

# Pulmonary Artery Enlargement: An Independent Risk Factor for Mortality in Patients Hospitalized With COVID-19

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## Abstract


**Objective:** To assess whether baseline pulmonary artery diameter (PAD), obtained from noncontrast nongated computed tomography (NCCT), can be associated with coronavirus disease 2019 (COVID-19) outcomes.

**Patients and Methods:** This is a retrospective study of patients hospitalized with COVID-19 admitted to Hôtel-Dieu de France university hospital (Beirut, Lebanon) between March 1, 2020 and March 1, 2021. Pulmonary artery diameter was measured at baseline NCCT. Various outcomes were assessed, including hospital length of stay, intensive care unit admission, invasive mechanical ventilation, mortality, and Post-COVID-19 Functional Status scale at discharge and at 2-month follow-up.

**Results:** Four hundred sixty-five patients underwent baseline NCCT, including 315 men (67.7%) with a mean age of  $63.7 \pm 16$  years. Baseline PAD was higher in critically ill patients admitted to the intensive care unit (mean difference, 0.8 mm; 95% CI, 0.4-1.59 mm) and those receiving invasive mechanical ventilation (mean difference, 1.1 mm; 95% CI, 0.11-2.04 mm). Pulmonary artery diameter at baseline correlated significantly with hospital length of stay ( $r=0.130$ ;  $P=.005$ ), discharge status ( $r=0.117$ ;  $P=.023$ ), and with Post-COVID-19 Functional Status scale at 2-month follow-up ( $r=0.121$ ;  $P=.021$ ). Moreover, multivariable logistic regression showed that a PAD of 24.5 mm and above independently predicted in-hospital all-cause mortality remained unaffected in patients with COVID-19 (odds ratio, 2.07; 95% CI, 1.05-4.09).

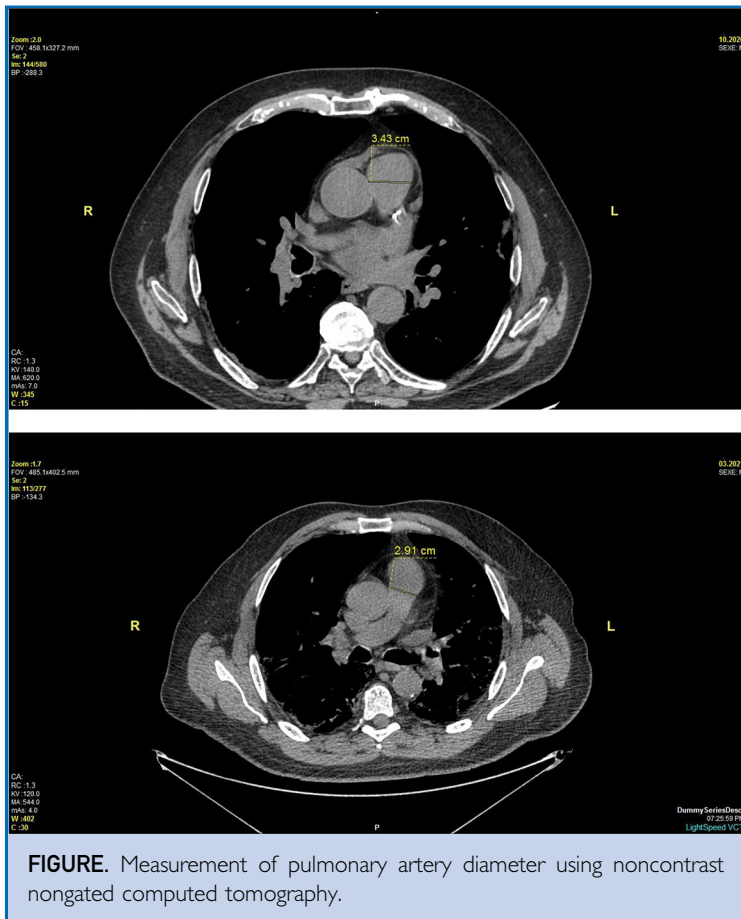
**Conclusion:** Baseline PAD measurement using NCCT can be a useful prognostic parameter. Its measurement can help to identify early severe cases and adapt the initial management of patients hospitalized with COVID-19.

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 In March 11, 2020, the World Health Organization declared the coronavirus disease 2019 (COVID-19)<sup>1</sup> a pandemic amid an alarming increase in the spread and severity of the disease.<sup>2</sup> Although a minority of patients infected with severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2) experience severe symptoms and require hospitalization, the outcomes for these patients may be devastating and often life-threatening. As of April 15, 2022, the COVID-19 pandemic is responsible for more than 6.1 million deaths around the world.<sup>3</sup> As a result, the impact of this dramatic death

toll on health care systems and economies around the world has made it a priority to identify prognostic risk factors to detect patients with poor prognosis and adapt an aggressive treatment plan.<sup>4</sup> Multiple risk factors for severe COVID-19 have been identified, including older age,<sup>5</sup> male sex,<sup>6</sup> history of lung and/or cardiovascular diseases,<sup>7</sup> diabetes,<sup>8</sup> and immunosuppression.<sup>9</sup> Noncontrast nongated computed tomography (NCCT) may be performed to assess lung involvement in patients hospitalized with infectious pneumonia<sup>10</sup> and has also reported an added value in the early identification and

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**FIGURE.** Measurement of pulmonary artery diameter using noncontrast nongated computed tomography.

management of severe COVID-19 cases.<sup>11</sup> Pulmonary artery dilation is associated with poor prognosis in various lung diseases, including cystic fibrosis,<sup>12-14</sup> chronic obstructive pulmonary disease,<sup>15,16</sup> and interstitial lung fibrosis.<sup>17</sup> An association between the pulmonary artery diameter (PAD) on NCCT and COVID-19 severity was first reported by Yildiz et al in January 2021,<sup>18</sup> and since then, a few reports have pointed to its potential prognostic utility. This study aimed to investigate the prognostic value of baseline PAD in short- and mid-term outcomes in patients hospitalized with COVID-19.

## PATIENTS AND METHODS

### Study Design

We conducted a retrospective study that included severe patients with COVID-19, admitted between March 2020 and March 2021 to Hôtel-Dieu de France, one of the

largest tertiary care centers in the capital of Lebanon, Beirut. The patients were admitted to dedicated wards of the departments of internal medicine, infectious diseases, and pulmonology and critical care. Adult patients ( $\geq 18$  years old) with positive real-time reverse transcriptase polymerase chain reaction for COVID-19 and a baseline NCCT were included. Patients aged less than 18 years, without a baseline NCCT at admission, as well as pregnant patients, and nonhospitalized patients were excluded.

### PAD Measurement

The measurement of the pulmonary artery was made on a dedicated workstation through which a radiologist identified the axial CT image that depicted the widest diameter of the pulmonary artery, perpendicular to the long axis of the vessel, near the midpoint between the base of the pulmonary trunk and the end of the right pulmonary artery (Figure). Each scan was interpreted by 2 independent radiologists with no prior knowledge of patient history.

### Data Collection

Various clinical outcomes were measured including hospital length of stay, admission to the intensive care unit (ICU), use of invasive mechanical ventilation, in-hospital mortality (COVID-19 related or all-cause mortality), the Post-COVID-19 Functional Status (PCFS) scale<sup>19</sup> at discharge and 2-month follow-up, and patients' status at discharge and 2-month follow-up. Patients' clinical data and National Early Warning Score 2 (NEWS2)<sup>20</sup> were obtained from the hospital's electronic medical records.

### Statistical Analyses

Categorical variables were presented as numbers and percentages, with their 95% CIs. Quantitative data with a skewed distribution (QQ plots, Shapiro-Wilk test) are presented as the mean  $\pm$  SD. Ordinal data and quantitative data with asymmetric distribution are presented as the median with its interquartile range (quartile 1-quartile 3) and range.

For the ordinal outcomes (NEWS2, PCFS at M0 and M2 and the functional state at discharge) and outcomes with asymmetric distribution (length of stay), correlation with PAD was done using the Spearman coefficient. Its

**TABLE 1. Baseline Characteristics of the Subjects Enrolled in the Study**

Variable	Statistic	Valid N	Result	
Age (y)	m±sd, min-max	465	63.7±16	16-96
Female gender	n(%), 95% CI		150 (32.3)	28.1%-36.6%
O Blood type	n(%), 95% CI		152 (38.1)	33.4%-42.9%
A Blood type	n(%), 95% CI		174 (43.6)	38.8%-48.5%
B Blood type	n(%), 95% CI		51 (12.8)	9.8%-16.3%
AB Blood type	n(%), 95% CI		22 (5.5)	3.6%-8.1%
Negative Rhesus antigen	n(%), 95% CI		37 (9.3)	6.7%-12.4%
Direct admission to ICU	n(%), 95% CI		48 (10.3)	7.8%-13.3%
Day symptoms started	m±sd, min-max	449	-6.7±5.2	-30 to 26
1st CT value	m±sd, min-max	261	22.5±5.6	8-37
Weight (kg)	m±sd, min-max	437	81.2±16.6	36-150
Hypertension	n(%), 95% CI		264 (56.8)	52.2%-61.2%
Diabetes mellitus	n(%), 95% CI		135 (29)	25%-33.3%
Immunosuppression	n(%), 95% CI		47 (10.1)	7.6%-13.1%
Cardiovascular disease	n(%), 95% CI		124 (26.7)	22.8%-30.8%
Chronic renal failure	n(%), 95% CI		74 (15.9)	12.8%-19.4%
Lung Disease	n(%), 95% CI		93 (20.5)	17%-24.4%
Smoker	n(%), 95% CI		114 (25.2)	21.3%-29.3%
ICU transfer day	Med (Q1-Q3), min-max	111	3 (1-7)	1-20
GGO (%) @ baseline NCCT	m±sd, min-max	465	25.2±18.3	0-90
PAD @ baseline NCCT (mm)	m±sd, min-max	465	26.7±3.8	18-50
Leucocytes (/cm <sup>3</sup> )	Med (Q1-Q3), min-max	465	7000 (5200-10,000)	920-65, 400
Neutrophils (/cm <sup>3</sup> )	Med (Q1-Q3), min-max	465	5370 (3590-8050)	230-56, 520
Lymphocytes (/cm <sup>3</sup> )	Med (Q1-Q3), min-max	465	830 (560-1250)	99-56, 240
Ferritin (µg/L)	Med (Q1-Q3), min-max	452	746.5 (378-1328.5)	10-35, 493
LDH (U/L)	Med (Q1-Q3), min-max	449	334 (251-436)	130-997
D-dimers (ng/L)	Med (Q1-Q3), min-max	452	0.9 (0.47-1.7)	0.2-483
CRP (mg/L)	Med (Q1-Q3), min-max	464	87.8 (36-149.5)	2-941
Procalcitonine (ng/L)	Med (Q1-Q3), min-max	427	0.2 (0.08-0.5)	0-366
HDL cholesterol (mmol/L)	Med (Q1-Q3), min-max	107	1.2 (0.94-1.4)	0.3-5.4
LDL cholesterol (mmol/L)	Med (Q1-Q3), min-max	108	2.9 (2.165-3.5)	0.8-6.7
Triglycerides (mmol/L)	Med (Q1-Q3), min-max	318	1.8 (1.32-2.5)	0.4-7.8
Serum Creatinin (µmol/L)	Med (Q1-Q3), min-max	454	78 (62-108)	11.5-1149
Baseline O <sub>2</sub> needs				
No O <sub>2</sub>	n(%), 95% CI		126 (27.1)	23.2%-31.3%
O <sub>2</sub> < 4 L/min	n(%), 95% CI		121 (26)	22.2%-30.1%
O <sub>2</sub> 4-8 L/min	n(%), 95% CI		135 (29)	25%-33.3%
HCM/Optiflow	n(%), 95% CI		83 (17.8)	14.6%-21.5%
NEWS2 score	Med (Q1-Q3), min-max	465	5 (3-6)	0-12

Categorical data are presented as frequencies, percentages and their 95% CIs (n[%], 95%CI). Continuous data not departing from normality assumptions are presented as mean and its SD (m±SD), min and max. Continuous data departing from normality assumptions are presented as median and its interquartile range, min and max (Med [Q1-Q3], min-max).

CRP, C-reactive protein; CT, cycle threshold; GGO, ground glass opacities; HCM, high concentration oxygen mask; ICU, intensive care unit; LDH, lactodehydrogenase; NCCT, noncontrast nongated computed tomography; NEWS2, National Early Warning Score 2; PAD, pulmonary artery diameter.

95% CI was constructed by bootstrapping on 10,000 random samples. For the binary outcomes, the average PAD was compared between the 2 categories by using the independent *t* test. For multicategory outcomes (including death from COVID-19), an analysis of variance was performed. Receiver operator characteristic type analysis was conducted to determine the PAD threshold with maximum sensitivity and specificity (Youden index) to detect the above-defined binary outcomes. The positive predictive value and negative predictive value of the found threshold were calculated. All the independent variables were then compared between the 2 subgroups formed by the PAD threshold, using the Chi<sup>2</sup> test (corrected by Fisher exact test where appropriate), the Mann-Whitney test, or the *t* test. For binary variables, a crude odds ratio (unadjusted) was calculated with its 95% CI. To adjust the odds ratio between all-mortality and PAD cutoff, all the independent variables with a univariate *P* value of  $\leq .10$  were entered in a multivariate logistic regression model for all-cause mortality. The model's *R*<sup>2</sup>, Hosmer-Lemeshow statistic, analog of cook's distances, and studentized ranges were calculated. The C statistic for the model was also calculated.

All the calculations were performed according to a prespecified statistical analysis plan, using IBM SPSS software (IBM Corp. Released 2021. IBM SPSS Statistics for Windows, Version 28.0, IBM Corp) and Python (Python Software Foundation. Python Language Reference version 3.4). The statistical code and the deidentified data are available on justified request from [crc@usj.edu.lb](mailto:crc@usj.edu.lb).

### Study Approval

The present work was approved by the Ethical Committee of the Saint Joseph University of Beirut, Lebanon (CEHDF letter). Protocols were carried out in accordance with the "Good Clinical Practice" described in the "Helsinki Declaration" (October 2013) and following the "International Ethical Guidelines for Biomedical Research Involving Human Subjects" developed by the Council for International Organizations of Medical Sciences in collaboration with the World Health Organization.

## RESULTS

### Baseline Characteristics and Outcomes

Between March 2020 and March 2021, 556 patients were hospitalized at Hôtel-Dieu de France university hospital; 89 patients did not have a baseline NCCT and were excluded from the study. Overall, 465 patients were included, and their demographic and clinical characteristics are shown in Table 1. The male patients were 315 (67.7%), with a mean (SD) age of 64 years (16 years). Most patients (264 [56.8%]) had a history of hypertension, the most frequent cardiovascular risk factor in the studied population. The mean baseline PAD was 26.7 mm (3.8 mm) (Table 1). In addition, 44.3% of patients had a NEWS2 score between 0 and 4, which indicates low clinical risk, whereas 55.7% of patients had a medium-to-high clinical risk. The median hospital length of stay (interquartile range) was 9 days (5-16 days). Although 110 patients (23.7%) were admitted to the ICU on median 3 days after admission, 63% of them were put on invasive mechanical ventilation for a median of 7 days (3-12 days) following their hospital admission. Table 1 also details the laboratory, and imaging characteristics of the subjects enrolled in the study.

Of the 465 admitted patients, 379 (81.5%) patients were discharged. At discharge, 272 (71.8%) patients did not require any supplemental oxygen, and at 2-month follow-up, 333 patients (91.2%) were completely autonomous on the respiratory level. At discharge, 108 (27.3%) patients had a PCFS score of 3 and above and needed a supervised rehabilitation in a specialized center. At 2-month follow-up, 30 patients (5.2%) still required supervised rehabilitation in a specialized center.

### Measure of Association Between Baseline PAD and In-Hospital Outcomes

In univariate analysis, the baseline PAD showed a weak correlation with most continuous and ordinal in-hospital and 2-month outcomes, that is, hospital length of stay, PCFS status at 2-month following discharge from hospital, and immediate and late (ie, 2-month) discharge status (Table 2). The correlation with NEWS2 score and PCFS at hospital discharge was not substantial. Larger mean PAD was associated with all-cause mortality (effect size, 0.256), intubation (effect size, 0.285), and a PCFS score

**TABLE 2. Correlation of Pulmonary Artery Diameter With In-Hospital and 2-Month Continuous and Ordinal Outcomes**

Variable	Spearman rho	P value	N	95% CI
NEWS2 score	0.069	.138	465	−0.022 to 0.159
Length of stay	0.130	.005	465	0.037 to 0.222
PCFS @ discharge	0.084	.108	368 <sup>a</sup>	−0.022 to 0.187
PCFS @ 2-month	0.121	.021	365 <sup>a</sup>	0.016-0.221
Discharge status	0.117	.023	375 <sup>a</sup>	0.018-0.212
2-month postdischarge status	0.128	.014	362 <sup>a</sup>	0.034-0.220

95% CIs for Spearman rho were built by bootstrapping based on 10,000 bootstrap samples. NEWS2, National Early Warning Score 2; PCFS, Post-COVID-19 Functional Status scale.

<sup>a</sup>Valid sample size is slightly less than the number of survivors (n=379) because of missing data.

of 3 and above at 2-month (effect size, 0.409), as shown in Table 3.

**Evaluation of Baseline PAD Measurement as a Screening Test for Increased Risk of Mortality**

A receiver operator characteristic analysis was performed and showed an area under the curve of 0.575 (95% CI, 0.507-0.643) with the cutoff 24.5 mm yielding 81.4% sensitivity and 32.7% specificity. The unadjusted odds ratio between PAD of 24.5 mm and above and all-cause mortality was 2.13 (95% CI,

1.19-3.81), PAD of 24.5 mm and above was also associated with increased weight, arterial hypertension, chronic renal failure, increased serum creatinine level, more extensive ground glass opacities, endotracheal intubation, and increased length of stay, as shown in Table 4.

**Multivariable Logistic Regression Analysis**

Using multivariable logistic regression, the adjusted odds ratio between PAD of 24.5 mm and above and all-cause mortality remained unaffected (multivariate OR, 2.07; 95%, CI 1.05-4.09). Pulmonary artery

**TABLE 3. Variation of Pulmonary Artery Diameter According to Categorical Outcomes**

Group	Categories	Group size	PAD at baseline		Effect size	P value
			NCCT (mm) (m±SD)			
Mortality	No	379	26.5±3.7		0.011	.072
	COVID-19-related	74	27.4±4.1			
	not COVID-19-related	12	28.3±4.1			
All-cause mortality	No	379	26.5±3.7		0.256	.033
	Yes	86	27.5±4.1			
ICU Admission	No	355	26.5±3.7		0.205	.061
	Yes	110	27.3±3.9			
Invasive mechanical ventilation	No	395	26.5±3.8		0.285	.028
	Yes	70	27.6±3.9			
PCFS at discharge <sup>a</sup>	PCFS 0-2	265	26.4±3.7		0.090	.441
	PCFS 3-4	103	26.7±3.8			
PCFS at 2-month <sup>a</sup>	PCFS 0-2	335	26.4±3.6		0.409	.032
	PCFS 3-4	30	27.9±4.5			

ICU, Intensive care unit; PAD, pulmonary artery diameter; PCFS, Post-COVID-19 Functional Status scale. P values correspond to analysis of variance and Student t test. The used effect sizes are Cohen's d for the t test and eta squared for analysis of variance test. <sup>a</sup>The group sizes are slightly less than the number of survivors due to missing data.

TABLE 4. Comparison of 2 Groups Defined by the 24 mm Pulmonary Artery Diameter Cutoff

	PA<24.5 mm	PA≥24.5 mm	Test	P value
Age	62±17	65±16	t	.112
Female gender	51 (36.4%)	99 (30.5%)	Chi <sup>2</sup>	.234
Blood type			Chi <sup>2</sup>	.367
O	42 (30%)	110 (33.8%)		
A	61 (43.6%)	113 (34.8%)		
B	11 (7.9%)	40 (12.3%)		
AB	7 (5%)	15 (4.6%)		
UNK	19 (13.6%)	47 (14.5%)		
Negative Rhesus antigen	12 (9.9%)	25 (9%)	Chi <sup>2</sup>	.851
Direct admission to ICU	10 (7.1%)	38 (11.7%)	Chi <sup>2</sup>	.183
Weight	76±14	83±17	t	<.001
Hypertension	70 (50%)	194 (59.7%)	Chi <sup>2</sup>	.066
Diabetes mellitus	34 (24.3%)	101 (31.1%)	Chi <sup>2</sup>	.149
Immunosuppression	13 (9.3%)	34 (10.5%)	Chi <sup>2</sup>	.741
Cardiovascular disease	30 (21.4%)	94 (28.9%)	Chi <sup>2</sup>	.109
Chronic renal failure	8 (5.7%)	66 (20.3%)	Chi <sup>2</sup>	<.001
Lung Disease	28 (20.6%)	65 (20.5%)	Chi <sup>2</sup>	.999
Smoker	30 (22.1%)	84 (26.5%)	Chi <sup>2</sup>	.346
Ground glass opacities (%)	21±16	27±19	t	<.001
Lobar condensation	9 (6.4%)	29 (8.9%)	Chi <sup>2</sup>	.462
Pulmonary embolism	0 (0%)	3 (0.9%)	F	.557
Leucocytes	6850 (5200-10,450)	7100 (5200-10,000)	MWU	.904
Neutrophiles	5165 (3625-7965)	5430 (3590-8050)	MWU	.746
Lymphocytes	870 (565-1280)	810 (540-1210)	MWU	.295
Ferritin	774 (456-1321)	732 (350.5-1328.5)	MWU	.682
LDH	318 (249-432)	336 (252-438)	MWU	.459
D-dimers	0.77 (0.44-2.1)	0.88 (0.48-1.67)	MWU	.61
CRP	76 (27-156)	94 (41.9-149)	MWU	.104
Procalcitonin	0.17 (0.07-0.33)	0.18 (0.09-0.48)	MWU	.193
HDL	1.13099 (0.86-1.42)	1.17 (0.99-1.34)	MWU	.715
LDL	3.17 (2.21-3.56868)	2.79 (2.07-3.46)	MWU	.236
Triglycerides	1.78 (1.25-2.46)	1.78 (1.34-2.48)	MWU	.469
Serum Creatinin	68.5 (54-90.5)	81 (65-116)	MWU	<.001
Oxygen (O <sub>2</sub> ) needs at baseline			MWU	.313
No O <sub>2</sub>	46 (32.9%)	80 (24.6%)		
O <sub>2</sub> < 4 L/min	29 (20.7%)	92 (28.3%)		
O <sub>2</sub> 4-8 L/min	42 (30%)	93 (28.6%)		
Optiflow	23 (16.4%)	60 (18.5%)		
NEWS2 score	5 (2-6)	5 (3-6)	MWU	.307
Length of stay	8.5 (5-14)	10 (6-18)	MWU	.028
ICU transfer	26 (18.6%)	84 (25.8%)	Chi <sup>2</sup>	.097
Intubation	11 (7.9%)	59 (18.2%)	Chi <sup>2</sup>	.004
Intubation day	8 (3-13)	6 (2-11)	MWU	.621

Continued on next page

TABLE 4. Continued

	PA<24.5 mm	PA≥24.5 mm	Test	P value
PCFS at discharge class 3-4	28 (23.0%)	75 (30.5%)	Chi <sup>2</sup>	.140
PCFS at 2-Month class 3-4	6 (5.0%)	24 (9.8%)	Chi <sup>2</sup>	.155

Chi<sup>2</sup>, Chi squared test; F, Fisher exact test; ICU, Intensive care unit; LDH, lactodehydrogenase; MWU, Mann-Whitney U test; PAD, pulmonary artery diameter; PCFS, Post-COVID-19 Functional Status scale; t, independent samples t test.

Categorical data are presented as frequencies and percentages. Continuous data not departing from normality assumptions are presented as mean ± SD. Continuous data departing from normality assumptions are presented as median and its interquartile range.

diameter of 24.5 mm and above was associated with all-cause mortality independently of hypertension, weight, chronic renal failure, cardiovascular disease, C-reactive protein, and ground glass opacities on CT-scan (Table 5). The model's C statistic was 0.750 (95% CI, 0.689-0.811), improving on univariate area under the curve.

## DISCUSSION

This retrospective study conducted at the Hôtel-Dieu of France, one of the largest tertiary centers and one of the main treatment centers for COVID-19 in Lebanon, suggests that a PAD of more than 24.5 mm, measured by NCCT at admission, is an independent risk factor for predicting mortality in patients hospitalized with COVID-19, with 81.4% sensitivity and 32.7% specificity, and can be of great help as a screening tool. These results are consistent with published results by Zhu et al<sup>21</sup>, and Esposito et al<sup>22</sup> reporting that pulmonary artery enlargement predicts overall

survival in patients with SARS-CoV-2. Although a higher cutoff for PAD could have been considered (taking into account normal PAD values in other populations), it would be less sensitive albeit more specific, a combination not optimal for screening purposes.

The NEWS2 Score is a validated scale for predicting clinical risk of mortality and life-threatening outcomes in patients with COVID-19.<sup>23</sup> Although on admission more than half the patients had a NEWS2 score indicating medium-to-high clinical risk for deterioration, the NEWS2 score was not correlated with PAD, suggesting that PAD enlargement could convey a risk not captured by NEWS2, because PAD was correlated hospital length of stay and was larger in patients requiring invasive mechanical ventilation.

Severe forms of COVID-19 can be complicated by an inflammatory response and a cytokine storm with leucopenia,<sup>24</sup> an elevation of D-dimer,<sup>25</sup> lactodehydrogenase,<sup>26</sup> C-reactive

TABLE 5. Multivariable Logistic Regression to Adjust the Odds Ratio Between PA Diameter ≥24.5 mm and All-Cause Mortality, Accounting for all Baseline Factors With a Univariate P value ≤ .10

Factor	Bêta	SE(Bêta)	Wald	df	P value	OR	95% CI
Hypertension	0.649	0.321	4.088	1	.043	1.913	1.020-3.588
Weight	-0.016	0.009	3.631	1	.057	0.984	0.967-1.000
Chronic renal failure	0.968	0.330	8.591	1	.003	2.634	1.378-5.032
Cardiovascular disease	0.774	0.301	6.630	1	.010	2.169	1.203-3.909
PA diameter ≥ 24.5 mm	0.727	0.348	4.371	1	.037	2.068	1.047-4.087
CRP	0.002	0.001	1.873	1	.171	1.002	0.999-1.004
Ground glass opacities (%)	0.014	0.008	3.593	1	.058	1.014	1.000-1.029
Constant	-2.248	0.763	8.687	1	.003	0.106	

CRP, C-reactive protein; PA, pulmonary artery.

Omnibus Test of Model Coefficients: P<.001.

-2 Log likelihood = 351.63.

Nagelkerke R Square = 0.196.

Hosmer-Lemeshow statistic: 6.49; P=.592.

protein (CRP),<sup>26</sup> ferritin,<sup>27</sup> interleukin (IL) 6,<sup>28</sup> and pro-calcitonin.<sup>29,30</sup> This storm of inflammatory cytokines leads to endothelial and epithelial dysfunction,<sup>31</sup> which can lead to an increase in pulmonary vascular resistance,<sup>32</sup> a dilation of the pulmonary vascular bed including the pulmonary artery. The early secretion of high levels of inflammatory cytokines (IL-6, IL-10, and tumor necrosis factor  $\alpha$ )<sup>33</sup> is responsible for the development of acute respiratory distress syndrome and pulmonary hypertension in patients with SARS-CoV-2.<sup>34,35</sup> The current study corroborates the existing literature<sup>22,36</sup> in that higher levels of IL-6, C-reactive protein, lactodehydrogenase, and D-dimers were found in patients requiring admission to the ICU, supporting the hypothesis that COVID-19–related pulmonary hypertension is induced by a thrombo-inflammatory syndrome.<sup>37</sup>

To the best of our knowledge, this is the first study to evaluate the relationship between the diameter of the pulmonary artery on admission and the PCFS and respiratory status on discharge and at 2-month follow-up in patients hospitalized with COVID-19. The alveolar–capillary insult leading to the development of acute respiratory distress syndrome and acute pulmonary hypertension can lead to debilitating and persistent symptoms (such as fatigue and dyspnea) 6–8 months after infection.<sup>38,39</sup> Thus, PAD measurement can be a quick and easy tool to guide and adapt effective treatment and rehabilitation strategies for patients hospitalized with COVID-19.

This work has some limitations. Patients with a history of pulmonary hypertension or chronic lung disease were not excluded. Second, we did not have any knowledge about patients' PAD before their hospitalization. Third, right ventricular function and pulmonary arterial pressure were not estimated by right heart catheterization, echocardiography and point-of-care ultrasound. Fourth, the Horowitz index for Lung Function (P/F ratio) to assess lung function is unavailable at baseline. In addition, the measurement of the pulmonary artery by NCCT is affected by “heart rate, acoustic window, operator experience”<sup>40</sup> and the presence of relevant lung disease.<sup>41</sup> Although to our knowledge this is one of the largest studies regarding PAD and COVID-19 outcomes to date, it is

retrospective and involves a single hospital with a Caucasian population, so it needs to be confirmed in other studies including the same and different ethnicities. Another caveat is that baseline characteristics of the patients were not combined and summarized in clinical scoring tools beyond the NEWS2 score, which could have been used to correlate the scoring tools with PA diameter and added to the multivariate model.

## CONCLUSION

The measurement of the pulmonary artery by NCCT on hospitalization is an independent risk factor for in-hospital mortality that can help identify severe cases and be a useful prognostic parameter of patients with COVID-19 as it is associated with overall survival and adapt rehabilitation strategies after discharge.

## POTENTIAL COMPETING INTERESTS

The authors report no competing interests.

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**Abbreviations and Acronyms:** COVID-19, coronavirus disease; NCCT, noncontrast nongated computed tomography; NEWS2, National Early Warning Score 2; PAD, pulmonary artery diameter; PCFS, Post-COVID-19 Functional Status; SARS-Cov-2, severe acute respiratory syndrome coronavirus 2

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