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# Prognostic Utility of the Ratio of Pulmonary Artery Diameter to Ascending Aorta Diameter in COVID-19 Patients

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## Abstract

**Aim:** Numerous hospital admissions of patients infected with Coronavirus disease-2019 (COVID-19) reveal the importance of managing clinical, radiological, and laboratory findings related to disease severity and mortality. Pulmonary artery (PA) trunk enlargement is a well-known indicator of hemodynamic instability. The purpose of this study was to assess the prognostic value of PA trunk diameter enlargement and the ratio of the PA diameter to the ascending aorta (AA) diameter on unenhanced computed tomography images in patients with severe COVID-19 infection.

**Materials and Methods:** Three hundred and ninety-three hospitalized patients in the pandemic ambulatory service, emergency department, and intensive care unit were retrospectively analyzed. Correlations between the PA diameter and the ratio of the PA diameter to the AA diameter with prognostic factors and values were examined.

**Results:** PA/AA rates were significantly higher in hospitalized patients who developed mortality. The optimum cut-off PA/AA ratio to predict mortality was 0.9386, with a sensitivity of 98% and specificity of 97%. The optimum cut-off PA diameter to predict mortality was 3.315 cm, with a sensitivity of 98% and specificity of 89%. The mortality risk was 221 times higher in patients with a PA/AA ratio higher than 0.93 and 65 times higher in patients with a PA diameter greater than 3.315 cm.

**Conclusion:** PA trunk diameter enlargement and the PA/AA diameter ratio can be valuable markers for predicting the mortality risk of COVID-19.

**Keywords:** Pulmonary artery diameter, ascending aorta diameter, COVID-19

## Introduction

Viral transmission has increased because of asymptomatic infections, limited testing, and inadequate personal protective equipment for healthcare providers worldwide (1). A new infection caused by Severe acute respiratory syndrome-Coronavirus-2 (SARS-CoV-2), named Coronavirus disease-2019 (COVID-19), has affected healthcare systems and communities. The numerous hospital admissions of patients infected with COVID-19 reveals the importance of managing clinical, radiological, and laboratory findings related to disease severity and mortality. Identifying potential risk factors that predict disease progression will help healthcare professionals triage patients effectively, personalize treatment, monitor clinical progress, and allocate appropriate resources at all levels of care to reduce morbidity and mortality (2).

A very high number of admissions to health centers or hospitals during an epidemic is essential (3). This high demand, especially the need for intensive care support, overwhelms human and mechanical capacities (4). An academician of the American Society for Radiation Oncology called for the immediate establishment of a computed tomography (CT)-based diagnostic method for COVID-19 and improvement of the detection rate of SARS-CoV-2 (5). In such an environment, another solution with sufficient accuracy is needed to guide the rapid management of patients admitted to the hospital during this pandemic. Therefore, early and effective predictors

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of clinical outcomes are urgently needed for risk stratification of COVID-19 patients.

The advantages of CT in diagnosing COVID-19 are clear because this method has great value for early screening, differential diagnosis, and assessment of disease severity (6). Although the virus prefers the lungs, the infection also severely affects the whole body and cardiovascular system (7). Pulmonary artery (PA) trunk enlargement is a well-known indicator of hemodynamic instability, such as acute central pulmonary embolism and heart failure (8,9). Enlargement of the PA body likely reflects cardiovascular injury, intrapulmonary inflammation, and abnormal blood coagulation. However, the prognostic value of this parameter and the optimal cut of the PA trunk diameter for predicting mortality on non-contrast CT images have not been well evaluated. The aim of this study was to investigate whether the ratio of PA diameter measured on CT imaging and PA diameter to ascending aorta (AA) diameter has a prognostic value in COVID-19 patients.

## Materials and Methods

### Study Design and Patient Population

This was a retrospective study conducted at the Department of Emergency Medicine, Ufuk University Faculty of Medicine. The study included 393 hospitalized COVID-19 patients in the pandemic service, emergency department, and intensive care unit (ICU) of Ufuk University Medical Faculty Dr. Rıdvan Ege Hospital, a tertiary reference center in Ankara, between 11.03.2020 and 24.03.2022. The Ufuk University Hospital Ethics Committee and the Ministry of Health approved the study protocol (decision no: 22.05.12.05/07, date: 12.05.2022). The inclusion criteria were hospitalized adult patients (aged 18 years or older) with laboratory (COVID-19-PCR)-confirmed COVID-19 who underwent at least one chest CT scan. Patients below 18 years of age, patients without CT imaging, patients with pulmonary hypertension, those with negative COVID-19-PCR results, and pregnant and non-hospitalized patients were not included. Patients with missing data were also excluded from the study.

All procedures applied in this study agreed with the Declaration of Helsinki. Clinical data of patients, length and type of hospital stay, and discharge status were obtained from the hospital registry database.

### Measurements

The patient's laboratory parameters and chest CT findings were recorded. Blood samples included white blood cell (WBC), lymphocytes, neutrophils, C-reactive protein (CRP), D-dimer, lactate dehydrogenase (LDH), and ferritin. PA diameter, AA diameter, and PA/AA ratio were recorded using CT scans. PA diameter, AA diameter, and the ratio of PA diameter to AA diameter were measured at the level of the PA bifurcation in the axial plane using computerized chest tomography. Correlations between the PA diameter and the ratio of the PA diameter to the AA diameter with prognostic factors and values were examined (Figure 1).

### Statistical Analysis

All statistical analyzes were performed using Statistical Package for the Social Sciences 22. The Kolmogorov-Smirnov test was applied as the normal distribution test. Parametric tests were used in the analysis of normally distributed data, and non-parametric tests were used when data were not normally distributed. The Mann-Whitney U test, t-test, binary logistic regression analysis, Spearman correlation analysis, and ROC analysis were used for statistical analyzes A p value of $<0.05$ is considered statistically significant.

## Results

Our study's mean age of 393 patients was 66.81±14.89 (minimum: 20-maximum: 99). The baseline demographic, clinical features, and comorbidities of the COVID-19 patients are given in Table 1.

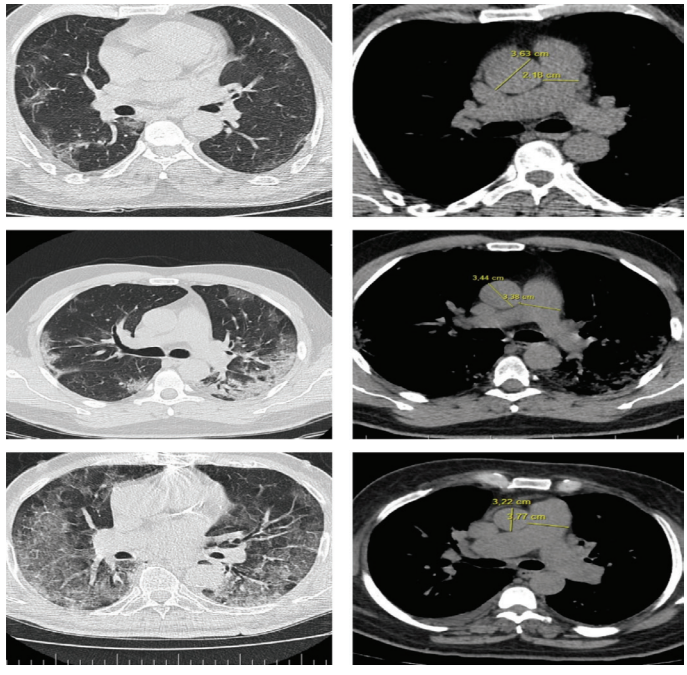

**Figure 1.** Axial images of non-contrast chest computed tomography demonstrating measurement of lung involvement due to Coronavirus disease-2019 and the corresponding pulmonary image in the parenchyma window. Increased pulmonary artery/ascending aorta (PA/AA) ratio was associated with the severity of lung involvement. The PA/AA ratios were 0.6-0.98-1.17, respectively

There was a statistically significant difference in laboratory parameters and the ratio of PA diameter to AA diameter according to the ICU requirement of patients. WBC, neutrophil, CRP, D-dimer, LDH, ferritin levels, and PA/AA ratios were statistically significantly higher in the ICU (Table 2).

There was a statistically significant difference in laboratory parameters and the ratio of PA diameter to AA diameter according to in-hospital mortality status. WBC count, neutrophil count, CRP, D-dimer count, LDH, ferritin level, and PA/AA ratio were statistically significantly higher in the non-survivor group compared to the survivor group (Table 3).

There was a weak negative correlation with the PA/AA ratio with lymphocytes and a weak positive correlation with WBC, neutrophils, CRP, D-dimer, LDH, and ferritin (Table 4).

Considering the usability of PA/AA ratio and PA diameter to discriminate between patients' mortality at the time of admission, the area under the curve was found to be 0.997 for PA/AA ratio and 0.974 for PA diameter. PA/AA ratio and PA diameter can be diagnostic markers for predicting the mortality risk for COVID-19 patients (Figure 2, Table 5).

The optimum cut-off PA/AA ratio to predict mortality was 0.9386 with a sensitivity of 98%, specificity of 97%, and Youden's J index of 0.95. The positive likelihood ratio (true positive/false positive ratio) was 33.7 and the negative likelihood ratio (true negative/false negative) was 0.02. These results show that the PA/AA ratio is a near-perfect diagnostic test for predicting mortality. The optimum cut-off PA diameter to predict mortality was 3.315 cm, with a sensitivity of 98% and specificity of 89%. Youden's J index was 0.87. The positive likelihood ratio (true positive/false positive ratio) was 9.33 and the negative likelihood ratio (true negative/false negative) was 0.02. These results indicate that PA diameter is a significant predictor of subsequent death (Table 6).

**Table 1. Demographics, clinical features, and comorbidities of Coronavirus disease-2019 patients**

| **Baseline features** | **n=393** | **%** |
|---|---|---|
| Gender (male) | 214 | 54.5 |
| Gender (female) | 179 | 45.5 |
| Hypertension | 194 | 49.4 |
| Diabetes mellitus | 112 | 28.5 |
| Coronary artery disease | 86 | 21.9 |
| Chronic obstructive pulmonary disease | 66 | 16.8 |
| Congestive heart failure | 41 | 10.4 |
| Asthma | 33 | 8.4 |
| Cancer | 26 | 6.6 |
| Cerebrovascular disease | 13 | 3.3 |
| **Clinical features** | | |
| Dyspnea | 223 | 56.7 |
| Cough | 168 | 42.7 |
| Fever (temperature ≥37.3 °C) | 146 | 37.2 |
| Myalgia or fatigue | 104 | 26.5 |
| Sore throat | 33 | 8.4 |
| Headache | 17 | 4.3 |
| Diarrhoea | 10 | 2.5 |
| Loss of taste | 3 | 0.8 |
| Anosmia | 2 | 0.5 |

The logistic regression analysis for predicting mortality was valuable (Omnibus test $p<0.001$). The independent predictors in the model determine 89.3% of the change in the dependent predictors. The accuracy rate of the model was 97.5%. The dependent variables of the model were mortality status and the independent variables were CRP, D-dimer, LDH, ferritin, PA diameter, and PA/AA ratio. The PA/AA ratio is divided into two categories according to the recommended cutoff value. Values above 0.9386 were considered risky. The PA diameter is divided into two categories according to the recommended cut-off value. Values above 3.315 cm are considered risky. The mortality risk was 221 times higher in patients with a PA/AA ratio higher than 0.93 and 65 times higher in patients with a PA diameter greater than 3.315 cm (Table 7).

## Discussion

Chest CT scanning is widely used for diagnostic and prognostic purposes in COVID-19 patients. The virus infects the lungs, affecting the whole body and especially severely affecting the cardiovascular system. PA trunk enlargement indicates

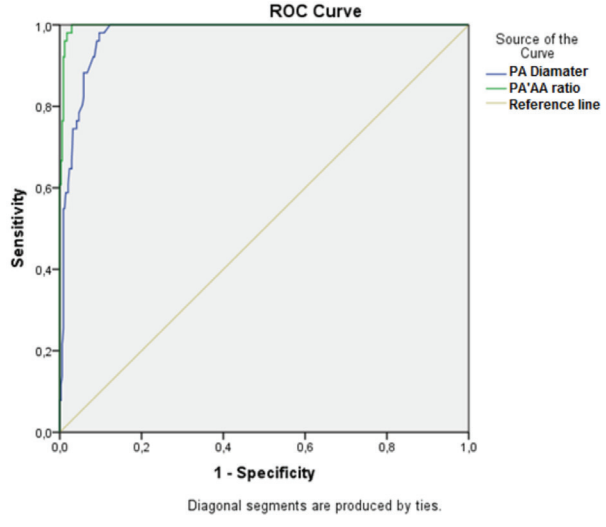


**Figure 2.** Area under the curve for PA/AA and PA
AA: Ascending aorta, PA: Pulmonary artery

| Table 2. Laboratory and radiographic features of COVID-19 patients in the intensive care unit and in-patients | | | | | | | |
|---|---|---|---|---|---|---|---|
| | Hospitalized patient (n=393) | | | | | | |
| | Intensive care unit (n=73) | | | In-patients (n=320) | | | p |
| | Average | Standard deviation | Median | Average | Standard deviation | Median | |
| WBC (cells/µL) | 15093.56 | 8326.91 | 13600 | 9789.22 | 6330.28 | 8885 | <0.001 |
| Lymphocyte (cells/µL) | 968.49 | 835.31 | 600 | 1602.54 | 1516.91 | 1300 | <0.001 |
| Neutrophile (cells/µL) | 13193.01 | 7841.42 | 11500 | 6939.53 | 4391.57 | 6100 | <0.001 |
| CRP (mg/L) | 137.72 | 92.59 | 121 | 72.51 | 70.34 | 53.95 | <0.001 |
| D-dimer (µg/L) | 3203.58 | 3434.85 | 1550 | 785.13 | 1190.33 | 362.50 | <0.001 |
| LDH (IU/L) | 463.37 | 257.27 | 407 | 249.48 | 116.32 | 225 | <0.001 |
| Ferritin (µg/L) | 1062.93 | 698.40 | 890 | 362.76 | 421.23 | 220.50 | <0.001 |
| PA/AA ratio | 1.00 | 0.08 | 0.98 | 0.78 | 0.07 | 0.78 | <0.001 |
| AA: Ascending aorta, PA: Pulmonary artery, CRP: C-reactive protein, WBC: White blood cells, LDH: Lactate dehydrogenase, COVID-19: Coronavirus disease-2019 | | | | | | | |

| Table 3. Laboratory and radiographic features of COVID-19 patients according to in-hospital mortality status | | | | | | | |
|---|---|---|---|---|---|---|---|
| | Mortality | | | | | | |
| | Survivor (n=342) | | | Non-survivor (n=51) | | | p |
| | Average | Standard deviation | Median | Average | Standard deviation | Median | |
| WBC (cells/µL) | 9944.21 | 6319.29 | 9090 | 16342.35 | 8959.56 | 14030 | <0.001 |
| Lymphocyte (cells/µL) | 1569.92 | 1491.21 | 1300 | 913.73 | 784.35 | 600 | <0.001 |
| Neutrophile (cells/µL) | 7147.05 | 4522.28 | 6300 | 14499.02 | 8403.67 | 12400 | <0.001 |
| CRP (mg/L) | 75.64 | 71.86 | 56.30 | 144.89 | 97.42 | 124.50 | <0.001 |
| D-dimer (µg/L) | 840.49 | 1269.67 | 409.50 | 3875.61 | 3716.35 | 2040 | <0.001 |
| LDH (IU/L) | 257.61 | 124.38 | 230 | 501.06 | 279.12 | 464 | <0.001 |
| Ferritin (µg/L) | 395.07 | 468.19 | 230.50 | 1148.31 | 647.01 | 1099 | <0.001 |
| PA/AA ratio | 0.79 | 0.08 | 0.79 | 1.03 | 0.07 | 1.02 | <0.001 |
| AA: Ascending aorta, PA: Pulmonary artery, CRP: C-reactive protein, WBC: White blood cells, LDH: Lactate dehydrogenase, COVID-19: Coronavirus disease-2019 | | | | | | | |

| Table 4. Spearman Rho correlation | | | |
|---|---|---|---|
| | | | PA/AA ratio |
| Spearman's Rho | WBC | R | 0.253 |
| | | P | **<0.001** |
| | Lymphocyte | R | -0.314 |
| | | P | **<0.001** |
| | Neutrophil | R | 0.321 |
| | | P | **<0.001** |
| | CRP | R | 0.240 |
| | | P | **<0.001** |
| | D-dimer | R | 0.368 |
| | | P | **<0.001** |
| | LDH | R | 0.375 |
| | | P | **<0.001** |
| | Ferritin | R | 0.326 |
| | | P | **<0.001** |
| AA: Ascending aorta, PA: Pulmonary artery, CRP: C-reactive protein, WBC: White blood cells, LDH: Lactate dehydrogenase | | | |

hemodynamic instability, such as acute central pulmonary embolism and heart failure (8,9). The dilation of the PA trunk likely reflects cardiac and vascular injury, abnormal blood coagulation, and intrapulmonary inflammation. However, the prognostic value of this parameter and the optimal cut-off of PA trunk diameter on unenhanced CT images to predict mortality have not been well evaluated.

Our study's mean age of 393 patients was 66.81±14.89. 81.4% of the patients were hospitalized, 18.6% had intensive care admission, and 13% of the patients died after hospitalization. Puhr-Westerheide obtained different results in a group of 89 COVID-19 ICU acute respiratory distress syndrome patients requiring mechanical ventilation or continuous positive airway pressure mask ventilation. This retrospective study suggested that CT severity scores and PA-to-AA ratios were not significantly associated with in-hospital mortality (10). WBC count, neutrophil count, CRP level, D-dimer level, LDH level, ferritin level, and PA/AA ratios were significantly higher in ICU patients and patients with mortality. There was a weak negative correlation between

PA/AA ratio and lymphocytes and a weak positive correlation between WBC, neutrophils, CRP, D-dimer, LDH, and ferritin. The optimum cut-off PA/AA ratio to predict mortality was 0.9386, with a sensitivity of 98% and specificity of 97%. The optimum cut-off PA diameter to predict mortality was 3.315 cm, with a sensitivity of 98% and specificity of 89%. It was found that the mortality risk was 221 times higher in patients with a PA/AA ratio higher than 0.93 and 65 times higher in patients with a PA diameter greater than 3.315 cm.

Main PA diameter (MPAD) enlargement is associated with pulmonary hypertension and mortality in patients without COVID-19. Esposito et al. (11) investigated the association between PA enlargement and overall survival in patients with COVID-19. A cohort study was conducted with 1.469 patients with COVID-19 who underwent chest CT within 72 h of admission to seven tertiary hospitals in Northern Italy between March 1 and April 20, 2020. Enlargement of the PA diameter (≥31 mm) was found to be a predictor of mortality. In patients with more than 31 mm PA diameter, the mortality risk was 1.592 times greater. Enlargement of MPAD (≥31 mm) was found to be an indicator of mortality in the corrected and multivariate regression analysis, with male gender, old age, high creatinine, low ventilated lung volume, and high pneumonia extension [c-index (95% confidence interval)]. Enlarged MPAD (≥31 mm) on CT has been reported as an independent predictor of mortality in COVID-19 (11).

The PA/AA ratio may be a predictor of poor prognosis. In our study, we had 320 in-patients whose mean PA/AA ratio was 0.78; 73 patients in the ICU whose PA/AA ratio was 1; and the mean PA/AA ratio of 51 patients who developed mortality was 1.03. Similarly, Yildiz et al. (12) examined the relationship between the severity of COVID-19 pneumonia and the diameter of the PA. A total of 101 patients with COVID-19 were included in this retrospective study. The patients were divided into three groups according to their CT images: 41 patients with mild pneumonia (group 1), 39 patients with moderate pneumonia (group 2), and 21 patients with severe pneumonia (group 3). In addition, the diameters of the MPAD, AA, and right and left PA diameters were calculated. Analyses show that increased MPAD is associated with poor prognosis in patients with COVID-19 pneumonia. In our study and a few other studies in the literature, PA diameter and the ratio of PA diameter to AA diameter are helpful for predicting clinical prognosis in patients with COVID-19.

The correlation between CT imaging parameters and clinical features in patients with patients has been investigated in recent studies. Eslami et al. (13) found that a PA/AA ratio >1 was

**Table 5. Area under the curve for PA/AA and PA**

| Variables | Area | SH | p | 95% CI | |
|---|---|---|---|---|---|
| | | | | Highest | Lowest |
| PA diameter | 0.974 | 0.007 | <0.001 | 0.960 | 0.988 |
| PA/AA ratio | 0.997 | 0.002 | <0.001 | 0.993 | 1.000 |

AA: Ascending aorta, PA: Pulmonary artery, CI: Confidence interval

**Table 6. Optimal cut-off values for the PA diameter and PA/AA ratio**

| | Cut-off | Sensitivity | Specificity | Youden's J index | Positive likelihood ratio | Negative likelihood ratio |
|---|---|---|---|---|---|---|
| **PA/AA ratio** | 0.9386 | 0.98 | 0.971 | 0.951 | 33.7931 | 0.020 |
| **PA diameter (cm)** | 3.315 | 0.98 | 0.89 | 0.875 | 9.33 | 0.022 |

AA: Ascending aorta, PA: Pulmonary artery

**Table 7. Prediction of in-hospital mortality in COVID-19 patients by logistic regression analysis**

| | B | p | OR | 95% CI OR | |
|---|---|---|---|---|---|
| | | | | Lowest | Highest |
| CRP | 0.004 | 0.396 | 1.004 | 0.995 | 1.013 |
| D-dimer | 0 | 0.670 | 1 | 1 | 1.001 |
| LDH | 0.003 | 0.202 | 1.003 | 0.998 | 1.009 |
| Ferritin | 0.001 | 0.412 | 1.001 | 0.999 | 1.002 |
| PA/AA ration | 5.402 | <0.001 | 221.890 | 17.918 | 2747.855 |
| PA diameter | 4.178 | 0.011 | 65.224 | 2.642 | 1609.932 |
| Constant | -5.397 | <0.001 | 0.005 | | |

AA: Ascending aorta, PA: Pulmonary artery, CRP: C-reactive protein, LDH: Lactate dehydrogenase, COVID-19: Coronavirus disease-2019, CI: Confidence interval, OR: Odds ratio

associated with extensive lung involvement and a nonsignificant increase in mortality (Odds ratio: 1.96 p=0.360) in 87 hospitalized COVID-19 patients. In addition, an increased cardiothoracic ratio is a strong predictor of mortality. According to Spagnolo et al. (14), previous chest CT scans of 45 COVID-19 patients showed that the PA/AA ratio increased after SARS-CoV-2 infection and was significantly correlated with the severity of pneumonia. In addition, enlargement of the PA diameter was associated with mortality in COVID-19 patients. Our study had a relatively more significant population than these two studies, with 255 patients. In our study, MPA was associated with in-hospital mortality according to the above cut-off values. MPA was an independent predictor of mortality as both a continuous and categorical variable in logistic regression analyzes In the logistic regression model, the PA/AA ratio and MPA diameter were independent predictors of mortality.

Pulmonary hypertension probably develops because of microvascular thrombi. Early diagnosis and aggressive anticoagulant treatment are crucial for these patients. Evaluating the PA/AA ratio with non-enhanced chest CT may predict the presence of underlying vascular thrombosis associated with poor prognosis. CT-measured indices may have predictive value for survival and extent of lung involvement in hospitalized COVID-19 patients and would be helpful for risk stratification of patients with COVID-19 and treatment decisions. In particular, increased PA diameter and PA/AA ratio are common in COVID-19 patients and can be strong predictors of mortality. Hayama et al. (15) examined the association between the PA/AA ratio and the clinical severity of COVID-19 infection. Twenty (19%) of 103 COVID-19 patients had severe respiratory exacerbations. Between the groups with and without severe respiratory exacerbation, the PA diameter (31.1±2.7 mm vs 25.4±3.5 mm, p<0.001) and the PA/AA ratio (0.97±0.11 vs 0.82±0.10 p<0.001) were significantly different. This difference in PA/AA ratio was also significant in 74 patients under 65 (1.03±0.1 vs 0.84±0.09 p<0.001). The group with a PA/AA ratio >0.9 had a more severe respiratory exacerbation (p<0.001) than the group with a median PA/AA ratio cut-off point of ≤0.9. Kaplan-Meier survival curves for the PA/AA ratio on admission showed an essential distinction between severe respiratory exacerbation and mortality during the hospital stay. Our study was conducted with a more significant population and found that mortality was significantly increased in patients with PA/AA >0.93.

### Study Limitations

This study has several limitations. First, this was a single-center, retrospective, and non-randomized study. We included patients with chest CT imaging and positive COVID-19 PCR test results in our study; therefore, these results cannot be generalized to all COVID-19 patients. Our study does not include data from transthoracic echocardiography and right heart catheterization that would allow us to draw more precise conclusions about hemodynamic status and PA enlargement. We also had no data from previous CT scans, which hindered us from suggesting that PA enlargement occurred after SARS-CoV-2 infection.

## Conclusion

PA dilation and the ratio of PA diameter to AA diameter strongly predict in-hospital mortality in patients with hospitalized COVID-19. The PA diameter and PA/AA diameter ratio can be easily calculated from chest CT imaging and may help predict the prognosis of COVID-19 patients.

### Ethics

**Ethics Committee Approval:** The Ufuk University Hospital Ethics Committee and the Ministry of Health approved the study protocol (decision no: 22.05.12.05/07, date: 12.05.2022).

**Informed Consent:** Retrospective study.

**Peer-review:** Externally peer-reviewed.

### Authorship Contributions

Surgical and Medical Practices: M.Ö., T.E., İ.Ç., Concept: M.Ö., T.E., İ.Ç., Design: M.Ö., T.E., Data Collection or Processing: M.Ö., Analysis or Interpretation: M.Ö., T.E., İ.Ç., Literature Search: M.Ö., T.E., İ.Ç., Writing: M.Ö., İ.Ç.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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