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Prognostic importance of pulmonary artery measurement in patients with COVID-19 and correlation with computed tomography severity score

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Abstract

Aim: To evaluate is the relationship of enlarged main pulmonary artery (mPA) diameter in COVID-19 with disease severity and early term prognosis by using computed tomography severity score (CTSS).

Materials and Methods: 906 of 1650 COVID-19 patients with chest computed tomography (CT) included in the study. The patient groups were divided in two as short (≤7 day) and long (> 7 day) hospitalization according to the length of hospital stay. The patients who were admitted to the intensive care unit (ICU) and those who died were also recorded. We assessed CTSS and PA diameter on CT images.

Results: 540 (60%) patients had pneumonia. 291 (54%) of them were found to have pure ground glass opacity (GGO), 168 (31%) of them were found to have both GGO and consolidation, 60 (11%) of them were found to have consolidation and 21 (4%) of them were found to have crazy paving pattern. There was a significant correlation between PA diameter and hospitalization time (r:0.339; $p < 0.001$), intensive care unit (ICU) need and mortality (r:0.398, 0.326; respectively; $p < 0.001$). There was a significant correlation between PA increase and CTTS increase (r:0.226; $p = 0.002$). The area under the curve of the mPA in predicting patient mortality was 0.805 (95% CI:0.695–0.915). The best cut-off value of mPA was taken as 28,4 sensitivity and specificity was found 78.9%, 74.5% respectively. CTSS of the cases who died because of COVID-19 were significantly higher ($p = 0.023$). The area under the ROC curve of CTSS in predicting patient mortality was 0.668 (95% CI:0.554-0.781). The best cut off value of CTSS was taken as 13 sensitivity and specificity was found 57.8%, 80.9% respectively.

Conclusion: mPA diameter increase is associated with poor prognosis including long term hospitalization, ICU hospitalization and mortality in COVID-19 cases.

Introduction

A pneumonia outbreak of unknown causes was reported to the World Health Organization (WHO) in Wuhan, Hubei province of China, on December 31, 2019 [1]. On January 7, 2020, the 2019 novel coronavirus (2019-nCoV) was shown as the cause of these reported cases, and it was later called coronavirus disease (COVID-19) [2]. The most common clinical symptoms of the disease are reported as fever, dry cough, shortness of breath, and common myalgia. In severe cases, dyspnea occurs after a week. In other severe cases, acute respiratory distress syndrome (ARDS), septic shock, metabolic acidosis difficult to treat, and coagulation dysfunction develop quickly. An increase in the risk for severe COVID-19 pneumonia has been reported in patients with underlying chronic health problems, especially cardiovascular and chronic pulmonary diseases [3]. The gold standard for diagnosis is a real-time reverse transcriptase polymerase chain reaction (rRT-PCR) test [4].

Pulmonary hypertension (PH) is a chronic and progressive disease affecting approximately 1% of the global popula-

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tion [5]. PH primarily causes right ventricle dysfunction, then biventricular dysfunction, leading to an increase in morbidity and mortality. An increase in the diameter of the main pulmonary artery (mPA) has been reported as a parameter in terms of predicting PH, and a cut-off value of 29 mm is highly likely to be considered PH [6, 7, 8]. As known, COVID-19 results pulmonary parenchymal fibrosis and these structural changes in lung parenchyma may lead decreased vascular compliance and this may result arterial resistance [9]. The pulmonary artery (PA) may be one of the important structures affected by pneumonia-related inflammation and hypoxia [10]. Chest computed tomography (CT), which has an important place in the diagnosis of COVID-19, allows an easy measurement of mPA and helps determine the risk of possible PH development in addition to lung parenchymal findings. Accordingly, the aim of our study is to determine the relationship between the enlarged mPA diameter in COVID-19 with disease severity and early term prognosis by using a CT severity score (CTSS).

Materials and Methods

Study design

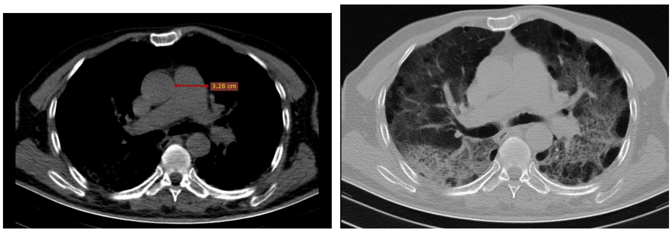
This retrospective study was approved by the Institutional Review Board (IRB protocol number: 2020/91) and the requirement for informed consent was waived. We retrospectively examined 1650 patients diagnosed with COVID-19 as proven by rRT-PCR at our university hospital between March and September 2020. Patients whose SARS CoV-2 infection was confirmed by rRT-PCR and who underwent a chest CT examination were included in our study. The patients who did not have a chest CT examination at the time of the initial diagnosis of COVID-19 were excluded from the study. The patients were divided into two groups as short (≤7 day) and long (> 7 day) hospitalization, according to the length of their hospital stay. The patients who were admitted to the intensive care unit (ICU) and those who died were also recorded.

Image acquisition

All CT examinations were conducted with a 16-slice spiral CT scanner (Emotion 16; Siemens Healthineers). The scanning range was from the apex to the base of the lung. Acquisitions were performed during a deep inspiration, breath-hold, without contrast administration. We implemented a low-dose scanning protocol with the following parameters: tube voltage, 80 kVp; tube current, 35–50 mA; rotation time, 0.75 s; pitch, 1.5; slice thickness, 3 mm; and detector width, 1.5 mm. In addition to the above-mentioned reduction dose strategy, we used iterative reconstruction algorithms. The dose length product and effective dose were 20.4 mGy.cm and 0.2856 mSv, compared with 260 mGy.cm and 3.64 mSv in a standard dose protocol.

Image analysis

The images were examined by two radiologists with 10 and 17 years of experience. The mPA diameter was measured at the bifurcation level of the pulmonary artery (Figure 1). Pulmonary parenchyma was evaluated in terms of ground glass opacity (GGO), consolidation, and crazy paving pattern. CTSS, which is a semi-quantitative scoring suggested by Pan et al., was used to predict the severity of pulmonary parenchymal involvement (11). Each of the five lung lobes were visually scored between 0 and 5: 0) no involvement; 1) < 5% involvement; 2) 5-25% involvement; 3) 26-49% involvement; 4) 50-75% involvement; and 5) > 75% involvement (Figure 2). Total CTSS was the sum of the individual lobar scores, and it ranged from 0 (no involvement) to 25 (maximum involvement).



(a) **(b)**

Figure 1. Axial unenhanced CT (a, b) of a 51-year-old female COVID-19 patient's main pulmonary artery diameter, shows bilateral ground glass opacities with superimposed inter and intralobular septal thickening (crazy-paving pattern) with CTSS 21.

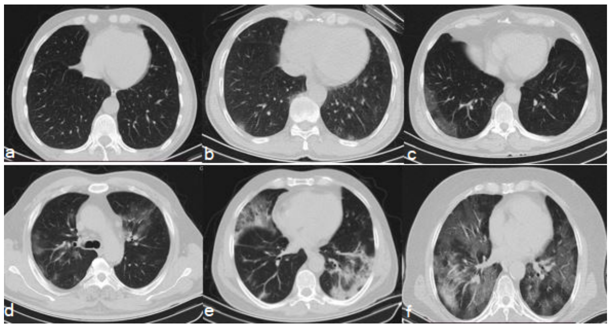


Figure 2. Lung parenchyma obtained from CT scans. Each of the five lung lobes were visually scored between 0 and 5: (a) no involvement; (b) < 5% involvement; (c) 5-25% involvement; (d) 26-49% involvement; (e) 50-75% involvement; and (f) > 75% involvement.

Statistical analysis

Statistical analyses were made with IBM SPSS V23.0. Normality distributions of quantitative data were made using the Kolmogorov-Smirnov and Shapiro-Wilk tests. The quantitative data that were normally distributed were compared with the Student's T-test, while the quantitative data that were not normally distributed were compared with the Mann Whitney-U test. Qualitative data were compared with the Pearson Chi-Square test. An ROC analysis was conducted for a diagnostic test assessment. The data were presented as mean±standard deviation, median (minimum–maximum), and frequency (%).

Table 1. Comparison of length of hospitalization and demographic data

	Total	≤7 days (n=579)	> 7 days (n=327)	p
Age (years) *	50 (18-95)	41 (18-95)	64 (24-91)	< 0.001
Female **	498 (55.0)	342 (59.1)	156 (47.7)	0.057
ICU Needs **	84 (9.3)	18 (3.1)	66 (20.2)	< 0.001
Comorbidities **	351 (38.7)	162 (28.1)	189 (57.8)	< 0.001
Hypertension	243 (26.8)	114 (19.8)	129 (39.4)	< 0.001
Diabetes mellitus	60 (6.6)	24 (4.2)	36 (11)	0.040
COPD	33 (3.6)	15 (2.6)	18 (5.5)	0.214
Astma	42 (4.6)	21 (3.6)	21 (6.4)	0.415
Malignancy	18 (2.0)	12 (2.1)	6 (1.8)	0.882
Ischemic CVD	21 (3.2)	3 (0.5)	18 (5.5)	0.010
Mortality **	57 (6.3)	18 (3.10)	39 (11.9)	0.005
Pulmonary artery diameter	26.3 ± 4.9	25.2 ± 4.5	28.2 ± 5.0	< 0.001

CVD: Cerebrovascular disease, COPD: Chronic obstructive pulmonary disease. *median (min-max), **n (%).

Table 2. Comparison of ICU needs and mortality and demographic data

	No need for ICU (n=274)	ICU needs (n=28)	p	Survive (n=849)	Exitus (n=57)	p
Age (years) *	46 (18-91)	76 (47-95)	< 0.001	46 (18-91)	76 (47-95)	< 0.001
Female **	474 (57.7)	24 (28.6)	0.003	477 (56.2)	21 (36.8)	0.101
Comorbidities **	285 (34.8)	66 (78.6)	< 0.001	309 (36.5)	42 (73.7)	0.001
Hypertension	192 (23.4)	51 (60.7)	< 0.001	210 (24.8)	33 (57.9)	0.003
Diabetes mellitus	45 (5.5)	15 (17.9)	0.028	51 (6.0)	9 (15.8)	0.122
COPD	21 (2.6)	12 (14.3)	0.013	24 (2.8)	9 (15.8)	0.026
Astma	39 (4.8)	3 (3.6)	0.776	42 (5.0)	0 (0.0)	1.000
Malignancy	15 (1.8)	3 (3.6)	0.446	15 (1.8)	3 (5.3)	0.326
Ischemic CVD	18 (2.2)	3 (3.6)	0.499	21 (2.5)	0 (0.0)	1.000
Pneumonia CT Score	10 (1 - 23)	15 (5 -23)	0.012	10 (1 - 23)	15 (5 -23)	0.023
Pulmonary artery diameter	25.7 ± 4.3	32.4 ± 5.8	< 0.001	25.9 ± 4.5	32.4 ± 6.1	< 0.001

CVD: Cerebrovascular disease, COPD: Chronic obstructive pulmonary disease. *median (min-max), **n (%).

Results

Population characteristics

Nine hundred six patients with positive rRT-PCR tests and chest CT examinations were included in the study. The demographic characteristics, length of hospitalization, need for the ICU, and prognosis of the patients are shown in Tables 1 and 2. The median age of the patients was found to increase in those who died or needed the ICU. The most common comorbidities were hypertension, diabetes mellitus, and chronic obstructive pulmonary disease (COPD).

There were 540 patients with a short hospitalization time and 366 patients with a long hospitalization time. Eighty-one (9%) patients needed the ICU, and 57 patients died after developing severe acute respiratory distress syndrome (ARDS).

Hospitalization time, need for ICU and mortality was higher significantly in elderly patients compared to younger patients ($p < 0.001$). Longer hospitalization time was observed in patients with hypertension, DM and cerebrovascular disease (CVD) ($p < 0.001$, $p = 0.04$, $p = 0.01$; respectively). The need for ICU was higher significantly in patients with hypertension, DM and COPD. ($p < 0.001$, p=0.028, p=0.013; respectively). Similarly, mortality was higher significantly in patients with hypertension, DM and COPD ($p = 0.003$, $p = 0.026$; respectively).

Pulmonary Parenchymal CT Characteristics

No sign of pneumonia was observed in 366 (40%) patients. Out of the 540 (60%) patients with pneumonia, 291 (54%) were found to have pure GGOs, 168 (31%) were found to have both GGO and consolidation, 60 (11%) were found to have consolidation, and 21 (4%) were found to have crazy paving pattern.

mPA Diameter and Prognosis Correlation

The mPA diameter was found to be high in both patients who needed the ICU and those who had died (Tables 1 and 2). A positive and moderate correlation was found between the mPA diameter and hospitalization time (r:0.339; $p < 0.001$). Similarly, a positive and moderate correlation was found between the mPA diameter and the need for the ICU and mortality (r: 0.398, 0.326, respectively; $p < 0.001$). The area under the curve of the mPA in predicting patient mortality was 0.805 (95% CI:0.695–0.915). In this context, when the best cut-off value of mPA was taken as 28.4 sensitivity was found as 78.9% (95% CI:54.43%-93.95%) and specificity was found as 74.5% (95% CI:69.07%-79.53%) (Figure 3).

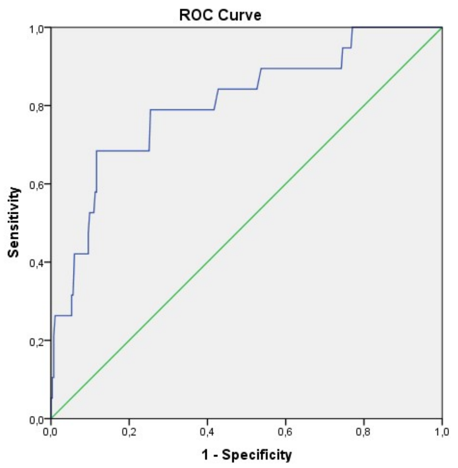


Figure 3. Receiver operating characteristic (ROC) curve of main pulmonary artery in predicting COVID-19 mortality.

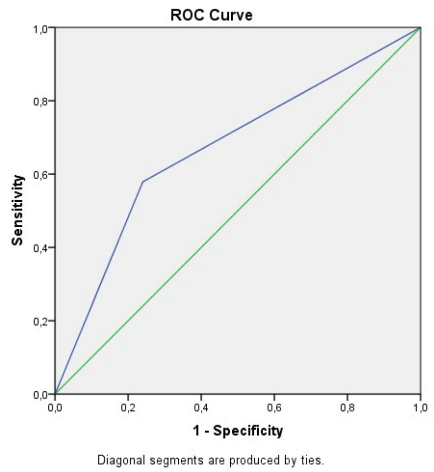


Figure 5. Receiver operating characteristic (ROC) curve of computer tomography severity score in predicting COVID-19 mortality.

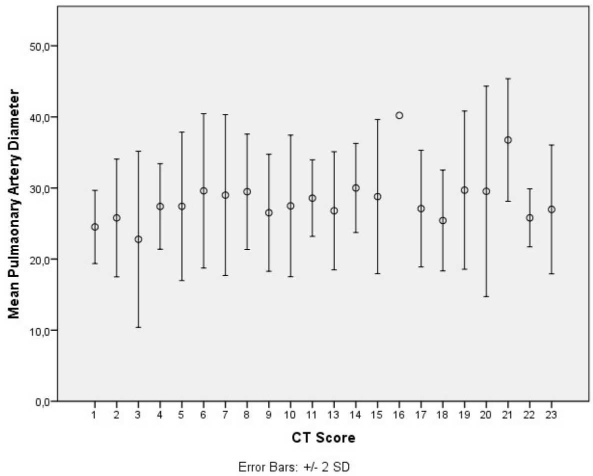


Figure 4. Comparisons between chest computed tomography severity score versus main pulmonary artery diameter.

Correlation of mPA Diameter and CTSS

There was a positive and weak correlation between the mPA increase and CTSS increase (r:0.226; $p = 0.002$) (Figure 4).

Correlation of CTSS and Mortality

The CTSS of the cases who died due to COVID-19 were significantly higher than the surviving patients ($p = 0.023$). The area under the ROC curve of CTSS in predicting patient mortality was 0.668 (95% CI:0.554-0.781). In this context, when the best cut-off value of CTSS was taken as 13, sensitivity was found as 57.8% (95% CI:33.50%-79.75%) and specificity was found as 80.9% (95% CI:75.85%- 85.33%) (Figure 5).

Discussion

The results of our study show that an enlarged in the mPA diameter is associated with a poor prognosis in COVID-19 patients, including longer hospitalization, an increase in the need for intensive care, and high mortality. In patients with a smaller mPA diameter and lower CTSS, the mortality rate was low, and the prognosis had a better course than the group with a larger mPA diameter the other group. There was a significant correlation between the CTSS and mPA diameter.

Enlargement in the mPA diameter can be the result of various pathological processes, such as primary and secondary hypertension, cardiac failure, an increase in circulating blood volume, pulmonary embolism, COPD, and interstitial pneumonia [12]. While an increase in the mPA diameter, which is an indicator of PH, is generally a long-term conditioning lung fibrosis, an acute mPA diameter increase may also occur depending on lung damage. In previous studies, an enlargement of them PA was observed within days in patients who progressed to ARDS [13]. In patients, the defined pathologies that may cause an mPA diameter increase, pulmonary hemodynamic processes (such as lung parenchymal damage, hypoxic vasoconstriction of pulmonary circulation, pulmonary endothelial damage, and thromboembolic events that may develop with COVID-19 pneumonia) may cause PH in non-advanced disease stages. A useful, non-invasive PA diameter measurement can easily be made to detect PH, which has prognostic significance in COVID-19 patients who undergo non-contrast CT examinations [14, 15]. There are several studies in the literature examining the effects of an mPA diameter enlargement on the clinical course of COVID-19 pneumonia. In their study with 200 COVID-19 patients, Pagnessi et al. found ICU hospitalizations and mortality rates in patients with PH were higher when compared to the non-PH group [16]. Unlike these studies, our study compared them PA diameter rate and patients' hospitalization times, ICU hospitalizations, and mortality rates, and a significant correlation was discovered between the findings.

In PH patients, secondary changes in pulmonary vascular hemodynamic (such as hypoxia, vascular remodeling, alveolar pressure increase, vasoconstriction, local thrombosis, pulmonary embolism, and decreased pulmonary compliance) are more frequent in pneumonia patients when compared with the normal population [17]. For this reason, COVID-19 pneumonia can have a more severe course and progress to ARDS in PH patients. In their study conducted to discover the role of mPA diameter increases in CTSS in COVID-19 pneumonia, Masomeh et al. found the mean mPA diameter was higher in patients with CTSS $\geq$ 12 when compared with CTSS $<$ 12 cases [18]. In their study, P. Spagnola et al. found a significant correlation between an increase in pulmonary vascular metric values (ΔPApost-pre, ΔPA/Aopost-pre values, PA/Ao ratio) and the degree of pneumonia in cases with COVID-19 pneumonia [19]. In our study, there was a statistically significant correlation between the CTSS score and an mPA diameter enlargement. In CTSS, we determined the severity of lung involvement in pneumonia cases. Sensitivity was found as 57.89% and specificity was found as 80.92% for a cut-off value of 13 in predicting mortality. The CT score was found to be significantly higher in patients who died, and our results were similar to those of previous studies [18, 20].

Our study had some limitations. First, there may be some differences in the mPA measurements in the thoracic CT of the patient depending on the examination. Second, there was a numerical inhomogeneity between the patients who died, who were hospitalized in the ICU, and who were discharged. Finally, neither a right heart catheterization nor an echocardiography examination was performed for PH diagnosis, and a method based on pulmonary artery measurement in tomography was used.

Conclusion

It has been shown that mPA diameter enlargement is associated with poor prognosis, including prolonged hospitalization, ICU need and mortality in COVID-19 cases. In addition, pneumonia involvement has a more aggressive course. The prognosis has a better course in patients with a lower CTSS and lower pulmonary artery CT diameter.

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