Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Pulmonary thromboembolism in COVID-19: Evaluating the role of D-dimer and computed tomography pulmonary angiography results

COVID-19 patients have a strong propensity to develop thrombosis and their respiratory symptoms often prompt clinicians to assess for the presence of a pulmonary thromboembolism (PTE) [1,2]. Prior research estimates that approximately 20% to 30% of patients with COVID-19 have a PTE demonstrated by computed tomography pulmonary angiography (CTPA) [3,4]. Some clinical decision rules such as the Pulmonary Embolism Rule-Out Criteria (PERC) and Wells' Criteria are used to assess a patient's risk of PTE. However, patients with COVID-19 can present with chest pain, tachycardia, tachypnea, and hypoxia even without a PTE; therefore, many of these clinical decision-making tools are unhelpful. Furthermore, elevations of d-dimer are frequent in COVID-19 given the pathophysiology of the disease. Recent studies have explored using higher thresholds for d-dimer testing among COVID-19 patients (e.g., from 2000 μg/L to 4000 μg/L) [5]. However, it is not clear that these are appropriate parameters based on their sensitivity and specificity [5,6].

We performed a retrospective cohort study at our hospitals in the NYU Langone Health System across Manhattan, Brooklyn and Long Island to evaluate the sensitivity and specificity of d-dimer testing to diagnose PTE among COVID-19 patients. We specifically compared CTPA studies performed in the emergency department (ED) versus those performed in the inpatient setting since d-dimer can increase during hospitalization due to disease progression [7]. From March 1, 2020 to June 1st, 2020, a total of 367 admitted COVID-19 positive patients had a CTPA study, as described in Table 1. Of these studies 157 (43%) were performed within 6 h of their arrival in the ED, and 210 (57%) were completed later during their inpatient hospitalization. Forty-five (29%) of the emergency department (ED) patients and 52 (25%) of the inpatients were diagnosed with an identifiable PTE.

We also compared the sensitivity and specificity of d-dimer levels drawn within 6 h of arrival for CTPA studies performed in the ED (139 of 157 ED patients) or within 48 h of inpatient CTPA studies (165 of 210 inpatients) to predict the presence of a PTE (Fig. 1). At a cutoff of 2000 μg/L (i.e., eight times the normal limit of 250 μg/L), a d-dimer test would have a 78% sensitivity and 67% specificity for an identifiable PTE in the ED and a 63% sensitivity and 66% specificity in the inpatient setting among patients who received a CTPA in our study. Even if we used a cutoff at just two times the normal limit (i.e., 500 μg/L), a d-dimer only had a 94% sensitivity and 30% specificity for an identifiable PTE in the ED, compared to a sensitivity of 89% and specificity of 23% in the inpatient setting. We should point out that this study is limited by its retrospective study design and reported rates of PTE may not accurately reflect the true prevalence of PTE among COVID-19 patients. Furthermore, we also noted that 31% and 40% of the ED and inpatient studies respectively were deemed to be suboptimal or inconclusive, e.g., unable to rule out a segmental or subsegmental PTE. This was largely due to motion artifact or mistimed contrast enhancement.

Our data supports the prior literature suggesting a relatively high incidence of PTE among COVID-19 patients [3,4]. Previously, it was reported that a cutoff of 2660 μg/L was 100% sensitive for PTE [6]. However, we find that a lower threshold may be required to identify more of these events. Furthermore, we found that a given d-dimer cutoff may be more sensitive or specific for identifying PTE in the ED when compared to the inpatient setting. This finding may be explained by the ongoing inflammation and coagulopathy given that d-dimer levels increase among some patients who experience disease progression [7].

In addition, 37% of patients in our study had a CTPA that was inconclusive for ruling out a PTE and some clots may have been missed. The actual rate of PTE among COVID-19 patients could be much higher than suggested by the rate of positive CTPA studies. It is also known, based on pathology reports, that even in the absence of a large thromboembolism identifiable by CTPA that COVID-19 patients have numerous microthrombi in their pulmonary vasculature, which is likely a critical component of the pathophysiology of the disease [8]. Given the poor sensitivity and specificity of d-dimer tests and high rate of non-diagnostic CTPA studies, the role of these diagnostic tests among COVID-19 patients should be reevaluated.

Table 1
Characteristics of COVID-19 patients with CTPA performed.

Patient characteristics	ED patients with CTPA performed	Inpatients with CTPA performed	*P*-value for difference
Patients, Number	157	210	
Age, Average	61.8	59.7	0.21
Male, Proportion	53.5%	69.1%	< 0.01
Race/Ethnicity			
White	31.9%	31.9%	0.25
Black	22.9%	14.8%	
Hispanic	26.8%	27.6%	
Asian	7.6%	10.9%	
Other	10.8%	14.8%	
BMI, Average	28.7	28.5	0.74
Comorbidities			
Hypertension	49.7%	43.8%	0.26
Hyperlipidemia	31.9%	33.8%	0.69
Diabetes	24.8%	34.8%	0.04
CAD	10.2%	9.1%	0.71
Asthma	10.2%	8.6%	0.60
COPD	7.0%	6.2%	0.75
Intubation Required	14.7%	33.3%	< 0.01
Inpatient Death	15.9%	17.1%	0.76
CTPA Result			
Negative	40.7%	35.7%	0.21
Indeterminate	30.6%	39.5%	
Positive	28.7%	24.8%	

Notes: Statistical difference between two groups calculated based on *t*-test or chi-squared as appropriate. Abbreviations: coronary artery disease (CAD), chronic obstructive pulmonary disease (COPD).

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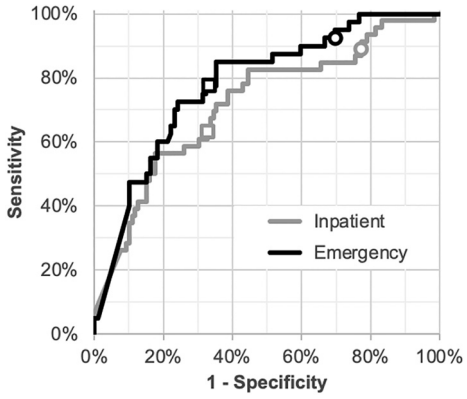

Fig. 1. Receiver Operating Characteristics Curves for D-Dimer and Pulmonary Thromboembolism among Inpatient versus Emergency Department Patients. Legend: Comparison of the sensitivity and specificity of d-dimer for COVID-19 patients with an identifiable pulmonary thromboembolism. Circles denote values at a d-dimer level of 500 μg/L. Squares denote values at a d-dimer level of 2000 μg/L.

Given the high risk of thromboembolism, surging COVID-19 patient volumes, and the difficulty of obtaining CTPA studies on all COVID-19 patients with an elevated d-dimer, empiric anticoagulation may be a more effective strategy than attempting to determine which patients should have a CTPA study based on any decision rule or d-dimer testing. Studies of anticoagulation are urgently needed to identify the most effective treatments to reduce morbidity and mortality of COVID-19. In these studies, laboratory markers, such as d-dimer, may help determine when to initiate or continue empiric anticoagulation.

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