Radiology

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Acute Pulmonary Embolism Associated with COVID-19 Pneumonia Detected by Pulmonary CT Angiography

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Summary Statement

In patients with severe clinical features of COVID-19 infection, the proportion of patients with acute pulmonary embolus was 23% (95% CI: 15%, 33%) on pulmonary CT angiography.

Abbreviations:

Pulmonary embolus: Acute Pulmonary Embolism

COVID-19: Coronavirus Disease 2019

CTA: Computed Tomography Angiography

IMV: Invasive Mechanical Ventilation

RT-PCR: real-time Reverse Transcriptase-Polymerase Chain Reaction

SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2

Introduction

Chest CT plays an important role in optimizing the management of patients with COVID-19 while also eliminating alternate diagnoses or added pathologies, particularly for acute pulmonary embolism (1). A few studies and isolated clinical cases of COVID-19 pneumonia with coagulopathy and pulmonary embolus have recently been published (2–4). The main objective of our study was to evaluate pulmonary embolus in association with COVID-19 infection using pulmonary CT angiography.

Materials and Methods

This retrospective study was approved by our institutional review board. It followed the ethical guidelines of the declaration of Helsinki. Written informed consent was waived. Three authors (F.G., J.B., P.C.) had access to the study data. No author has any conflict of interest to declare in relation to this study.

Patients

The inclusion criteria were consecutive adult patients (≥ 18 years old) with a RT-PCR diagnosis (NucleoSpin RNA Virus kit, Macherey-Nagel Inc., Bethlehem, PA, USA) of SARS-CoV-2 or a strong clinical suspicion of COVID-19 (fever and/or acute respiratory symptoms, exposure to an individual with confirmed SARS-CoV-2 infection) who underwent a chest CT scan between March 15 to April 14, 2020 at a single center. In patients with suspected or confirmed SARS-CoV-2 infection, chest CT scan was performed when clinical features of severe disease were present (e.g., requirement for mechanical ventilation [IMV]) or underlying comorbidities). Patients with non-contrast chest CT scans were excluded.

CT Protocol

Our routine protocol for patients with severe clinical features of COVID-19 infection was multidetector pulmonary CT angiography using 256 slice multi-detector CT (Revolution, GE Healthcare, Milwaukee, WI) after intravenous injection of 60 ml iodinated contrast agent (Iomeprol

400 Mg I/mL, Bracco Imaging, Milan, IT) at a flow rate of 4 mL/s, triggered on the main pulmonary artery. CT scan settings were 120 kVp, 80 x .625 mm, rotation time .28 s, average tube current 300 mA, pitch .992 and CTDIvol 4.28 mGy.

Imaging Analysis. Chest CT scan pattern of COVID-19 and presence of pulmonary embolus were independently analyzed by two chest radiologists (J.B. and F.G. with 11 and 6 years of experience) on a PACS workstation (Carestream Health, Rochester, NY). Readers were blinded to patient status as well as clinical and biological features. In cases of discordance, a simultaneous reading to reach consensus was achieved.

Statistical Analysis

Comparisons between continuous variables were performed using Student t-test when distribution was normal. Comparison between categorical variables were performed using Pearson's chi-squared test or Fisher's exact test. To determine the clinical factors associated with pulmonary embolus, we considered the CT extent of lesions, need for invasive mechanical ventilation, demographics, and the presence of comorbidities as potential independent variables in a logistic regression model. A P value of less than .05 indicated a significant difference. All analyses were performed with R version 3.4.4 (R Core Team 2017).

Results

Of 2003 patients diagnosed with COVID-19, 280 patients were hospitalized during the study period. Of these, 129 of 280 (46%) hospitalized patients underwent CT scan at an average of 9 ± 5 days after symptom onset. Twenty-nine patients had non-contrast chest CT due to contraindication to iodinated contrast or non-severe clinical features and thus were excluded. Finally, 100 patients with COVID-19 infection and severe clinical features were included were examined with contrast enhanced CT (Figure 1). The mean age of the included patients was 66 ± 13 years old, with 70 men and 30 women (Table; Appendix E1 [online]).

Of 100 patients meeting inclusion criteria, 23 (23%, [95%CI, 15-33%]) patients had acute pulmonary embolism (Figure 2; Appendix E1 [online]). Patients with pulmonary embolus were more frequently in the critical care unit than those without pulmonary embolus (17 (74%) vs 22 (29%) patients, p<.001), required mechanical ventilation more often (15 (65%) versus 19 (25%) patients, p<.001) and had longer delay from symptom onset to CT diagnosis of pulmonary embolus (12 ± 6 versus 8 ± 5 days, p<.001), respectively (Table). In multivariable analysis, requirement for mechanical ventilation (OR = 3.8 IC95% [1.02 - 15], p=.049) remained associated with acute pulmonary embolus.

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Discussion

Our study points to a high prevalence of acute pulmonary embolism in patients with COVID-19 (23%, [95%CI, 15-33%]). Pulmonary embolus was diagnosed at mean of 12 days from symptom onset. Patients with pulmonary embolus were more likely require care in the critical care unit and to require mechanical ventilation than those without pulmonary embolus (Table).

Current guidelines (1,5,6) recommend performing non-contrast chest CT to assess the COVID-19 CT pattern and its extension. However, prior reports suggested coagulopathy associated with COVID-19 infection [e.g. (2,3)]. Further, these patients have frequent risk factors for pulmonary embolus (e.g. mechanical ventilation, intensive care unit admission). Therefore, we routinely performed contrast enhanced CT for COVID-19 patients with severe clinical features to evaluate the lung parenchyma as well as to evaluate other complications that may result in respiratory distress.

Our results showed frequent (23%) pulmonary embolus in patients with COVID-19. In multivariate analysis, pulmonary embolus was associated with invasive mechanical ventilation and male gender. Interestingly, extent of lesions was not a associated with pulmonary embolus. We acknowledge the preliminary nature of these findings, including its retrospective nature and limited sample size. Important clinical markers were not available that may explain or be associated with pulmonary embolus, including D-dimer (only 22 of 100 patients had D-dimer levels available). Nevertheless, our

results suggest that patients with severe clinical features of COVID-19 may have associated acute pulmonary embolus. Therefore, the use of contrast enhanced CT rather than routine non-contrast CT may be considered for these patients.

Author contributions: Guarantors of integrity of entire study, all authors; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; approval of final version of submitted manuscript, all authors; agrees to ensure any questions related to the work are appropriately resolved, all authors; literature research, F.G., J.B., E.D..; radiological analysis F.G., J.B.; statistical analysis, P.C.; and manuscript editing, all authors.

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Table. Patient Characteristics

	Total (n, % or SD)	Pulmonary embolus on chest CT (n, % or SD)	No Pulmonary embolus on chest CT (n, % or SD)	p value
	n= 100	n=23	n=77	
Age (years)	66 ± 13	67 ± 11	66 ± 13	.80
Male	70 (70)	21 (91)	49 (64)	.02
Comorbidities				
Cardiovascular disease	39 (39)	10 (43)	29 (38)	.81
Chronic respiratory insufficiency	15 (15)	4 (17)	10 (13)	.76
Diabetes, type 2	20 (20)	6 (23)	14 (18)	.55
Malignancy	20 (20)	3 (23)	16 (21)	.39
Care status				
Conventional care	61 (61)	6 (26)	55 (71)	
Critical care	39 (39)	17 (74)	22 (29)	<.001
Invasive mechanical ventilation	34 (34)	15 (65)	19 (25)	<.001
Delay from onset of symptoms to CT scan (days)	9 ± 5	12 ± 6	8 ± 5	<.001

SD = standard deviation

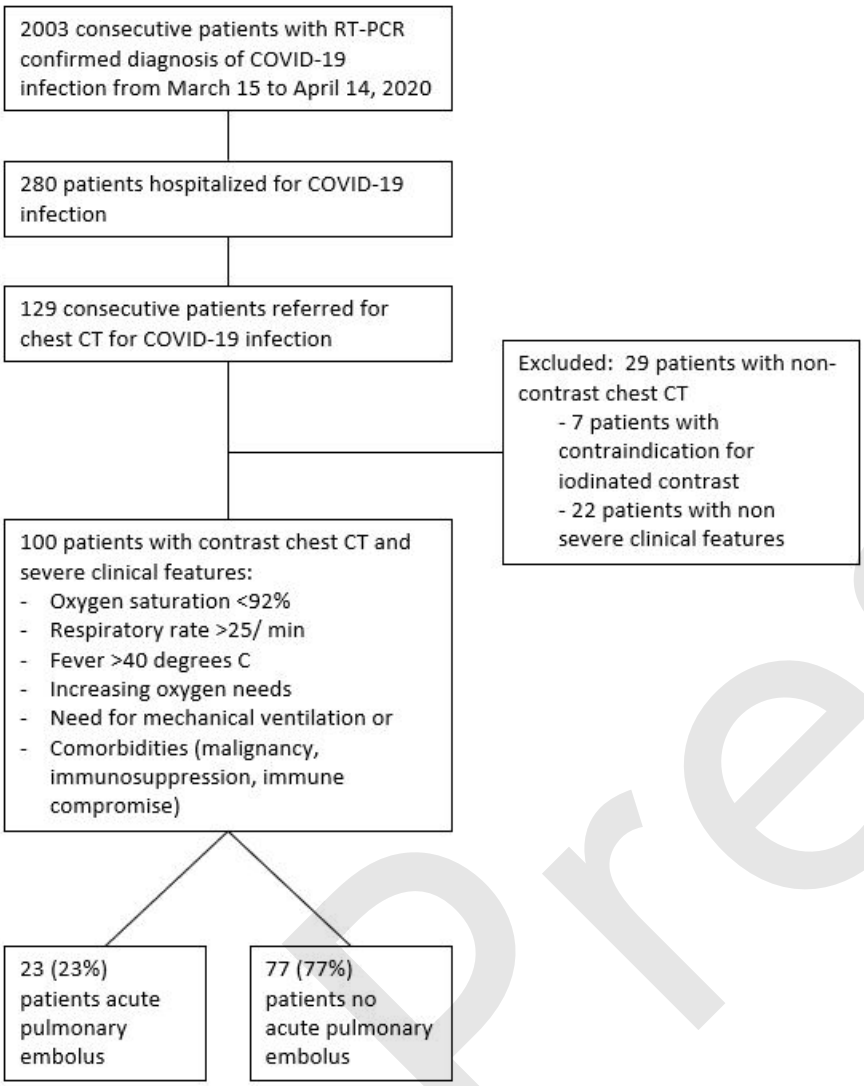

Figure 1: Flow chart of the study.

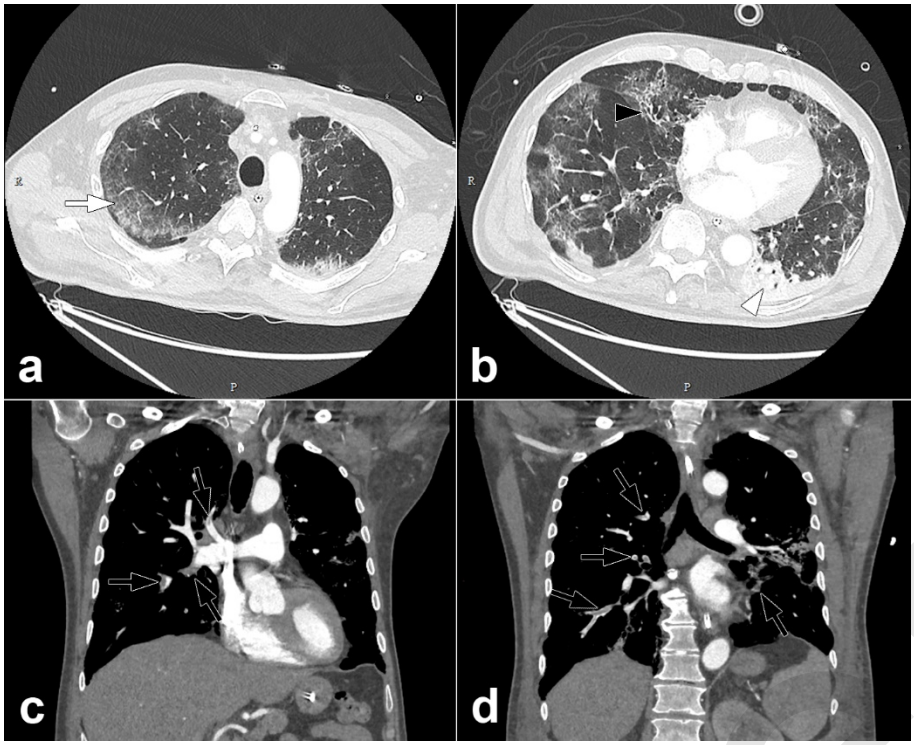

Figure 2: Pulmonary CT angiography of a 68 year old male. The CT scan was obtained 10 days after the onset of COVID-19 symptoms and on the day the patient was transferred to the intensive care unit. Axial CT images (lung windows) (a,b) show peripheral ground-glass opacities (arrow) associated with areas of consolidation in dependent portions of the lung (arrowheads). Interlobular reticulations, bronchiectasis (black arrow) and lung architectural distortion are present. Involvement of the lung volume was estimated to be between 25% and 50%. Coronal CT reformations (mediastinum windows) (c,d) show bilateral lobar and segmental pulmonary embolism (black arrows).