus. To determine the CT severity index, we evaluated ground-glass opacity (GGO), crazy-paving pattern, and consolidation described by Pan et al. (15). The score was calculated for each of the lungs considering the extent of anatomic involvement, as follows: 0 = no involvement; 1 = <5% involvement; 2 = 25% involvement; 3 = 26%–49% involvement; 4 = 50%–75% involvement; and 5 = >75% involvement (15).

In this study, we categorized the patients with a CT severity index of 0–2 as a mild infiltration and 3–5 as a severe infiltration. The right pulmonary artery area was calculated as 1.5 cm distally to the pulmonary artery bifurcation, the left pulmonary artery area was calculated as 1 cm distally to the pulmonary artery bifurcation, and the main pulmonary artery area was calculated as 1.5 proximally to the pulmonary artery bifurcation (Fig. 1) (RadiAnt DICOM Viewer 64 bit 2020). The measurements of the pulmonary artery area were performed manually by the same person (R2).

Statistical analysis

The categorical variables were presented using frequency and percent; parametric continuous variables were presented with mean ± standard deviation; and non-parametric continuous variables were presented with median (interquartile range [IQR]). Patients with progression were separated into three groups for right, left, and both lungs: progression from mild-to-mild infiltration (Group A, CT severity index of 0–2); the progression from mild to severe infiltration (Group B, CT severity index of 0–2 to 3–5) (Fig. 2); and progression from severe-to-severe infiltration (Group C, CT severity index of 3–5). The normal distributions of the right, left, and main pulmonary artery areas were assessed with the Shapiro–Wilk test. The number of cases in each group was >30 and distributed normally. The initial and follow-up values of the pulmonary artery areas of right, left, and main pulmonary artery were compared in these groups of CT severity index (Groups A, B, and C) for right, left, and both lungs, respectively. In addition, we compared the percentage differences of the pulmonary artery areas between the deceased and the surviving patients. The paired t-test was used for comparison if variables were normally distributed, and the Wilcoxon signed-ranks test was used for non-parametric

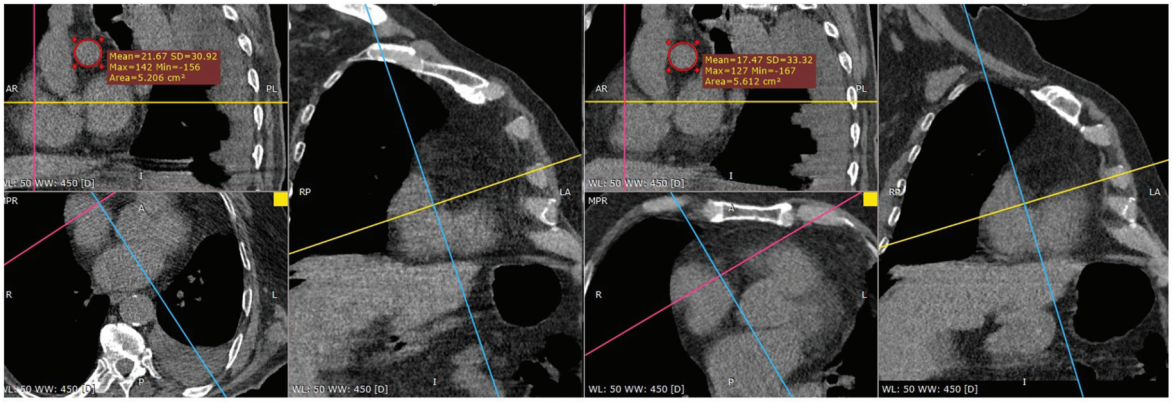

Fig. 1. Pulmonary artery measurement method. Initial and follow-up exam images are placed side by side and evaluated according to adjacent anatomical landmarks.

variables after removing outliers. The percentage differences were calculated by the following equation: $(r_2 - r_1) / r_1 \times 100$ (r_1: initial area, initial CT severity index; r_2: follow-up area, follow-up CT severity index). The association between changes of CT severity index and pulmonary artery areas was assessed using correlation analyses. $P <$ 0.05 was considered statistically significant. In correlation analysis, attention was focused on the R-value if the P value was <0.05. Those with an R-value of <0.40 were interpreted as poor correlation, 0.40–0.60 as mild correlation, and 0.60–0.80 as strong correlation. SPSS version 23.0 (IBM Corp., Armonk, NY, USA) was used for the statistical analyses.

Results

A total of 81 patients (44 men, 37 women; mean age = 56 ± 12 years) were included. Regarding the patients showing progression in the CT images, the number of patients in Groups A, B, and C was 29, 40, and 12 on the right lung, and 32, 45, and 4 on the left lung, and 23, 45, and 13 on both lungs, respectively. The time between CT exams was in the range of 2–38 days (median = 9 days).

In Group A, the right pulmonary artery area was increased from 4.39 (1.63) cm^2 to 4.46 (1.85) cm^2; the left pulmonary artery area was increased from 4.27 ± 1.19 cm^2 to 4.43 ± 1.26 cm^2 but the main pulmonary artery area was similar (6.02 (2.11) cm^2 to 6.02 (1.16) cm^2). There was no significant difference between the main, right, and left pulmonary artery areas in Group A ($P > 0.05$).

In Group B, the right pulmonary artery area was increased from 4.7 ± 1.42 cm^2 to 5.26 ± 1.42 cm^2, and the left pulmonary artery area was increased from 4.31 ± 1.07 cm^2 to 4.76 ± 1.21 cm^2. The main pulmonary artery area was increased from 6.73 ± 1.6 cm^2 to 7.74 ± 1.68 cm^2. In Group B, there were significant increases in the diameters of main, right, and left pulmonary arteries ($P < 0.05$).

In Group C, the right pulmonary artery area was increased from 4.7 (1.29) cm^2 to 5.3 (0.98) cm^2 and left pulmonary artery area was increased from 4.11 (2.88) cm^2 to 5.02 (3.42) cm^2, and the main pulmonary artery area was increased from 6.68 (2.64) cm^2 to 8.12 (3.42) cm^2. There were also significant increases in the diameters of the right and main pulmonary arteries in Group C ($P < 0.05$).

The comparisons between the initial and follow-up values of pulmonary artery areas are presented in Table 1, and the relevant box-plot graphs for percent changes in the pulmonary artery areas are presented in Fig. 3.

The correlation between the change in CT severity index and area of the pulmonary artery was analyzed using linear regression analysis, which showed that the CT severity index of both lungs was positively but poorly correlated with the pulmonary artery area in progressed cases ($P <$ 0.05). There was no significant association between the remaining measurements. The results of the linear regression are presented in Table 2.

Comparing between the deceased (n = 8) and the surviving patients (n = 73), in the surviving patients, a percentage difference of the main pulmonary artery area was 10.4 ± 14.64, the right pulmonary artery area was 5.72 ± 13.5, and the left pulmonary artery was 7.03 ± 17.33. In the deceased patients, the percentage difference of the main pulmonary artery was 24.86 ± 42.47, the right pulmonary artery was 14.25 ± 23.85, and the left pulmonary artery was 14.2 ± 13.6. There was a significant increase in the main pulmonary artery area in deceased cases compared to survivors ($P = 0.011$) (Table 3).

Discussion

Pulmonary arteries may be affected secondary to infectious and non-infectious diseases. In these cases, increases in pulmonary artery diameters, pulmonary thromboembolism, or pulmonary hypertension may develop (11). COVID-19 pneumonia causes diffuse pulmonary parenchymal

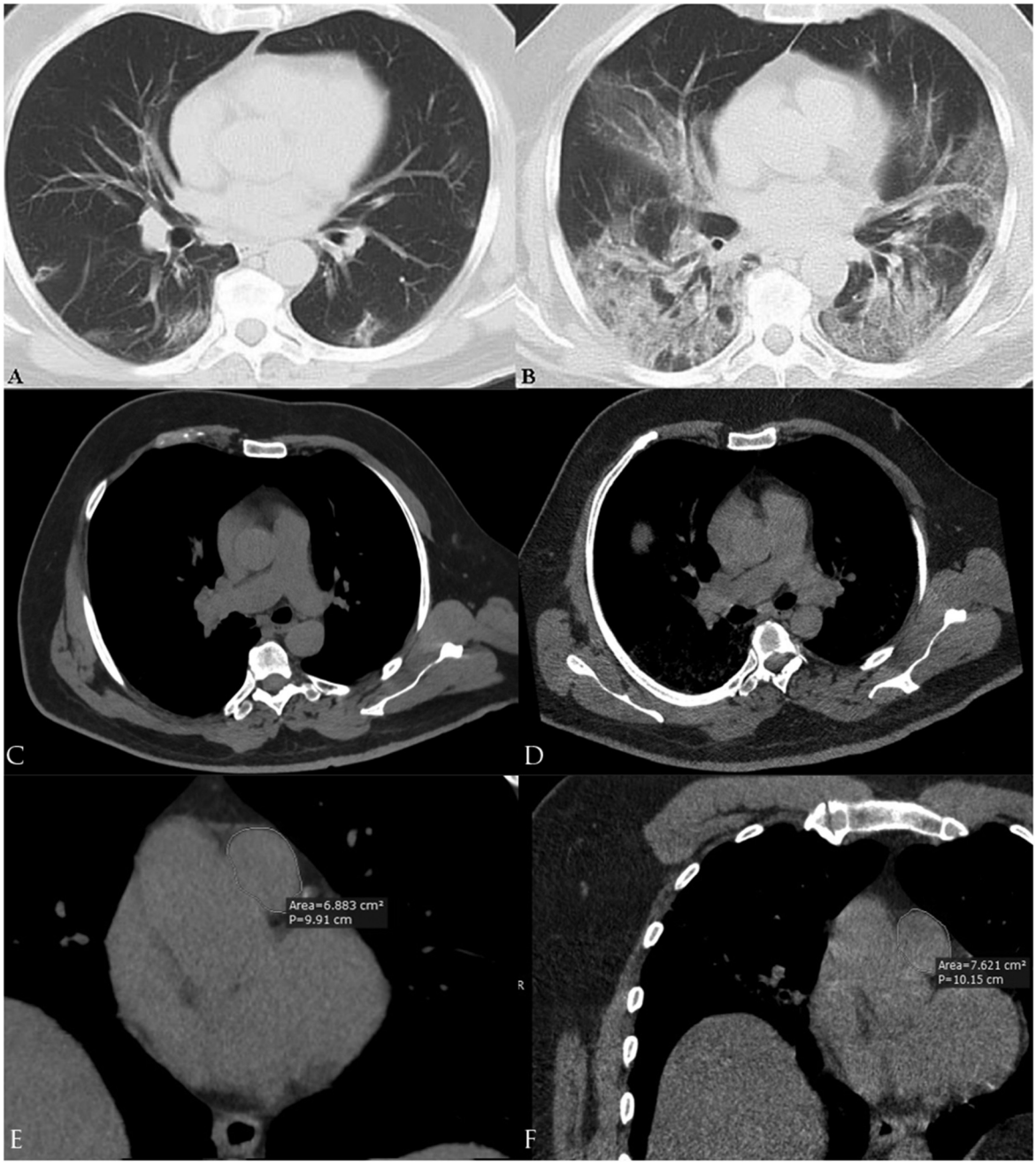

Fig. 2. A case with progressive infiltration in both lungs (Group B, CT severity index of 0–2 to 3–5). (a, c) Initial CT images; (b, d) CT images obtained two days later. (a) Bilateral peripheral and subpleural ground-glass opacity was seen, (b) two days later, severe ground-glass progression was obtained. (c, d) The main pulmonary artery diameter was increased from 26 mm to 31 mm, right pulmonary artery diameter was increased from 20 mm to 25.7 mm, left pulmonary artery diameter was increased from 21 mm to 25.8 mm. (e, f) The main pulmonary artery area was increased from 6.88 cm^2 to 7.62 cm^2. The interval between the two images was two days, and the patient died.

involvement by causing vascular endothelial injury, which subsequently advances with vascular diameter changes (9). The most frequently underlying mechanism is progression of ARDS due to thromboembolism and viral pneumonia that develops secondary to endothelial injury and deteriorations in the coagulation cascade (16).

Moreover, the frequent involvement of the pulmonary vascular structures may be associated with the thinness of the muscular layer in the pulmonary arteries and veins (17). Menter et al. reported their findings in 21 post-mortem cases in Switzerland, which showed that 76% of cases had a diffuse exudative alveolar disease, 38% of cases diffuse

Table 1. The initial and follow-up values of the pulmonary artery area in each group.

	Group	Initial area (cm^2)	Follow-up area (cm^2)	*P*
Right pulmonary artery	A	4.39 (1.63)	4.46 (1.85)	0.21
	B	4.7 ± 1.42	5.26 ± 1.42	<0.001
	C	4.7 (1.29)	5.3 (0.98)	0.005
Left pulmonary artery	A	4.27 ± 1.19	4.43 ± 1.26	0.14
	B	4.31 ± 1.07	4.76 ± 1.21	<0.001
	C	4.11 (2.88)	5.02 (3.42)	0.068
Main pulmonary artery	A	6.02 (2.11)	6.02 (1.16)	0.08
	B	6.73 ± 1.6	7.74 ± 1.68	<0.001
	C	6.68 (2.64)	8.12 (3.42)	0.001

Values are given as mean ± SD or median (interquartile range).

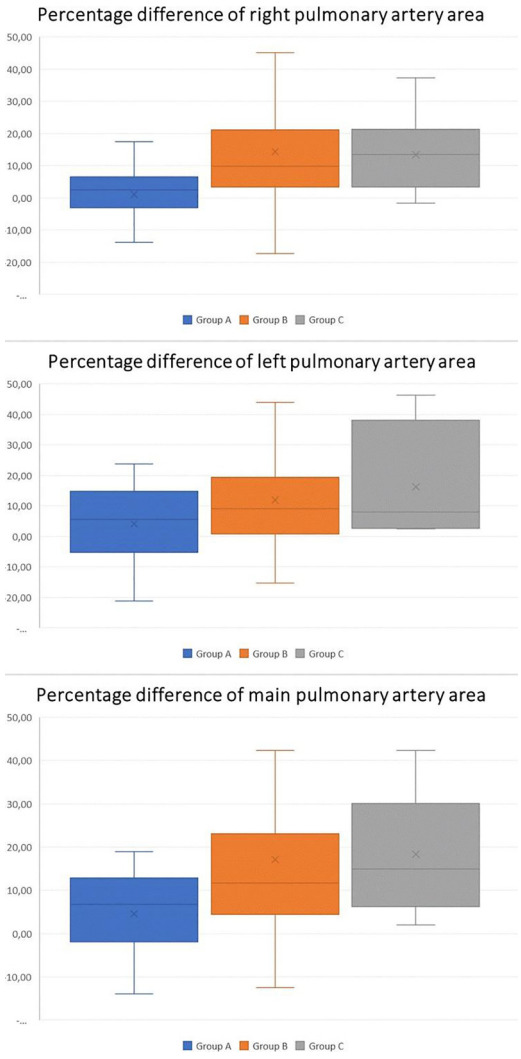

Fig. 3. Percentage differences in the right, left, and main pulmonary artery areas in each group.

proliferative alveolar disease, massive capillary congestion, and microthrombi in the alveolar capillaries (5/11,45%), and 19% of cases had a pulmonary embolism (18). All these findings were also suspected to be caused by edema and exudation in the intercellular distance associated with secretion of proinflammatory cytokines (tumor necrosis factor alpha, interleukine-1, etc.) against inflammation by the organism (5,18,19). Marini et al. reported that endothelial injury associated with inflammatory changes might result in reflex vasoconstriction and ventilation-perfusion injury as an underlying mechanism (20). The severity of vasoconstriction in pulmonary parenchyma is mainly thought to be associated with increased pulmonary artery diameter and a cause of hypertension.

Moreover, Yang et al. reported in their study on SARS in 2005 that autoantibodies against the virus may cause vascular endothelial injury (21). The changes in the coagulation parameters in patients' follow-up for COVID-19 pneumonia are associated with poor prognosis, such as increases in D-dimer and troponin, and associated with prolonged hospitalization and death rates (22). In addition, in two different studies, 23%–30% of patients with COVID-19 pneumonia were reported to have had at least one episode of pulmonary embolism (23,24). Besides thromboembolic complications, COVID-19 pneumonia can cause cardiac damage as SARS-CoV-2 can infect the myocardium. Moreover, hypoxemia, which develops in severe patients, is among the other causes of cardiac failure. These factors may be responsible for the increasing diameter of the pulmonary artery (25).

Pulmonary artery diameters can be measured by several methods using a chest CT. The pulmonary artery is often measured transversely in the axial section (26). There are two studies on the measurement of pulmonary artery diameters in the literature (16,27). In both studies, pulmonary artery diameters were compared with ascending aorta, and measurements were made only in the axial plane. Instead of transverse measurement of the diameter, the measurement on the plane perpendicular to the arterial axis in oblique reformatted images in all three planes is a more objective approach to the measurement of pulmonary artery diameters. In this study, in addition to the measurement of the main pulmonary artery area, we compared the areas of the right and left pulmonary artery areas with the CT severity index because the main pulmonary artery and its main branches may be affected differently by the severity of disease involvement.

Yildiz et al. reported that in patients with severe infiltration, pulmonary artery diameters were larger than in patients with mild infiltration (27). In our study, there was no significant difference between changes of main and right, left pulmonary arteries in Group A (mild to mild)

Table 2. R and *P* values for correlation analyses of percentage change of pulmonary artery areas and CT severity index change.

	Percentage difference in CT severity index					
	Right lung		Left lung		Both lungs	
	R	*P*	R	*P*	R	*P*
Percentage difference in pulmonary artery area						
Right pulmonary artery	0.034	0.762	0.15	0.181	0.108	0.338
Left pulmonary artery	0.107	0.344	0.097	0.391	0.148	0.189
Main pulmonary artery	0.158	0.16	0.216	0.052	0.248	0.025

Table 3. The pulmonary artery areas percentage differences between deceased patients and survivors.

	Survivors	Deceased patients	*P*
Right pulmonary artery	5.72 (13.5)	14.25 (23.85)	0.15
Left pulmonary artery	7.03 (17.33)	14.2 (13.6)	0.1
Main pulmonary artery	10.4 (14.64)	24.86 (42.47)	0.011

Values are given as median (interquartile range).

($P > 0.05$). However, all areas in Group B (mild to severe) and the main and right areas in Group C (severe to severe) significantly increased ($P < 0.05$). The significant difference between the pulmonary artery area in lung involvement in Group B and Group C suggest that severe pulmonary artery area changes occur in severe disease.

In the deceased patients, the percentage difference in the right, left, and main pulmonary artery areas was increased compared to that of the surviving patients. However, only the increase in the main pulmonary artery area was statistically significant ($P = 0.011$). Although there was a rise in the right, left, and main pulmonary arteries in Groups B and C, the main pulmonary artery change was only statistically significant in the deceased group, from which it can be assumed that the deceased group had a small number.

A poor meaningful positive correlation was found between the CT severity index of both lungs and the main pulmonary artery area. The correlation itself is a good indicator of the relationship between these two factors despite it being poor, which shows an increase in CT severity index results with an increase in pulmonary artery area. Since the pulmonary artery area is affected by many other factors, we do not expect a linear relationship between the pulmonary artery area and severity index.

The present study has some limitations. These include the low number of cases and the retrospective design of the study. We did not evaluate inter-observer variability and use of intravenous contrast medium in the imaging studies. In addition, we did not know the cardiac compliance of patients, laboratory findings, and if there was a presence of pulmonary artery embolism.

In conclusion, the area of pulmonary arteries increases as the disease involvement advances in cases with COVID-19 pneumonia and are thought to be associated with hypoxemia, infiltration, and maybe reflex vasoconstriction. These changes in the pulmonary artery area were remarkable in the deceased patients. For this reason, an increase in the pulmonary artery area should be assessed by the radiologists along with the CT severity index. Radiological findings that appeared from respiratory and cardiac systems highlighted in this study should be supported by further clinical studies.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship and/or publication of this article.

ORCID iDs

Gokhan Ongen https://orcid.org/0000-0002-7348-0813
Gokhan Gokalp https://orcid.org/0000-0002-3682-2474
Omer Fatih Nas https://orcid.org/0000-0001-6211-4191
Rifat Ozpar https://orcid.org/0000-0001-6649-9287
Selman Candan https://orcid.org/0000-0002-4742-296X

References

1. World Health Organization. Novel Coronavirus (2019-nCoV). Available at: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200121-sitrep-1-2019-ncov.pdf (accessed 15 June 2021).
2. World Health Organization. Coronavirus disease (COVID-19) technical guidance: The Unity Studies: Early Investigation Protocols. Available at: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/early-investigations (accessed 15 June 2021).
3. Johns Hopkins Whiting School of Engineering website. Coronavirus COVID-19 global cases. Available at: https://Gisanddata.maps.arcgis.com/apps/opsdashboard/index.html#/bda7594740fd40299423467b48e9ecf6 (accessed 15 June 2021).
4. Chan JF, Yuan S, Kok KH, et al. A familial cluster of pneumonia associated with the 2019 novel corona virus indicating person to-person transmission: a study of a family cluster. Lancet 2020;395:514–523.

5. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020;395:497–506.
6. Salehi S, Abedi A, Balakrishnan S, et al. Coronavirus disease 2019 (COVID-19): a systematic review of imaging findings in 919 patients. AJR Am J Roentgenol 2020;215:87–93.
7. Bernheim A, Mei X, Huang M, et al. Chest CT findings in coronavirus disease-19 (COVID-19): relationship to duration of infection. Radiology 2020;295:200463.
8. Raptis CA, Hammer MM, Short RG, et al. Chest CT and coronavirus disease (COVID-19): a critical review of the literature to date. AJR Am J Roentgenol 2020;215:839–842.
9. Zhao W, Zhong Z, Xie X, et al. Relation between chest CT findings and clinical conditions of coronavirus disease (COVID-19) pneumonia: a multicenter study. AJR Am J Roentgenol 2020;214:1072–1077.
10. Xu R, Du M, Li L, et al. CT Imaging of one extended family cluster of corona virus disease 2019 (COVID-19) including adolescent patients and "silent infection". Quant Imaging Med Surg 2020;10:800–804.
11. Oswald-Mammosser M, Weitzenblum E, Quoix E, et al. Prognostic factors in COPD patients receiving long-term oxygen therapy: importance of pulmonary artery pressure. Chest 1995;107:1193–1198.
12. Olschewski H, Simonneau G, Galiè N, et al. The aerosolized iloprost randomized study group inhaled iloprost for severe pulmonary hypertension. N Engl J Med 2002;347:322–329.
13. Tan RT, Kuzo R, Goodman LR, et al. Utility of CT scan evaluation for predicting pulmonary hypertension in patients with parenchymal lung disease. Chest 1998;113:1250–1256.
14. Marongiu F, Grandone E, Barcellona D. Pulmonary thrombosis in 2019-nCoV pneumonia? J Thromb Haemost 2020;18:1511–1513.
15. Pan F, Ye T, Sun P, et al. Time course of lung changes on chest CT during recovery from 2019 novel coronavirus (COVID19) pneumonia. Radiology 2020;295:715–721.
16. Spagnolo P, Cozzi A, Foà RA, et al. CT-derived pulmonary vascular metrics and clinical outcome in COVID-19 patients. Quant Imaging Med Surg 2020;10:1325–1333.
17. Tekcan Şanlı DE, Yıldırım D. A new imaging sign in COVID-19 pneumonia: vascular changes and their correlation with clinical severity of the disease. Diagn Interv Radiol 2021;27:172–180.
18. Menter T, Haslbauer JD, Nienhold R, et al. Postmortem examination of COVID-19 patients reveals diffuse alveolar damage with severe capillary congestion and variegated findings in lungs and other organs suggesting vascular dysfunction. Histopathology 2020;77:198–209.
19. Rankin JA. Biological mediators of acute inflammation. AACN Clin Issues 2004;15:3–17.
20. Marini JJ, et al. Management of COVID-19 respiratory distress. JAMA 2020;323:2329–2330.
21. Yang YH, Huang YH, Chuang YH, et al. Autoantibodies against human epithelial cells and endothelial cells after severe acute respiratory syndrome (SARS)-associated coronavirus infection. J Med Virol 2005;77:1–7.
22. Tang N, Li D, Wang X, et al. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. J Thromb Haemost 2020;18:844–847.
23. Léonard-Lorant I, Delabranche X, Séverac F, et al. Acute pulmonary embolism in patients with COVID-19 at CT angiography and relationship to d-dimer levels. Radiology 2020;296:189–191.
24. Grillet F, Behr J, Calame P, et al. Acute pulmonary embolism associated with COVID-19 pneumonia detected with pulmonary CT angiography. Radiology 2020;296:186–188.
25. Ruan Q, Yang K, Wang W, et al. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. Intensive Care Med 2020;46:846–848.
26. Ieki H, Nagatomo Y, Tsugu M, et al. Impact of pulmonary artery-to-aorta ratio by CT on the clinical outcome in heart failure. J Card Fail 2019;25:886–883.
27. Yildiz M, Yadigar S, BŞ Y, et al. Evaluation of the relationship between COVID-19 pneumonia severity and pulmonary artery diameter measurement. Herz 2021;46:56–62.