## COVID-19 Increased Incidence of Acute Pulmonary Embolism in Emergency Department Patients During the COVID-19 Pandemic

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E arly detection of acute pulmonary embolism (PE) in patients with SARS-CoV-2 infection is integral to the clinical management of these patients. Many recently published studies have evaluated incidence of PE in hospitalized patients with COVID-19;<sup>1–9</sup> however, there are relatively limited data describing patients with SARS-CoV-2 infection and concomitant diagnosis of acute PE upon initial presentation. Therefore, the purpose of this study is to 1) evaluate the incidence of acute PE in patients undergoing computed tomography pulmonary angiography (CTPA) in the emergency department (ED) across six hospitals in New York City during the height of the COVID-19 pandemic compared to a nonpandemic period and 2) compare the characteristics and early outcomes of patients presenting with PE during the pandemic (n = 87) to patients presenting with PE during a nonpandemic period (n = 34).

This retrospective review was approved by the institutional review board, and informed written consent was waived. No authors had any conflict of interest to declare.

The inclusion criteria included all patients > 18 years of age who underwent CTPA in the ED. Data were collected for all patients who underwent imaging between April 1 and May 1, 2019, and April 1 and May 1, 2020, representing studies performed during nonpandemic and pandemic times, respectively. Demographic information was manually extracted from the electronic medical record and each record was reviewed by two independent authors for accuracy. Date of testing for SARS-CoV-2 infection by reverse transcriptase polymerase chain reaction (RT-PCR) was recorded. For the purposes of classifying patients as positive, negative, or not tested, the following criteria were used. Patients were classified as COVID positive if the patient had a documented positive test from an encounter prior to presenting to the ED with PE or if the patient had a positive test obtained within 2 days of CTPA. If a patient was not tested or tested negative within 2 days of the CTPA,

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the patient was classified as not tested or negative, respectively. Patients who > 2 days after CTPA tested positive were classified according to results available within 2 days of PE detection.

Outcome data on each patient were recorded for 14 days following hospital discharge. Patients transferred to an outside hospital after admission were excluded from the short-term outcomes analysis. For the patients diagnosed with PE between April 1 and May 1, 2020, date of symptom onset was recorded, with any described symptom of SARS-CoV-2 infection recorded as day 1 of symptoms.<sup>10</sup>

Axial images from the thoracic inlet to the iliac crests were obtained of the chest during administration of an IV contrast bolus timed for pulmonary arterial opacification. 3D and thin-section reformats were performed on a separate workstation. Dose reduction techniques were utilized including kVp/mA dose modulation based on patient size and iterative reconstruction. Reports of CTPA studies performed were queried from the radiology information system using Montage (Montage Health, Monterey, CA), and images were reviewed by a board-certified radiologist on a PACS workstation. CTPA studies performed in 2020 were additionally evaluated for commonly reported imaging features of COVID-19 pneumonia.<sup>11</sup>

To compare continuous data between the 2019 and 2020 groups, a Mann-Whitney U-test was used for nonnormally distributed data, and a Student's t-test was used for normally distributed data. Pearson's chisquare test was used to compare categorical variables between groups. Normality of continuous data was determined by the Shapiro-Wilk test. Normally distributed data were reported and means with standard deviations (SDs), and nonnormally distributed data were reported as medians with interquartile ranges. All statistical tests were performed between the 2019 cohort and aggregate 2020 data, including all patients presenting with PE to the ED during the study time period, regardless of result of SARS-CoV-2 test. All analyses were performed with GraphPad Prism Version 8.4.2.

Between April 1 and May 1, 2020, a total of 464 CTPAs were performed at initial presentation to the ED compared to 446 studies performed during the same date range in 2019. Eighty-seven of 464 (18.8%) studies were positive for acute PE in 2020 compared with 34 of 446 (7.6%) in 2019 (odds ratio [OR] = 2.6, 95% confidence interval [CI], 1.7% to 4.1%; absolute increase of 10.9%).

Among the 87 patients with acute PE in 2020, 49 of 82 (59.8%) tested positive for SARS-CoV-2 infection by RT-PCR analysis performed on samples obtained via nasopharyngeal swab, and 70 of 87 (80.5%) had commonly reported imaging features of COVID-19 pneumonia. Of the 49 patients who tested positive, 43 patients were tested upon index visit to the ED, having undergone no prior SARS-CoV-2 testing, with no prior encounter in the health care system or indication of previous hospitalization for COVID or suspected COVID. Notably, six patients who presented to the ED had tested positive between 9 and 18 days prior to presentation to the ED during prior hospitalizations, and represented with shortness of breath.

Patients in the 2020 cohort were on average younger compared to the 2019 cohort (57.2 years vs 65.7 years; 95% CI, 1.2 to 16 years), were more tachycardic  $(108.2 \pm 19.5 \text{ beats/min vs. } 96.8 \pm 19.0 \text{ cardic}$ beats/min; p = 0.004), and had fewer documented instances of unilateral lower extremity edema (9% vs. 26%; p = 0.02) compared to the 2019 cohort. Additionally, there were more male patients in 2020 comparted to 2019 cohort (58.6% vs 35.3%; OR = 2.6, 95% CI = 1.1% to 5.7%). In 2019, a total of 31 of 34 (91.2%) patients presenting to the ED and found to have PE were admitted to the hospital, and in 2020, 73 of 87 (83.9%) of patients presenting to the ED and found to have PE were admitted to the hospital. Additionally, in 2019 and 2020, one and five patients, respectively, transferred care to outside hospitals. Therefore, hospital course and disposition information was reported for a total of 30 and 68 patients in 2019 and 2020, comprising patients who were admitted to the hospital and did not transfer care elsewhere.

There was no significant difference in number of patients who underwent intensive care unit admission, length of hospital stay, 14-day readmission, or disposition of the patients between the groups. Detailed characteristics of the cohorts and short-term outcomes are described in Table 1.

Our study demonstrats that 18.8% of studies performed during the height of the pandemic were positive for PE, which is significantly higher than the year prior in which 7.6% of CTPA studies performed in the ED were positive for PE. Notably, a prior study performed by a single center in France reported an incidence of PE of 18.0% in patients presenting to the ED with COVID-19 pneumonia.<sup>12</sup> An important limitation of this study includes selection bias because individuals who may have otherwise presented to the emergency room may have chosen to stay at home or seek care elsewhere during the pandemic. In addition, while there is not enrichment in traditional risk factors of PE including obesity, malignancy, smoking, and recent major surgery in the 2020 cohort, there were likely differing practice patterns, hospital policies, and ordering tendencies of ED physicians during the pandemic compared to during the same time period in 2019.

Although differences in practice patterns cannot be accounted for when comparing the two time periods, our study highlights the importance of considering PE in patients presenting with respiratory distress, and suggests PE as a potential early manifestation of

Table 1

Comparison of Characteristics and Short-term Outcomes of Patients With PE Diagnosed in the ED Between April 1 and May 1, 2019, Compared to the Same Period in 2020

		CTPA Positive for PE in 2020 ( $n = 87$ )					
	CTPA Positive for PE in 2019 (n = 34)	COVID Positive (n = 49)	COVID Negative (n = 33)	All Patients in 2020	OR	95% CI	p-value
Demographics							
Age (years)	$65.7\pm16.9$	$58.1\pm19.2$	$58.0\pm17.7$	$57.2\pm18.7$		_	0.02
Male	12/34 (35)	30/49 (61)	18/33 (55)	51/87 (59)	2.6	1.1 to 5.7	0.02
Non-White race	22/34 (65)	39/49 (78)	24/33 (73)	67/87 (77)	1.8	0.8 to 4.3	0.2
Obesity (BMI > 30)	9/34 (27)	25/49 (51)	12/33 (36)	39/87 (45)	2.3	0.9 to 5.3	0.06
Diabetes	5/34 (15)	19/49 (39)	5/33 (15)	24/87 (28)	2.2	0.8 to 5.7	0.2
Asthma or COPD	15/34 (44)	7/49 (14)	7/33 (21)	18/87 (21)	0.3	0.1 to 0.8	0.009
Major surgery within 4 weeks	1/34 (3)	1/49 (2)	2/33 (6)	3/87 (3)	1.2	0.2 to 16	0.9
History of PE/DVT	11/34 (32)	10/49 (20)	4/33 (12)	17/87 (20)	0.5	0.2 to 1.2	0.1
Active smoker	6/34 (18)	3/49 (6)	5/33 (15)	9/87 (10)	0.5	0.2 to 1.7	0.3
Clinical presentation							
Chest pain or shortness of breath	25/34 (73.5)	37/49 (76)	27/33 (82)	69/87 (79)	1.4	0.6-3.5	0.5
Heart rate (beats/min)	$96.8\pm19.0$	$114\pm18.5$	$102.3\pm19.7$	$108.2\pm19.5$		_	0.004
Oxygen saturation (%)*	$96.5\pm3.3$	$94.0\pm9.8$	$95.4 \pm 2.8$	$94.8\pm7.4$		_	0.03
Unilateral leg swelling	9/34 (26)	4/49 (8)	3/33 (9)	8/87 (9)	0.3	0.1-0.8	0.02
Laboratory values							
White blood cell count (×10 <sup>6</sup> )	$\textbf{8.8}\pm\textbf{4.8}$	$10.9\pm4.0$	$11.2\pm5.0$	$10.5\pm4.3$		-0.8 to 2.8	0.5
D-dimer > 0.5 mg/L	14/17 (82)	45/46 (98)	30/32 (94)	78/81 (96)	5.4	1.1 to 24	0.07
Troponin > 0.03 ng/mL	12/32 (38)	18/47 (38)	13/31 ( 42)	31/82 (38)	1.0	0.5 to 2.3	0.9
COVID positive by RT-PCR	_	49/49 (100)	0/33 (0)	49/82 (61)†			_
Imaging findings							
Proximal PE (main or lobar artery)	15/34 (44)	22/49 (45)	21/33 (64)	44/87 (50)	1.3	0.6 to 2.8	0.5
Imaging findings of COVID-19	_	46/49 (94)	23/33 (70)	70/87 (81)		_	_
COVID positive by RT-PCR and/or imaging findings of COVID-19	—			72/87 (83)	—	—	_
Hospital course‡							
Admitted from ED	31/34 (91)	46/49 (94)	27/33 (82)	73/87 (84)	0.7	0.2 to 2.3	0.5
Transferred care to outside hospital	1/31 (3)	4/46 (9)	1/33 (3)	5/73 (7)	2.2	0.3 to 27	0.7
Length of hospital admission (days)	4.0 (3.0-7.8)	5.0 (3.0-8.5)	5.6 (2.0-10.0)	5.4 (3.0-9.9)	_	-2.3 to 3.6	0.7
BiPAP and/or intubation	6/30 (20)	15/42 (36)	6/26 (23)	21/68 (31)	1.8	0.7 to 5.0	0.3
Admission to ICU	13/30 (43)	16/42 (38)	5/26 (19.2)	21/68 (31)	0.6	0.2 to 1.4	0.3
14-day readmission	2/30 (7)	3/42 (7)	1/26 (4)	4/68 (6)	0.9	.2 to 4.8	1.0
Disposition of hospitalized patients:							
Returned home	18/30 (60)	32/42 (76)	20/26 (77)	52/68 (76)	1.6	0.7 to 4.0	0.3
Acute or subacute rehabilitation	4/30 (13)	3/42 (7)	3/26 (11)	6/68 (9)	0.4	0.1 to 1.5	0.2

## Table 1 (continued)

		CTPA Positive for PE in 2020 ( $n = 87$ )					
	CTPA Positive for PE in 2019 (n = 34)	COVID Positive (n = 49)	COVID Negative (n = 33)	All Patients in 2020	OR	95% CI	p-value
Still hospitalized 14 days after admission	3/30 (10)	9/42 (21)	3/26 (11)	12/68 (18)	1.9	0.5 to 6.8	0.5
Death within 14 days of admission	5/30 (17)	4/42 (10)	1/26 (4)	5/68 (7)	0.4	0.1 to 1.4	0.3

Data are reported as mean  $\pm$  SD, No./total No. (%), or median (IQR). Data for the 2020 cohort are subdivided into RT-PCR positive and negative for SARS-CoV-2 infection. Statistical tests were performed between the 2019 and 2020 groups. Unpaired parametric Student's t-test was used for continuous variables with normal distributions, the nonparametric Mann-Whitney test was used to compare groups with nonnormally distributed data, and chi-square analysis was used to compare categorical variables between groups.

BiPaP = bilevel positive airway pressure; BMI = body mass index; COPD = chronic obstructive pulmonary disease; COVID-19 = coronavirus disease; CTPA = computed tomography pulmonary angiography; DVT = deep venous thrombosis; ICU = intensive care unit; PE = pulmonary embolism; RT-PCT = reverse transcriptase polymerase chain reaction.

\*Oxygen saturation on room air was recorded for 28 patients in 2019 and 64 patients 2020 with results provided.

†Five patients were not tested for SARS-CoV-2 infection. Of the 49 patients who tested positive, 43 patients were tested upon presentation to the ED at their index visit, having undergone no prior SARS-CoV-2 testing, and no prior hospitalization for COVID or suspected COVID. Notably, six patients who presented to the ED and found to have PE had tested positive between 9 and 18 days prior to presentation with PE.

<sup>‡</sup>Hospital course and disposition do not include patients who were discharged from the ED without hospital admission or patients who were transferred to an outside hospital. Overall, there were 30 patients in 2019 and 68 patients in 2020 who were hospitalized without transfer of care elsewhere.

SARS-CoV-2 infection. CTPA is a vital diagnostic tool and can identify an urgent diagnosis of acute PE in patients with SARS-CoV-2 infection leading to further medical, surgical, and endovascular management that could potentially be lifesaving.

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