Radiology

ORIGINAL RESEARCH • RESEARCH LETTER

Acute Pulmonary Embolism in Patients with COVID-19 at CT Angiography and Relationship to D-Dimer Levels

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Conflicts of interest are listed at the end of this article.

Online supplemental material is available for this article.

Radiology 2020; 296:E189–E191 • https://doi.org/10.1148/radiol.2020201561 • Content codes: CH CT •

Reports of acute pulmonary embolism associated with coronavirus disease 2019 (COVID-19) have emerged in the literature. For example, Chen et al (1) described 25 pulmonary CT angiographic examinations from 1008 patients with COVID-19; 10 were positive for pulmonary embolism, mostly as segmental or subsegmental acute pulmonary embolism. In addition, D-dimer levels have been reported as elevated in patients with COVID-19 (2,3), with the suggestion of an independent association between the severity of the disease and the level of D-dimer (4). The purpose of this report is to describe the rate of pulmonary embolus in patients classified as having COVID-19 infection who underwent chest CT at a tertiary referral center.

Materials and Methods

Patient Population

The local ethics committee of Strasbourg University Hospital approved this retrospective study and waived the need for informed consent. Full methods are provided in Appendix E1 (online). From March 1 to March 31, 2020, medical records of all consecutive patients who underwent a CT examination *(a)* including the chest and *(b)* performed for either suspicion or follow-up of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection at one of our two hospital sites (Nouvel Hôpital Civil and Hôpital de Hautepierre, Hôpitaux Universitaires de Strasbourg, France) were evaluated. CT examinations that included pulmonary CT angiographic images were evaluated for further study. Clinical and demographic parameters for patients with and patients without pulmonary embolus on CT pulmonary angiograms were evaluated.

CT Pulmonary Angiography

CT angiograms were acquired with 64-row or greater scanners after injection of 50–75 mL of contrast material with a high concentration of iodine. Imaging was performed with use of a bolus-tracking technique and a threshold of 160–250 HU in the main pulmonary artery. Images were reconstructed with a slice thickness of 1 mm in mediastinal and parenchymal windows. One reader (I.L.L., with 4 years of experience) classified pulmonary embolism location as main pulmonary arteries, lobar,

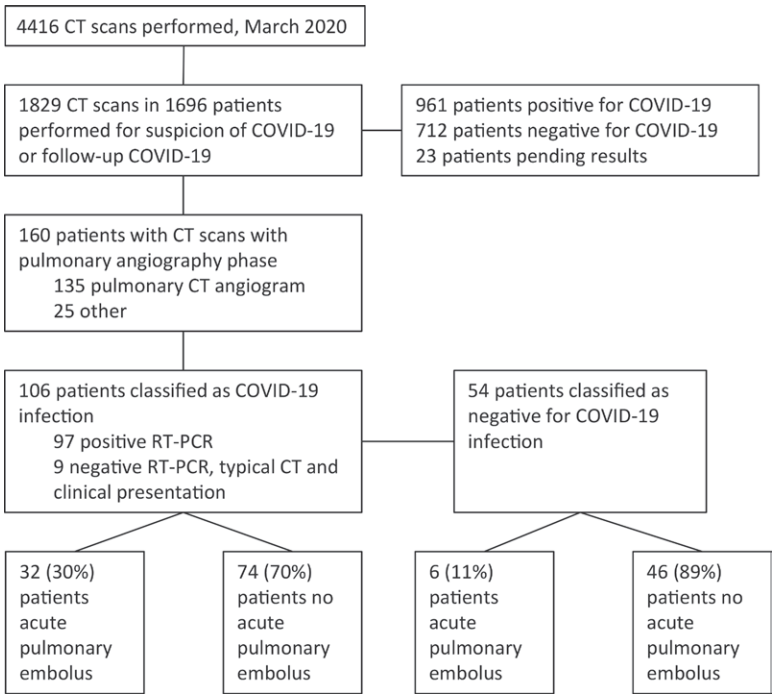

Figure 1: Flowchart of the study. COVID-19 = coronavirus disease 2019, RT-PCR = reverse-transcriptase polymerase chain reaction.

segmental, or subsegmental on the basis of the location of the most proximal luminal defect.

Laboratory Analysis

Fibrinogen and D-dimer levels were recorded for all patients who underwent pulmonary CT angiography. All patients who underwent pulmonary CT angiography were evaluated for reverse-transcriptase polymerase chain reaction (RT-PCR) results for SARS-CoV-2. All initial samples were obtained by means of nasopharyngeal swab; some patients had a second or third sampling using sputum or bronchoalveolar lavage. Any positive result was classified as confirmed COVID-19 infection. When RT-PCR results were negative, chest CT images were reviewed by a senior chest radiologist (M.O., with 14 years of experience) to look for characteristic COVID-19 lung parenchyma lesions. When CT findings were considered typical for COVID-19 (ie, extensive bilateral and peripheral ground glass opacities and/or alveolar consolidation) and clinical data were compatible, the patient was also adjudicated as having COVID-19 (4,5).

Results

A flowchart of all patients with CT scans obtained from March 1 to March 31, 2020, is shown in Figure 1. During this period, 1696 patients underwent CT for suspicion or follow-up of COVID-19 infection. Dedicated pulmonary CT angiography was performed in 135 of the 1696 patients (8%); 25 additional patients had pulmonary arterial phase images included in chest-abdomen-pelvic CT (total, 160 patients). Of these 160 patients, 106 were classified as having COVID-19 infection (97 patients with RT-PCR and nine with positive CT findings and negative RT-PCR test). In these 106 patients, CT angiography was performed owing to suspicion of pulmonary embolus in 67 patients (63%) and other CT indications in 39 (37%).

Thirty-two of the 106 patients (30% [95% confidence interval: 22%, 40%]) with COVID-19 who underwent pulmonary CT angiography were positive for acute pulmonary embolus (Fig 2); 74 were negative for pulmonary embolus at CT. Relevant clinical and biologic data are summarized in the Table.

Patients with COVID-19 infection and pulmonary embolus had higher D-dimer levels than those without pulmonary embolus (median: 15385 μg/L [interquartile range, 8180-22590 μg/L] vs 1940 μg/L [interquartile range, 410-3470 μg/L], respectively; $P < .001$), were more likely to be in the intensive care unit (24 of 32 patients [75%] vs 24 of 74 patients [32%], $P < .001$), and were treated more often with low-molecular-weight heparin before CT angiography (25 of 32 patients [78%] vs 17 of 74 patients [23%], $P < .001$) (Table). In these patients with COVID-19 infection, a D-dimer level greater than 2660 μg/L had a sensitivity of 100% (32 of 32 patients; 95% confidence interval: 88%, 100%) and a specificity of 67% (49 of 74 patients; 95% CI: 52%, 79%) for pulmonary embolism at CT angiography.

Discussion

Our study demonstrated that of 106 pulmonary CT angiograms performed for patients with COVID-19 over a 1-month period in a tertiary care center, 32 of 106 patients (30%) had acute pulmonary embolus. This rate of pulmonary embolus is higher than usually encountered in critically ill patients without COVID-19 infection (1.3% [6]) or in patients treated in the emergency department (3%–10% [7]). In our patient population, a D-dimer threshold of 2660 μg/L enabled the detection of all patients with pulmonary embolus at chest CT. This threshold of 2660 μg/L is higher than previously reported median levels of 2400 μg/L (8) and 900 μg/L (2) and is higher than cut-off values used to exclude pulmonary embolus in patients not in the intensive care unit (9). High values of D-dimer could be related to a higher activation of blood coagulation in patients with COVID-19 secondary to a systemic inflammatory response syndrome, or as a direct consequence of the SARS-CoV-2 itself. Although a single-center retrospective report, our results of the potential for pulmonary embolism associated with COVID-19 infection may serve to alert the medical community to heighted vigilance of this complication.

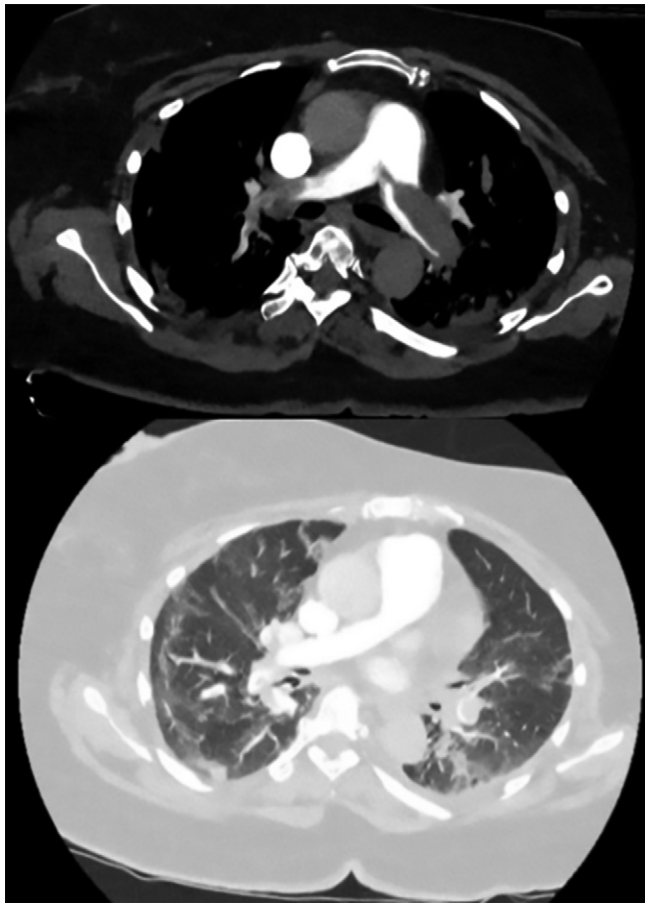

Figure 2: Images from CT pulmonary angiography (top, mediastinal window; bottom, parenchymal window) in a 71-year-old woman at day 3 of intensive care unit stay for acute respiratory distress syndrome secondary to coronavirus disease 2019. Pulmonary CT angiography was performed to investigate an elevated D-dimer value of more than 20000 μg/L. CT angiogram demonstrates bilateral filling defects in the main pulmonary arteries (top). Bilateral peripheral ground-glass opacities and small areas of consolidation are present (bottom).

Acknowledgments: The authors thank Cédric Hintzpeter, Joris Muller, MD, and Pierre Emmanuel Zorn, MSc, for their precious help in the data collection.

Clinical and Biologic Data for Patients Undergoing Pulmonary CT Angiography Classified as Having COVID-19 Infection

Clinical and CT Features	Pulmonary Embolism Present (n = 32)	Pulmonary Embolism Absent (n = 74)	P Value
RT-PCR positive for COVID-19	30 (94)	67 (91)	.59
Male sex	25 (78)	45 (61)	.04
Age (y)*	64 ± 22	63 ± 15	.60
BMI (kg/m^2)*	27 ± 8	29 ± 10	.10
ICU hospitalization	24 (75)	24 (32)	<.001
SAPS II (if patient was in ICU)*	46 ± 16	42 ± 13	.37
Worst PaO_2/FiO_2 ratio over the course of the hospital stay (if patient was in ICU)*	116 ± 50	168 ± 74	.06
Clinical suspicion for pulmonary embolus	17 (53)	50 (68)	
Thromboembolic prophylaxis before CT pulmonary angiography	25 (78)	17 (23)	<.001
Anticoagulation before CT pulmonary angiography	2 (6)	5 (7)	>.99
Interval between initial symptoms and CT pulmonary angiography (d)†	14 (11–18)	10 (7–13)	.001
Patients with a high D-dimer level (μg/L)	28 (88)	50 (68)	
Median D-dimer level (μg/L)†	15,385 (8180–22 590)	1940 (410–3470)	<.001
D-dimer level <5000 (μg/L)	5 (18)	39 (78)	…
D-dimer level 5000–20 000 (μg/L)	12 (43)	9 (18)	…
D-dimer level >20 000 (μg/L)	11 (39)	2 (4)	…
Median higher fibrinogen level (g/L)†	7.89 (6.33–9.45)	7.03 (5.39–8.68)	.19
Location of embolus on chest CT scans			
Main pulmonary artery	7 (22)	…	…
Lobar artery	11 (34)	…	…
Segmental artery	9 (28)	…	…
Subsegmental artery	5 (16)	…	…

Note.—Except where indicated, data are numbers of patients, with percentages in parentheses. The normal D-dimer level is less than 500 μg/L, and the normal fibrinogen level is between 2 and 4 g/L. BMI = body mass index, COVID-19 = coronavirus disease 2019, FiO_2 = fractional inspired oxygen (expressed as a fraction), ICU = intensive care unit, PaO_2 =arterial oxygen partial pressure (in millimeters of mercury), RT-PCR = reverse-transcriptase polymerase chain reaction, SAPS II = Simplified Acute Physiology Score.

* Data are medians ± standard deviations.

† Data are medians, with interquartile range in parentheses.

Author contributions: Guarantors of integrity of entire study, I.L.L., O.C., F. Schneider, A.L., P.B., C.R., M.O.; 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, I.L.L., X.D., J.H., C.P., F. Schneider, A.L., P.L., M.O.; clinical studies, I.L.L., X.D., J.H., O.C., F. Schneider, A.L., P.B., P.L., C.R., M.O.; experimental studies, X.D.; statistical analysis, F. Séverac, M.O.; and manuscript editing, I.L.L., X.D., F. Séverac, J.H., C.P., O.C., F. Schneider, A.L., S.M., M.O.

Disclosures of Conflicts of Interest: I.L.L. disclosed no relevant relationships. **X.D.** disclosed no relevant relationships. **F. Séverac** disclosed no relevant relationships. **J.H.** disclosed no relevant relationships. **C.P.** disclosed no relevant relationships. **O.C.** disclosed no relevant relationships. **F. Schneider** disclosed no relevant relationships. **A.L.** disclosed no relevant relationships. **P.B.** disclosed no relevant relationships. **S.M.** disclosed no relevant relationships. **P.L.** disclosed no relevant relationships. **C.R.** disclosed no relevant relationships. **M.O.** Activities related to the present article: disclosed no relevant relationships. Activities not related to the present article: is a paid consultant for Canon Medical Systems Europe; receives payment for lectures including service on speakers bureaus from Canon Medical Systems Europe. Other relationships: disclosed no relevant relationships.

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