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Association of the changes in pulmonary artery diameters with clinical outcomes in hospitalized patients with COVID-19 infection: A cross-sectional study

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ABSTRACT

Objective: Enlarged pulmonary artery diameter (PAD) can be associated with mortality risk in coronavirus disease 2019 (COVID-19) patients. Our aim is to find the factors that cause changes in PAD and the relationship between radiological findings and clinical outcomes in COVID-19 patients.

Patients and Methods: In this descriptive, retrospective, and single centered study, among the hospitalized 3264 patients, 209 patients with previous chest computed tomography (CT) were included. Findings of current chest CTs of patients obtained during COVID-19 were compared with that of previous chest CTs. Pulmonary involvements, World Health Organization (WHO) Clinical Progression Scale scores and laboratory variables were recorded. Intensive Care Unit (ICU) admission, intubation and mortality were clinical outcomes that were evaluated by using uni – and multivariate analyses.

Results: Patients with high D-dimer had significantly increased risk for enlarged PAD and increase in PAD compared to previous chest CT (ΔPAD) (OR=1.18, p<0.05, OR=1.2 p<0.05). Both high D-dimer and an increase over 2 mm in PAD (ΔPAD 2mm) had significant risks for ICU admission, intubation, and mortality (OR= 1.18 p<0.01, OR=1.22 p<0.01, OR=2.62 p<0.05, OR=2.12 p<0.01, OR=2.32 p<0.01, OR=2.09 p<0.001 respectively). It was found that with enlarged PAD, risk of ICU admission and mortality increased. (OR=3.03 p<0.001, OR=2.52 p<0.01). Combined with age and lymphocyte counts, PAD predicted mortality with a 50% sensitivity, 88% specificity (AUC=0.83, p<0.001).

Conclusion: PPatients with an increase over 2 mm (ΔPAD 2mm) in PAD had significantly increased clinical severity, ICU admission, intubation, and mortality. High levels of D-dimer and CRP in patients suggest that increased inflammation and thrombosis may be effective in pathogenesis.

Keywords: Pulmonary artery diameter, COVID-19, Thromboembolism, CoRad, WHO score

1. INTRODUCTION

It is well known that increased pulmonary thromboembolic events are responsible for increased morbidity and mortality in patients with coronavirus disease 2019 (COVID-19) infection [1-5]. The detection of diffuse thromboembolism in the pulmonary arteries (PA) and dilatation of the right ventricle according to autopsy studies and clinical studies suggest that severe pulmonary hypertension (PH) secondary to pulmonary thromboembolism that develops in a large proportion of patients [6-8].

It has been stated that the enlarged pulmonary artery diameter (PAD) and PAD/Aorta ratio measurement in non-contrast chest computed tomography (CT) is a useful non-invasive method in determining pulmonary hypertension. Reference values of PAD for healthy persons have been previously established and revealed good sensitivity for excluding PH [9].

Some studies reported a relationship between enlarged PAD and severity [10,11] and mortality of COVID-19 12-14]. In a study with a small patient population comparing the change in PAD in chest CT scans between COVID-19 and pre COVID-19 periods, it was shown that increased PA diameter (ΔPAD), PAD/Aorta ratio were significantly associated with the degree of lung involvement, but no significant relationship was found with clinical severity and mortality [14].

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The aim of this study is to investigate factors that influence the changes in PAD and the relationship between the change in PAD and clinical severity, radiological involvement, and mortality in hospitalized COVID-19 patients.

2. PATIENTS and METHODS

This study is a descriptive study. A total 3264 patients aged 18 and above, who were tested positive for SARS-CoV2 PCR and diagnosed with COVID-19 and hospitalized in tertiary university hospitals between March 2020 and June 2021 were scanned from the hospital information system and analyzed. Among them, 209 patients who had chest CT scans before the COVID-19 pandemic and whose PAD could be measurable were included in the study. Sample size was based on previous studies. Patients with missing data were excluded from the study. Chest CT scans and laboratory values of the patients obtained during the administration, as well as previous chest CT scans obtained with different indications within the last 5 years were analyzed. PAD was measured perpendicular to the vessel surfaces where the vessel walls were parallel to each other, within 3 cm of the bifurcation point, in both pre – and post-COVID-19 chest CT scans of 209 patients.

The diameter of the ascending aorta (Ao), detected in the same cross-section as the maximum PAD, was measured horizontally and vertically and averaged. PAD was evaluated by Framingham-Based on gender-specific references. Females with a diameter over 27 mm and males with a diameter 29 mm were considered having enlarged PAD, and patients were categorized into two groups as normal PAD and enlarged PAD. The normal PA/Ao ratio was considered as ≤ 0.9 [9, 15].

In addition, patients also were divided into two groups: those with an increased PAD (ΔPAD) and those without an increase in PAD, regardless of reference values, but according to the degree of change in PAD between previous chest CT scans and chest CT scans done during the COVID-19 infection.

Considering the highest Likelihood Ratio (LR) in the ROC analysis, the patients were divided into two groups as those with an increased PAD over 2 mm (ΔPAD_{2mm}) and those with PAD less than 2mm (ΔPAD_{2mm^-}). In radiological evaluation, parenchymal involvement was classified in increasing percentage intervals with 0%, 5%, 25%, 50% ,75% to 100% for each lung lobe. In sum, total scores between 0 and 25 were calculated by adding scores for each lobe, such as 0, 1, 2, 3, 4, and 5 respectively [16, 17].

Two pulmonologists evaluated the chest CT scans independently, and a consensus was reached between the different results; at the point without agreement, the decision of a more senior pulmonologist was consulted. All chest CT examinations were performed on multidetector scanners with 256 rows (Philips ICT). The WHO Clinical Progression Scale was used for clinical severity [18]. Data of the patients was taken from the hospital information system. Laboratory variables including C-reactive protein (CRP), D-dimer, ferritin, fibrinogen, LDH, MPV, neutrophil, lymphocyte neutrophil/lymphocyte, lymphocyte/CRP ratios obtained in the first day of admission, and the worst values during hospitalization were used [19-22].

Human rights

The study was approved by the Marmara University, School of Medicine Clinical Research Ethic Committee (protocol number: 09.2020.1316, date: 04-12-2020). All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standard.

Statistical Analysis

The statistical analysis was performed using the STATA SE 17 software (Stata Corp 2021. *Stata Statistical Software: Release 17*. College Station, TX: StataCorp 2021 lLC). Data were expressed median and interquartile range (IQR) according to normal distribution for continuous ones; counts and percentage for categorical ones. The normality assumption was tested with Shapiro Wilk W test. Chi-square is applied between categorical variables; Mann-Whitney U Test was used for two independent groups in numerical variables. Spearman's correlation test was applied to evaluate variables like radiologic involvement and pulmonary artery. Logistic regression analysis was used to examine the factors affecting the dependent outcomes. Survival analysis and multivariate analyzes in PAD and ΔPA groups were performed using the Cox proportional hazards model. Receiver Operating Characteristics (ROC) analysis was applied to see the mortality estimation of PAD and the Area Under Curve was calculated. Confidence intervals (CIs) were computed at a 95% level. If the P value was less than 0.05, it was considered statistically significant.

3. RESULTS

The Patient Characteristics

This study enrolled 209 patients (132 male, 63.16%) with previous chest CT scans. The median age of the patients was 64 years (IQR=55-75). The number of patients with oxygen requirement was 168 (80.3%), 72 patients (34.4%) were admitted to ICU. The median duration of hospitalization was recorded to be 7 days (IQR, 5-12) for patients admitted to the medical ward, and 7 days (IQR, 4-12) for patients admitted to ICU.

The previous CT scans used as baseline examinations had been performed with a median of 1.8 years (IQR, 1.04-2.65) before COVID-19 for another reason. The median PAD value of the patients before COVID-19 (PAD_{pre}) was 25.72 mm (IQR,23.54-26.63), while PAD was 27.29 mm (IQR,24.84-30.62) during COVID-19 ($p<0.001$).

Assessment of Lung Parenchyma

Radiological score distribution of patients were as follows: 0-5 points: 48 patients (23%), 6-10 points: 85 patients (41%) 11-15 points: 42 patients (19%), 16-20 points: 26 patients (13^%) 21-25 points: 8 patients (4%).

Radiological score showed a weak positive correlation with WHO score (R=0.28, $p<0.001$), and the risk of ICU admission

(OR=1.10, LR=13.34, p<0.001, 95% CI) and intubation (OR=1.05, LR=4.22, p=0.03, 95% CI) (Table II).

The enlarged PAD incidence was found to be higher in patients with a radiological score of 5 and above (OR=7.01, p<0.01, 95% CI). The increased ICU admission was found in those with a radiological score of 10 and above (p=0.008), and this relationship was clearer in those with a radiological score of 20 and above (OR = 9.64, p<0.001, 95% CI). A tendency to increase in the need for intubation was found in those with a radiological score of 15 and above (p=0.086). However, there was no significant relationship between the radiological score and mortality.

The enlarged PAD was found to be higher in patients with a radiological score of 5 and above (OR= 7.01; p<0.01). A radiological score of 5 or higher was found in 85 of 88 patients (96.6%) with enlarged PAD.

Patients with enlarged PAD

Relationship between the enlarged PAD and different variables are shown in the Table I. Risk factors affecting enlarged PAD and effect of PAD to clinical outcomes are given in Table II and Table III.

The PAD solely was a significant predictor of mortality (61% sensitivity, 65% specificity, AUC = 0.69, p<0.001). When the PAD was evaluated with age and lymphocyte, it predicted mortality better (50% sensitivity, 88% specificity, AUC = 0.83, p<0.001) (Table III). (Figure 1).

The optimal cutoff value of PAD for mortality was detected as 27.61 mm (sensitivity 67.7%, specificity 63.9%), and the cutoff for maximum effectiveness was determined as 33.54 mm (17.7% sensitivity, 97.7% specificity) (Figure 1).

Table I. *The comparisons of patients' characteristics and outcomes between normal vs enlarged PAD and without increase vs increased ΔPAD_{2mm}*

Variables	Normal PAD (n=121)	Enlarged PAD (n=88)	Without increase ΔPAD_{2mm} (n=121)	Increased ΔPAD_{2mm} (n=88)	Total (n=209)
Age	61 (54-72)	68 (59-76.5) **	65(55-75)	64 (54-73)	64 (55-75)
Female	30 (38.96%)	47 (61.04%) ***	44(%57%)	33 (%43%)	77 (%37%)
CRP	71 (121-124)	79 (37-141)	126 (62-207)	149 (84.5-214.5)	74 (27-127)
D-dimer	0.7 (0.4-1.22)	1.02 (0.6-.2.4) ***	0.71 (0.43-1.15)	1.14 (0.54-2.24) ***	0.86 (0.46-1.57)
LDH	314 (249-452)	351 (284-449)	317 (253-425)	339 (274-494)	336 (259-452)
Lymphocyte	0.8 (0.6-1.2)	0.8 (0.5-1.1)	0.9 (0.5-1.2)	0.7 (0.5-1) *	0.8 (0.5-1.1)
N/L Ratio	5.75 (3-9.6)	6.79 (3.4-11)	5.6 (2.6-10)	7.5 (4.4-11) **	5.8 (3-10.4)
L/CRP Ratio	0.01(0.004-0.05)	0.01 (0.003-0.2)	0.1 (0.005-0.05)	0.008 (0.004-0.02) **	0.1 (0.005-0.05)
WHO Score	5 (5-6)	6 (5-10) ***	5 (5-7)	5 (5-10) *	5 (5-10)
ICU Admission	29 (%40.28%)	43 (%59.72%) ***	33 (%45.83%)	39 (%54.17%) **	72 (%34%)
LOS in ICU	0(0-1)	0 (0-6.5) ***	5(2-11)	8 (5-12) **	7 (4-12)
Intubation	29(%41.43^%)	41 (%58.57%) ***	31(%44.3%)	39 (%55.7%) **	70 (%33%)
Radiological Score	97 (80.2%)	85(96.6%)	6(6-12)	8 (6-14)	9 (6-13)
Mortality	26 (41.94%)	36 (58.06%) **	28(%45.2%)	34 (%54.8%) **	62 (%29%)

p<0.05, p<0.01**, p<0.001*** CRP: C-reactive protein, LDH: Lactate dehydrogenase, N/L Ratio: Neutrophil/Lymphocyte ratio, L/CRP: Lymphocyte/ CRP ratio LOS: Length of stay, ICU: Intensive care unit.*
Data are reported as median (Interquartile Range, IQR) or number(percentage).

Table II. *The factors effecting outcomes according to Multivariable Logistic Regressions Analysis*

Variables	ICU (OR)	Intubation (OR)	Mortality (OR)
Age	1.02*	1.05***	1.07***
Covid PAD	1.16***	1.15**	1.17***
CRP	1.007***	1.007***	1.005**
D-Dimer	1.18**	1.22***	2.62*
Lymphocyte	0.3**	0.1***	0.17***
Radiological Score	1.10***	1.05*	1.03
PAD_{pre} (U)	1.21***	1.21***	1.24***
Enlarged PAD(U)	3.03***	2.76**	2.52**
ΔPAD (U)	1.09	1.14	1.02
ΔPAD_{2mm} **(U)**	2.12**	2.32**	2.09***

U: Univariate Regression, OR: Odds Ratio, p<0.05, p<0.01**, p<0.001****

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Table III. *The group of independent non-categoric variables that affect PAD and change in PAD and outcomes according to Multivariable Logistic Regression Analysis*

Dependent variables	Independent non-categoric initial variables	Accuracy	Sensitivity	Specificity	AUC
Enlarged PAD	DD, L/CRP, Ferritin, PAD_{pre}	0.803	0.807	0.680	0.893
Δ PAD	DD, L	0.569	0.547	0.585	0.635
ΔPAD2mm	DD, L, Age	0.713	0.740	0.674	0.787
ICU admission	DD, L, Age, PAD, CRP	0.732	0.708	0.745	0.801
Intubation	DD, L Age, PAD	0.78	0.71	0.81	0.85
Mortality	L, Age, PAD	0.727	0.742	0.721	0.832

DD:D-Dimer, L/CRP: Lymphocyte/ CRP ratio, PADpre, :PAD before COVID-19 L: Lymphocyte, AUC: Area Under Curve

Table IV. *The variables effecting PAD and change in PAD according to Multiple Logistic RegressionAnalysis*

Variables	Enlarged PAD	ΔPAD	ΔPAD2mm
Age	1.02**	0.9	0.9
CRP	1.001*	1.005*	1.002
D-Dimer	1.12*	1.18*	1.18***
Ferritin	1.0004*	1.0004	0.9
Lymphocyte	0.8	0.6	0.4**

The values are Odds Ratio, p<0.05= p<0.01=** p<0.001*

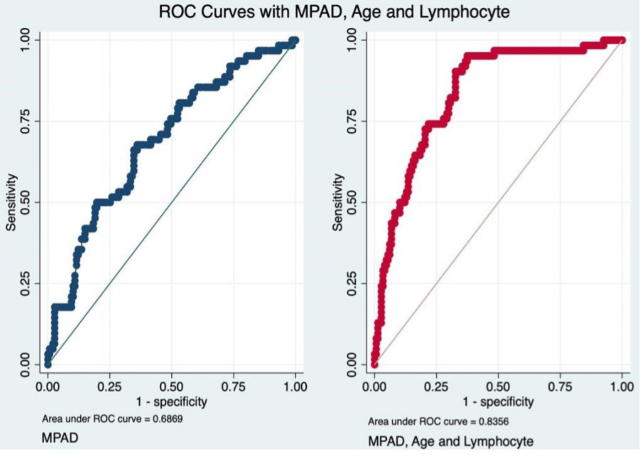

Figure 1. *Receiver Operating Characteristic Curve of PAD for predict death. The optimal cutoff value of PAD for mortality was detected as 27.61 mm (sensitivity 67.7%, specificity 63.9%), and the cutoff for maximum effectiveness was determined as 33.54 mm (17.7% sensitivity, 97.7% specificity).*

Patients with ΔPAD

It was found that the median PAD of the patients before COVID-19 (PAD_{pre}) was 25.72 mm, while PAD was 27.29 mm during COVID-19 (p<0.001). The median value changed by 1.5 mm (IQR, 0.35-3.04).

Patients were divided into two groups as increased PAD (ΔPAD) and without an increase in PAD according to the change in PAD relative to their previous chest CTs. ΔPAD increased in 144 out of 209 patients (68.9%). There was no difference in terms of demographic characteristics (age and gender). CRP, D-dimer, LDH, neutrophil, neutrophil/lymphocyte levels were significantly higher in patients with ΔPAD (p=0.005, p<0.001, p=0.04, p=0.03, p=0.007). The ratio of lymphocytes and lymphocytes/CRP were found to be significantly lower in patients with ΔPAD (p<0.001, p=0.002). While ICU admission increased significantly in patients with ΔPAD (p=0.04), there was no significant difference in WHO and radiological scores, medical ward length of stay (LOS) and ICU admission, and mortality (p=0.2, p=0.5, p=0.9, p=0.05, p=0.4). According to Cox regression analysis, it was also found that the risk of mortality significantly increased with the increase in PAD (HR=1.09, p=0.01, 95% CI).

Patients with $ΔPAD_{2mm}$

Considering the highest LR in the ROC analysis, the patients were divided into two groups: those with an increase over 2 mm ($ΔPAD_{2mm}$) and those with PAD less than 2 mm ($ΔPAD_{2mm}$).

Relationship between the $ΔPAD_{2mm}$ and different variables are shown in the Table I. Effect of $ΔPAD_{2mm}$ to clinical outcomes are given in the Table II.

When the PAD/Aorta ratio and various parameters were examined, no significant relationship could be found.

It was found that age, CRP, D-dimer, ferritin, and lymphocyte count are responsible for the change in PAD according to multiple logistic regression analysis (Table IV).

4. DISCUSSION

Pulmonary artery diameter in the chest CT of patients with COVID-19 was found to be significantly increased when compared to previous chest CT scans. In patients with enlarged PAD or $ΔPAD_{2mm}$ ICU admission, intubation rate, and mortality increased significantly. The radiological score was found to be significantly higher in patients with enlarged PAD. In patients with ΔPAD, ICU admission was increased. It was determined that the WHO scores, ICU admission, and mortality were higher in the patients with enlarged PAD_{pre}. While, CRP levels increased significantly in patients with enlarged PAD and ΔPAD, they tended to increase in patients with $ΔPAD_{2mm}$. D-dimer levels were also found to be significantly higher in all patients with changes in PAD.

In this study, enlarged PAD was higher in older age, but ΔPAD was the same in both genders and among the age groups. It was reported that there was no difference between genders regarding change in PAD in a previous study [13]. It has been known that there is a positive but weak correlation between age and PAD in a healthy person [9]. So, the increase in PAD with age could be secondary to COVID-19 infection, however, it remains unknown whether this finding can be related to COVID-19

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infection or age. Age can be a confounder for the relationship between COVID-19 and PAD.

High D-dimer, low L/CRP, high ferritin and enlarged PAD_{pre} were significantly increased parameters in patients with enlarged PAD. It was determined that high D-dimer and low lymphocyte count were factors that were seen in patients with significant increase in ΔPAD and $ΔPAD_{2mm}$. It has been reported that there is a correlation between PAD and CRP, N/L, body temperature, oxygen requirement, LDH, D-dimer, and lymphocyte during hospitalization and an increase in PAD indicates a poor prognosis [7,10,23]. Our findings are consistent with the literature. The fact that D-dimer and CRP values in the clinical course are higher in patients with enlarged PAD than in those with normal PAD, could suggest that inflammation and coagulopathy were more serious in these patients.

In our study, it was found that CRP, ferritin, lymphocyte, D-dimer had significant effects on PAD changes. It is also a crucial point that only high D-dimer levels were significantly associated with a change in PAD (Table IV). Ferritin, CRP, L/CRP are markers that show inflammation [24,25]. D-dimer is a fibrin degraded product that shows the presence of thrombi in circulation. With these findings, it can be thought that inflammation and thrombosis may be responsible for the changes in PAD. Therefore, changes in PAD were associated with poor prognosis [10].

In our study, PAD_{pre} was found to be larger than normal in 60 of 209 (28.7%) patients. In 55 of them (91%), PAD was also found to be large during COVID-19 infection. In 33 (22.14%) of 149 patients with normal PAD before COVID-19, PAD was found to be enlarged during COVID-19. As a result, PAD was found to be enlarged in 88 (42.10%) of 209 patients. ΔPAD was not found to be significantly different between patients with a previously normal or enlarged PAD. These findings suggest that patients with an enlarged PAD before COVID-19 have an increased requirement of hospitalization and increase in all the clinical outcomes.

Although, 20 of the 121 patients did not have PAD enlargement, it was noteworthy that ΔPAD2mm was significantly associated with mortality in these patients. Furthermore, $ΔPAD_{2mm}$ was found to be more significantly associated with mortality than enlarged PAD ($p<0.01$ vs $p<0.001$). At this point, it may be important to examine patients according to previous chest CT, both to determine the risk of patients with enlarged PAD_{pre} as we mentioned above and to predict the mortality increased by $ΔPAD_{2mm}$ in patients without enlarged PAD_{pre} or PAD.

In our study, although a median of 1.5 mm increase in PAD was detected ($p=0.001$), there was no significant relationship between ΔPAD and clinical outcomes. It has been reported that PAD increased by 3 mm ($p=0.001$) in chest CT in COVID-19 patients when compared with previous chest CT [14].. Due to the large number of patients with enlarged PAD before COVID-19 (28.7 %) in our study, a smaller increase in PAD was observed after COVID-19 when compared to the ones reported in the literature and we think that the correlation between the clinical endpoints and the ΔPAD could not reach a significant level. The increase in the size of the pulmonary artery during COVID-19 infection and the amount of this increase significantly affect the prognosis of the patients. In our study, the admission for ICU, intubation, and mortality are significantly increased in patients with enlarged PAD and/or an increase in PAD over 2 mm.

A significant correlation was found between radiological involvement and clinical severity. It was determined that the need for ICU increased significantly in patients with a radiological score of 20 and above, more specifically in patients with a radiological score of 10 and above. A significant correlation was determined between a radiological score of 15 and above and the need for intubation. A radiological score of 5 and above is significantly associated with enlarged PAD. It has been reported that there is a significant correlation between the amount of parenchymal involvement and PAD increase ($p=0.032$) and PAD/Aorta increase ($p<0.001$) [14]. Again, in parallel with the severity of pulmonary involvement, it was stated that PAD was 26.11± 3.72 mm in those without lung involvement, 26.65± 2.95 mm in those with mild pneumonia, and 28.59± 3.63 mm in those with severe pneumonia were reported ($p=0.027$) [10]. Our study helped us to make a meaningful prediction for important clinical endpoints by using different threshold values of the radiological score.

$ΔPAD_{2mm}$ was found to be more significantly associated with mortality than enlarged PAD ($p<0.01$ vs $p<0.001$). There was no significant difference between $ΔPAD_{2mm}$ and enlarged PAD in terms of intensive care and intubation requirements. The D-dimer level was found to be much higher in patients with $ΔPAD_{2mm}$ compared to patients with an incase in enlarged PAD. So, it can be considered that coagulopathy is a more important feature for ΔPAD2mm than enlarged PAD.

In our study, mortality increased when PAD was 27.61 mm and above according to the ROC analysis (Sensitivity= 67.7%, Specificity =63.9%); If we selected the threshold as 33.54 mm we observed that the sensitivity decreased but the specificity increased significantly (17.7% Sensitivity, 97.7% specificity). In addition, we also found that the risk of mortality significantly increased with every 1 mm increase in PAD (HR=1.09, $p=0.01$, 95% CI) (Figure 1).

It has been reported that there was a significant increase in mortality with an increase in PAD; it was determined as an independent risk factor for mortality, and an increase in mortality in COVID-19 patients with PAD≥ 31 mm (HR=1.592[1.154–2.196], $p=0.005$, 95%CI) [13]. Likewise, it was found that mortality increased significantly with a PA over 29.15 (75% sensitivity 84% specificity) [26].

There are some studies that found both significance and insignificance between the PA/Ao ratio and mortality [26,27]. PA/Ao ratio did not reach the level of significance in our study, although, this rate tended to increase in COVID-19.

While, no significant relationship was found between ward LOS and changes in PAD, there was a significant correlation between enlarged PAD, ΔPAD and $ΔPAD_{2mm}$ and LOS of ICU (respectively $p=0.001$, $p<0.05$ and $p=0.01$). The enlarged PAD and $ΔPAD_{2mm}$ were significantly associated with ICU admission.

In the literature, severity of the pneumonia was significantly associated with ΔPAD and enlarged PAD [10,23,38. It was mentioned that there was no significant relationship between parenchymal abnormalities and pulmonary embolism [7,29]. These suggest that severity of parenchymal involvement could not be associated with severity of vascular involvement. In our study, the fact that the radiological score increased the risk of ICU admission, intubation, and correlated with the WHO score, but not showing its effect on mortality; could suggest that vascular involvement rather than parenchymal involvement has a greater effect on mortality. Therefore, radiological involvement increases the clinical severity, but vascular pathologies are at the forefront at the point of the issue is mortality.

This study has the following limitations. Firstly, the lack of data on etiologies that could cause enlarged PAD and PAD_{pre} like pulmonary embolism. Secondly, lack of data related to pressure pulmonary artery pressure estimated by right heart catheterization or echocardiography. Thirdly, single-center design of the study cause bias.

Conclusion

Our study indicated that PAD increased significantly in COVID-19 patients compared to previous chest CT. For the first time in the literature, this was associated with the risk of ICU admission. It was established that the clinical severity, ICU admission, the risk of intubation and mortality increased significantly in patients whose PAD increased over 2 mm. The high D-dimer level and inflammation markers in these patients suggest that increased inflammation and thrombosis may be effective in the pathogenesis.

Compliance with the Ethical Standards

Ethical Approval: This study was approved by the Marmara University, School of Medicine Clinical Research Ethics Committee (approval number: (2020/164).

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Conflict of Interest: The authors have no potential conflicts of interest to disclose.

Authors' Contributions: CI.: Medical practice, SK: Conceptualization, AS and SK: Data collection and processing, AS and CI.: Formal analysis and interpretation, AS and SK.: Writing the draft and editing. All authors read and approved the final version of the article.

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