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BRIEF REPORT

Infectious Disease

Utility of D-dimer in predicting pulmonary embolism in patients with COVID-19 presenting to the emergency department

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Abstract

Objectives: While our understanding of coronavirus disease 2019 (COVID-19) has evolved, uncertainty remains regarding utility of previously established pulmonary embolism (PE) screening guidelines in patients with COVID-19. Many studies have investigated the efficacy of D-dimer (DD) screenings for patients with COVID-19 admitted to inpatient services, but few have evaluated patients in the emergency department (ED). The purpose of this study was to investigate utility of DD threshold for PE screening in patients with COVID-19 presenting to the ED.

Methods: This was a retrospective, multicenter cohort including patients presenting to three EDs between March 1, 2020 and February 1, 2021 who tested positive for COVID-19 during ED visit or in 60 days prior to presentation and had DD ordered in ED. Patients were grouped by those who underwent computed tomography pulmonary angiogram (CTPA) to evaluate for PE and those who did not, and descriptive statistics were performed. Those who underwent CTPA were further divided into PE-positive and PE-negative groups. The discriminative ability of DD in predicting PE in patients with COVID-19 was analyzed using the receiver operating characteristic (ROC) curve.

Results: A total of 570 patients with COVID-19 were included in the study, of which 107 underwent CTPA to evaluate for PE. History of diabetes, elevated glucose, elevated lactate dehydrogenase, elevated white blood cell count, elevated platelets, elevated respiratory rate, and lower temperature were associated with increased risk for PE. Compared to those without PE, patients with PE were significantly more likely to be hospitalized (100% vs. 82%, $p = 0.020$) and admitted to the ICU (64% vs. 24%, $p = 0.002$). Those with PE had a significantly higher median DD value (21,177 ng/mL) compared to PE-negative group (952 ng/mL, $p < 0.001$). The ROC curve for DD in predicting PE had an area under the curve of 0.91 (95% confidence interval [0.84, 0.98]). In our study population, the optimal DD threshold for predicting PE was 1815 ng/mL

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(sensitivity 93% and specificity 80%). A conservative threshold of 1089 ng/mL could be used with sensitivity 100% and specificity 58%.

Conclusion: DD is often elevated in patients with COVID-19, regardless of PE. While the classically used DD cutoff is 500 ng/mL, our study demonstrated a threshold of 1089 ng/mL safely predicted PE in patients with COVID-19 .

1 | INTRODUCTION

1.1 | Background

Coronavirus disease 2019 (COVID-19) can cause a dysfunctional coagulopathy with increased risk for thrombosis.[1,2] Severe acute respiratory syndrome coronavirus 2 (SARS CoV-2) has been shown to infect epithelial cells, triggering a cascade that results in vascular endothelial dysfunction and predisposition to formation of microthrombi.[3] Studies have shown that pulmonary embolism (PE) is the most common thromboembolic complication.[4-6] In the emergency department (ED), a study found that 19% of computed tomography (CT) scans ordered to evaluate for PE in patients with COVID-19 were positive compared to a pre-pandemic rate of 8%.[7]

Clinically validated decision tools such as the Wells' Criteria and the Pulmonary Embolism Rule-Out Criteria can be used to assess risk of PE and guide workup in the ED.[8,9] Furthermore, D-dimer (DD) is classically used to obviate need for further imaging studies in working up venous thromboembolism (VTE) in low- to intermediate-risk patients. Negative DD screening is sufficient to rule out PE in such patients.[10] However, the overlap between signs and symptoms of COVID-19 and PE such as chest pain, tachypnea, tachycardia, and hypoxia challenge clinical utility of these tools. Additionally, DD is often increased in patients with COVID-19, irrespective of concurrent thromboembolic complications.[11] Elevation in DD is predictive of poor clinical course and increased disease severity in patients with COVID-19, with or without PE.[12] Thus, identifying patients with COVID-19 who should undergo further imaging to evaluate for PE remains a challenge.[13,14]

1.2 | Importance

Given the continued burden of patients with COVID-19 on EDs and challenges with resource utilization, it is important to consider a risk assessment strategy to avoid performing imaging on every COVID-19 patient with an elevated DD. Recent studies have explored using higher DD thresholds when evaluating for PE in COVID-19 patients with cut-offs ranging from 2000 to 2903 ng/mL.[15–21] Most of these studies had a small sample size, included patients with severe COVID-19 admitted to the floor or ICU, or took place outside the United States.[15–21]

1.3 | Goals of this investigation

We sought to investigate utility of DD in evaluating for PE in patients with COVID-19 in the ED. Our hypothesis was that a higher DD threshold could be used to safely predict PE in our patient population.

2 | METHODS

2.1 | Study design and setting

This was a retrospective multi-center cohort including patients who presented to Loyola University Medical Center, Gottlieb Memorial Hospital, or MacNeal Hospital between March 1, 2020 and February 1, 2021. The study was approved by the Institutional Review Board of Loyola University Chicago Health Sciences Division.

2.2 | Selection of participants/exposures

All consecutive patients presenting to the ED in the indicated timeframe were considered. Patients were included if they tested positive for COVID-19 on reverse transcription-polymerase chain reaction (RT-PCR) or antigen testing during or within the 60 days preceding an ED visit and had a DD ordered in the ED during diagnostic workup. Primary analysis was performed on patients who had computed tomography pulmonary angiogram (CTPA) performed while in the ED to evaluate for PE. Exclusion criteria were as follows: direct admissions, transfers from another hospital, <18 years old, pregnant, trauma patients.

2.3 | Measurements

Our data collection used the COVID-19 Clinical Research Registry provided by Loyola University Chicago's Clinical Research Office to pull charts for review. The registry uses the U.S. Centers for Disease Control and Prevention case report form for persons under investigation. Data from the registry were transferred using the secure web-based software program REDCap hosted at Loyola University Chicago. Additional data not included in the registry was manually extracted from patient charts, including date of presentation to the ED, DD while in the ED, associated symptoms, vitals and lab values on

arrival, prior anticoagulation, known risk factors for PE, and presence or absence of PE on CTPA. All manually extracted data were reviewed and verified by a second investigator for quality assurance. Discordant manual extractions were adjudicated by a third investigator.

2.4 | Outcomes

The primary outcome of interest was presence or absence of acute PE on CTPA. At Loyola, CTPE images were acquired on 64–256 slice scanners after injection of 65–85 mL of Isovue 370 contrast media, with contrast bolus-tracking after 4-s monitoring delay. Images were reconstructed with a slice thickness of 1.25 mm. At Gottleib and MacNeal, images were acquired on 64 slice scanners after injection of 90 mL of Isovue 370 contrast media, with contrast bolus-tracking after 5-s monitoring delay. Images were reconstructed with a slice thickness of 1.25 mm. The presence of PE was determined by manual extraction from radiographic reports using the same quality assurance techniques mentioned above. Reports identifying acute PE, regardless of location or extent, were considered positive for PE. Reports with indeterminate readings were considered negative for PE. If PE was confirmed, data on location of PE were manually extracted from the radiographic report and assigned to one or more of the following categories: central, segmental, subsegmental, unilateral, bilateral, and saddle. Secondary outcome measures included hospitalization and morality. Hospitalization was considered positive if admitted directly from ED. Data on mortality were extracted from the COVID-19 Clinical Research Registry.

2.5 | Data analyses

Patients were grouped by those who underwent CTPA to evaluate for PE while in the ED and those who did not. Patients who underwent alternative imaging to evaluate for PE (ie, venilation-perfusion (VQ) scan or CT with or without contrast) or who underwent CTPA after admission were categorized into the group who did not receive CTPA in the ED. Descriptive statistics were used to compare groups. Those who underwent CTPA were further divided into PE-positive (PE+) and PE-negative (PE−) groups, and descriptive statistics were again performed. Normality of continuous data were assessed using the Shapiro–Wilks test. Wilcoxon rank sum test was used to compare continuous characteristics. Pearson's chi-squared test, or Fisher exact test when appropriate, was used to compare categorical characteristics. Single logistic regression models were fitted to examine associations and conduct discriminant analysis between PE diagnosis and various individual predictors. Univariate models were applied for each of the patient characteristics, without adjusting for other covariates. We calculated sensitivity and specificity for predicting PE at various DD thresholds. The discriminative ability of DD in predicting PE in patients with COVID-19 was analyzed using the receiver operating characteristic (ROC) curve. The optimal DD cutoff to predict PE in this patient population was obtained from the ROC curve using Youden's J statistic. We divided patients >50 years old into 10-year age groups and constructed ROC curves for DD for each of these groups. The optimal DD threshold was plotted against the age group and linear regression analysis was performed to obtain the regression coefficient, representing the increase in DD cut-off value per decade over 60 years old. Analyses were performed using the R statistical programming language, version 4.1.3.

The Bottom Line

This retrospective, multicenter cohort investigated the discriminative ability of D-dimer (DD) in screening patients with active or recent COVID-19 for pulmonary embolism (PE). A DD threshold of 1089 ng/mL was found to safely predict PE in this population across three emergency departments (ED). Larger, prospective studies are required to determine an optimal DD threshold to rule out PE in COVID-19 patients in the ED.

3 | RESULTS

3.1 | Characteristics of study subjects

A total of 1290 patients presented to the ED during the study period who tested positive for COVID-19 during the ED visit or in the preceding 60 days, of which 29 patients met exclusion criteria for our study. Of these, 570 patients had DD performed while in the ED and were included in statistical analysis. In the study group, 107 patients underwent CTPA to evaluate for PE while in the ED and 14 were found to have acute PE (Figure 1). A comparison of patient characteristics in those who underwent CTPA versus those who did not is shown in Table 1. The median DD was 816 ng/mL in the overall population. Median DD was significantly higher in those who had CTPA performed compared to those who did not (1086 vs. 764 ng/mL, $p < 0.001$). Those who had CTPA performed were significantly less likely to be male (47% vs. 58%, $p = 0.036$) and to be hospitalized (84% vs. 93%, $p = 0.003$).

3.2 | Outcomes

For the group who underwent CTPA, 14 patients were diagnosed with PE with an overall incidence of 13.1% (14/107). Patient characteristics in PE− versus PE+ patients are shown in Table 2. Those with PE had a higher median DD value (21,177 ng/mL) compared to the PE− group (952 ng/mL, $p < 0.001$). Patients with PE were significantly more likely to have a history of diabetes and have baseline elevated glucose, lactate dehydrogenase (LDH), white blood cell (WBC) count, platelets, and respiratory rate. They were more likely to have lower temperature. All patients with PE were hospitalized (14/14), while PE− patients were

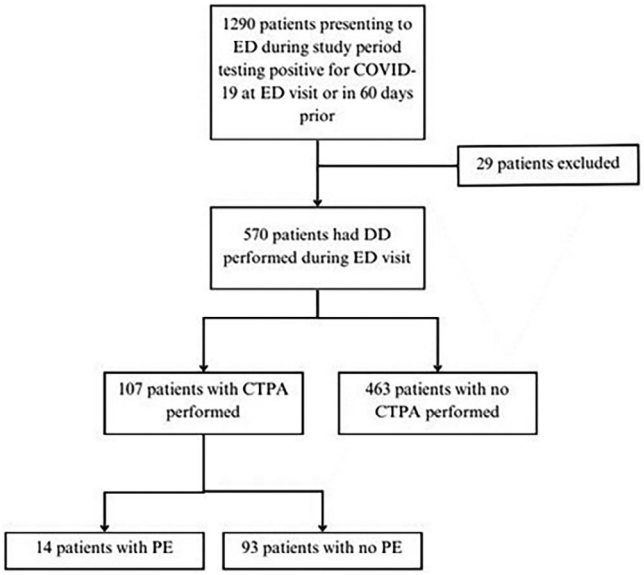

FIGURE 1 Flowchart of study population. Abbreviations: COVID-19, coronavirus disease 2019; CTPA, computed tomography pulmonary angiography; DD, D-dimer; ED, emergency department; PE, pulmonary embolism.

hospitalized 82% of the time (76/107, $p < 0.020$), resulting in a discharge rate from ED of 18%. Those with PE were more likely to be admitted to the ICU (64% of PE+ patients vs. 26% of PE− patients, $p < 0.002$). In our cohort, the location of PE was central and/or saddle in 79% of patients (11/14). There were bilateral PEs in 57% of patients (8/14) (Figure 2).

Table 3 displays the sensitivity and specificity for predicting PE at various DD thresholds. We have included the optimal threshold of 1815 ng/mL, identified using Youden's J statistic as well as a conservative threshold of 1089 ng/mL, which was the value with a sensitivity of 100% and the highest corresponding specificity. Lastly, the currently accepted DD threshold of 500 ng/mL for patients without COVID-19 was included for reference. The optimal threshold of 1815 ng/mL yielded a sensitivity of 93% and specificity of 80%. A more conservative threshold of 1089 ng/mL had a sensitivity of 100% in our cohort and a specificity of 58%. The classically used DD cutoff of 500 ng/mL had a sensitivity of 100% in our patient population, but with a specificity of only 9%.

The ROC curve illustrating performance of DD in the evaluation of PE is shown in Figure 3. The area under the curve (AUC) was 0.91 (95% confidence interval [0.84, 0.98]), indicating excellent discriminative performance of DD in our patient population. When broken down by 10-year age groups, the ROC curve performed similarly across groups.

Figure S1 shows the optimal DD threshold for age groups ≤60 years old, 61–70 years old, and ≥71 years old, obtained from the ROC curve for each age group. The threshold increased in each age group with a regression coefficient of 1655 (SE 536.6) ng/mL or 165.5 ng/mL increase per year ($r^2 = 0.9049$).

4 | LIMITATIONS

There are several limitations to our study. First is the small sample size and retrospective nature of our analysis. Second is selection bias as

TABLE 1 Patient characteristics: Computed tomography pulmonary angiography (CTPA) performed versus no CTPA performed in the emergency department (ED).

Patient characteristic	*N*	All patients (*N* = 570)	CTPA performed (*N* = 107)	No CTPA performed (*N* = 463)	*p*-value[a]
D-Dimer, ng/mL	570	816 (487.5, 1351.8)	1086 (733.5, 2359.5)	764 (454.0, 1294.0)	**<0.001**
Age, years	570	58 (46.0, 69.0)	59 (41.5, 69.5)	58 (46.0, 69.0)	0.558
Male, *n* (%)	570	318 (56%)	50 (47%)	268 (58%)	**0.036**
Race, *n* (%)	570				0.632
White		254 (45%)	49 (46%)	205 (44%)	
Black		179 (31%)	36 (34%)	143 (31%)	
Other/unknown		137 (24%)	22 (21%)	115 (25%)	
Ethnicity, *n* (%)	570				0.410
Hispanic/Latino		244 (43%)	42 (39%)	202 (44%)	
BMI, kg/m^2	551	31.0 (26.5, 36.6)	29.9 (26.3, 34.5)	31.3 (26.6, 36.9)	0.171
Outcomes, *n* (%)	570				
Hospitalized		521 (91%)	90 (84%)	431 (93%)	**0.003**
Death from COVID-19		72 (13%)	12 (11%)	60 (13%)	0.625
Death from other cause		8 (1%)	0 (0%)	8 (1%)	0.363

Note: Data are presented as median (interquartile range) or *n* (%). Bolded p-values highlight categories with $p < 0.05$.
Abbreviations: BMI, body mass index; COVID-19, coronavirus disease 2019.
[a]Wilcoxon rank sum test and Pearson's chi-square test were used for continuous and categorical characteristics, respectively.

TABLE 2 Patient characteristics: pulmonary embolism (PE)-negative (PE−) versus PE-positive (PE+).

Patient characteristic	*N*	PE− (*N* = 93)	PE+ (*N* = 14)	*p*-value[a]
D-dimer, ng/mL	107	952 (714.0, 1553.0)	21,177 (2881.3, 40,557.8)	**<0.001**
Age, years	107	55 (41.0, 68.0)	68.0 (55.8, 76.8)	0.088
Male, *n* (%)	107	40 (43%)	10 (71%)	0.056
Race, *n* (%)	107			
White		45 (48%)	4 (29%)	
Black		29 (31%)	7 (50%)	0.136
Other/unknown		19 (20%)	3 (21%)	0.479
Ethnicity, *n* (%)	107			
Hispanic/Latino		38 (41%)	4 (29%)	0.384
Time from the first COVID-19 + test to ED presentation, days	106	0 (0.0, 6.0)	2.5 (0.0, 12.0)	0.340
Risk factors, *n* (%)				
Current smoker	105	6 (6%)	2 (15%)	0.275
Former smoker	106	31 (33%)	5 (38%)	0.715
Cardiovascular disease	107	54 (58%)	12 (86%)	0.064
Diabetes	107	32 (34%)	9 (64%)	**0.040**
Anticoagulation prior to arrival, therapeutic or prophylactic	107	3 (3%)	2 (14%)	0.095
Estrogen prior to arrival	107	2 (2%)	1 (7%)	0.320
Recent surgery/admission	107	1 (1%)	0 (0%)	0.992
Signs and symptoms				
Absolute body weight, kg	105	84.8 (71.2, 102.0)	85.2 (75.0, 107.7)	0.727
Height, cm	105	165.1 (157.5, 175.3)	169.3 (165.1, 176.5)	0.295
BMI, average, kg/m^2	104	29.9 (26.6, 34.2)	29.8 (25.7, 38.8)	0.966
Temperature, °C	107	37.3 (36.9, 37.8)	36.9 (36.7, 37.1)	**0.010**
Heart rate	107	91 (81.0, 103.0)	104 (78.8, 110.0)	0.318
Oxygen saturation	107	96 (94.0, 98.0)	94 (92.3, 96.0)	0.082
Respiratory rate, breaths per min	107	21 (18.0, 26.0)	27 (21.3, 30.8)	**0.041**
Systolic blood pressure	107	128 (116.0, 142.0)	125 (119.3, 142.0)	0.974
Diastolic blood pressure	107	75 (69.0, 84.0)	74 (69.3, 82.0)	0.631
Mean arterial pressure	107	94 (85.0, 102.3)	95 (86.4, 99.8)	0.868
Cough, *n* (%)	107	68 (73%)	10 (71%)	0.895
Shortness of breath, *n* (%)	107	76 (82%)	11 (79%)	0.778
Chest pain, *n* (%)	107	41 (44%)	5 (36%)	0.557
Unilateral leg swelling, *n* (%)	107	0 (0%)	0 (0%)	
Hemoptysis, *n* (%)	107	2 (2%)	0 (0%)	
Labs				
Lactate dehydrogenase	52	324 (275.0, 414.5)	504 (389.3, 525.3)	**0.019**
C-reactive protein	72	66 (37.0, 148.6)	76 (60.6, 108.9)	0.909
Ferritin	50	289 (137.5, 936.0)	525 (346.0, 1011.0)	0.171
Troponin	102	0.03 (0.03, 0.03)	0.04 (0.02, 0.09)	0.085
Brain natriuretic peptide	74	40 (20.0, 85.3)	46 (37.8, 129.5)	0.314
White blood cells	107	6.4 (4.6, 9.0)	9.5 (7.2, 11.5)	**0.009**
Hemoglobin	107	13.5 (12.6, 14.4)	12.9 (12.0, 14.3)	0.383
Platelets	107	223 (164.0, 274.0)	278 (232.8, 342.8)	**0.019**
Lymphocyte count	105	0.9 (0.7, 1.3)	1.3 (1.0, 1.8)	0.102

(Continues)

TABLE 2 (Continued)

Patient characteristic	N	PE− (N = 93)	PE+ (N = 14)	p-value[a]
Bicarbonate (CO_2)	107	23 (21.0, 24.0)	22 (19.3, 23.0)	0.095
Glucose	107	115 (101.0, 137.0)	147 (115.3, 273.0)	**0.043**
Creatinine	107	0.95 (0.79, 1.19)	0.97 (0.78, 1.47)	0.644
Outcomes, *n* (%)				
Hospitalized	107	76 (82%)	14 (100%)	**0.020**[b]
Admitted to ICU	107	20 (26%)	9 (64%)	**0.002**
Death from COVID-19	107	9 (10%)	3 (21%)	0.207
Death from other cause	107	0 (0%)	0 (0%)	

Note: Data are presented as median (interquartile range) or *n* (%). Bolded p-values highlight categories with $p < 0.05$.
Abbreviations: BMI, body mass index; COVID-19, coronavirus disease 2019.
[a]Wilcoxon rank sum test was used for continuous variables. Pearson's chi-square test was used for categorical variables unless otherwise noted.
[b]Fisher's exact test.

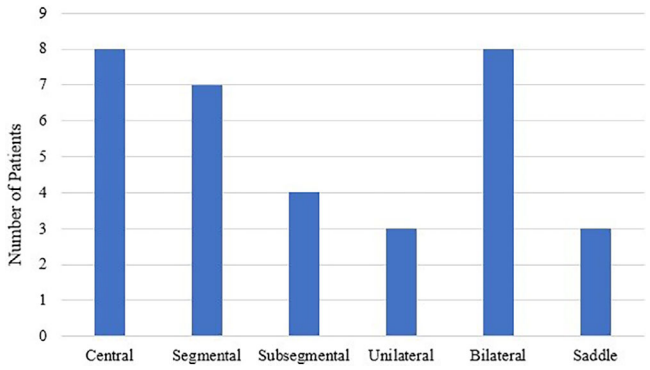

FIGURE 2 Locations of pulmonary emboli.

TABLE 3 Specificity and sensitivity of various D-dimer thresholds for predicting pulmonary embolism.

D-Dimer threshold, ng/mL	Specificity, % (95% CI)	Sensitivity, % (95% CI)
500	9 (3–15)	100 (100–100)
1089	58 (48–68)	100 (100–100)
1815	80 (71–87)	93 (79–100)

Note: Data are presented as % (confidence interval).
Abbreviation: CI, confidence interval.

patients selected for DD and CTPA were based on clinical gestalt rather than standardized clinical guidelines. Decisions to pursue these tests likely varied between providers and institutions. Details on thought process regarding decision to order DD and CTPA were not explicitly documented and thus could not be identified in a retrospective chart review. Further, our study excluded patients who were unable to undergo CTPA or in whom imaging was deferred because of prior anticoagulation or initiation of anticoagulation as part of treatment.

While most patients in our study tested positive for COVID-19 during the same ED visit, we chose to include those who tested positive up to 60 days prior to presentation due to the known lasting thrombotic sequalae seen after infection.[22] This is a feature that differentiates our study from other similar ones which tend to look at a much shorter time frame. However, the exact time frame of these effects following initial infection are not known, and thus the large window could skew data.

In the evolving landscape of COVID-19, it is unclear whether newer viral strains are associated with the same risk of thrombosis as strains investigated during the early pandemic. Larger, prospective studies focused on different strains of COVID-19 are required. Lastly, the effect of COVID-19 vaccination and antiviral treatments could mitigate some risk of thrombosis.

5 | DISCUSSION

Our study adds to literature on patients with COVID-19 and utility of pre-pandemic guidelines that consider pretest probability in conjunction with DD to guide workup of PE. Consistent with other studies,[20,23] our population had a median DD of 816 ng/mL, which is significantly higher than that expected in the general non-COVID-19 population presenting to the ED. Our findings confirm that patients with COVID-19 often have elevated DD regardless of PE status.

We found that patients in our cohort chosen for CTPA were significantly less likely to be hospitalized. One explanation for this finding is that in sick patients needing admission regardless of PE status, the decision to pursue imaging may have been deferred to the inpatient setting, or forgone due to anticoagulation recommendations for severe COVID-19 at this stage of the pandemic.[24] Another explanation is that patients requiring hospitalization can have contraindications to CTPA, including hemodynamic instability or comorbidities such as kidney disease.[25,26]

In those who underwent CTPA, we found an incidence of PE of 13% in our population. We found that median DD was significantly higher in COVID-19 patients with PE. This is similar to recent published findings.[20,21,27] In our cohort, PE+ patients were more likely to have a history of diabetes. They were more likely to have baseline elevated respiratory rate, glucose, LDH, WBC count, and platelets, and a lower temperature. While not significant, there is a considerable difference in other vitals and labs between groups, especially the troponin, which is substantially

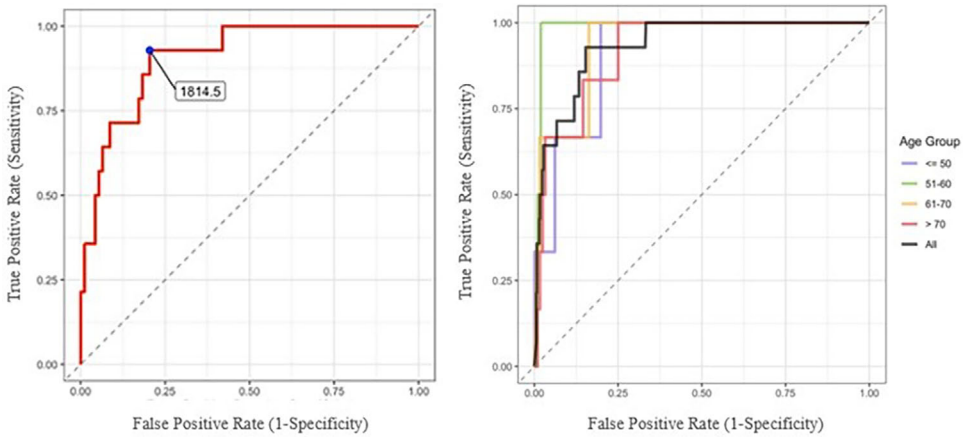

FIGURE 3 Receiver operating characteristic (ROC) curves. Left ROC for all patients: optimal threshold of 1814 ng/mL via Youden's J statistic (area under the curve [AUC] of 0.908, 95% confidence interval [CI] = 0.83–0.97). Right ROC by age group: all patients, ≤50 years old, 51–60 years old, 61–70 years old, and > 70 years old.

higher in our PE+ group. It is possible that studies with larger cohorts may find significant differences between these markers in the future. In our study, those with PE were significantly more likely to be hospitalized and admitted to the ICU. However, there was no significant difference in rates of mortality between PE+ and PE− patients, which may reflect successful PE identification and treatment.

When evaluating various DD thresholds, the ROC analysis in our study had a high AUC of 0.91. This suggests high overall performance of DD as a diagnostic test for PE in COVID-19 patients in our ED. The optimal threshold of 1815 ng/mL had a sensitivity of 93% and specificity of 80%. In our cohort, using this threshold to guide further imaging would have resulted in 32 total CT scans with one missed PE and 19 false positives. Thus, 75 scans could have been avoided resulting in a 70% reduction in CT scans ordered. A conservative threshold of 1089 ng/mL could be used with 100% sensitivity and 58% specificity. Using this threshold would result in 53 total CT scans with no missed PEs and 39 false positives. Thus, in our patient population, 50% of CT scans could have been avoided with no compromise in diagnosis.

When divided by age, the ROC curve for each group shows an increasing optimal DD threshold for predicting PE in our patient population. This trend is well-known and has been studied in patients without COVID-19 to derive age-adjusted DD thresholds to evaluate for PE.[28–31] Studies with larger sample sizes are required for meaningful derivation of age-adjusted DD thresholds that could be applied to patients with COVID-19.

Several studies have also looked at DD thresholds in COVID-19 with various findings. Mouhat et al. found that in inpatients with severe COVID-19, an optimal threshold of 2590 ng/mL had a sensitivity of 83% and specificity of 84%.[17] Ventura-Díaz et al. report a cutoff of 2903 ng/mL that could be used with a sensitivity of 81% and specificity of 59% in hospitalized patients, while a cutoff of 1221–1721 ng/mL yielded a sensitivity of 91%–94% and specificity of 37%–45%.[18] However, these studies focused on inpatients who have a higher prevalence of PE and more severe COVID-19 disease.[32] Further, inpatient studies do not differentiate between those who develop PE as a result of COVID-19 from those with embolization from deep vein thrombosis due to hospitalization.

Our study focuses specifically on ED patients in which disease severity ranges widely. Ramadan et al. found that DD performed better as a diagnostic test in the ED when compared to the inpatient setting, with higher AUC and increased sensitivity and specificity at any given threshold.[19] In the ED, DD has been shown to perform similarly in diagnosing PE in COVID+ and COVID− patients.[33] However, literature focused on the ED is limited and mostly focuses on populations outside the United States. A study in the UK reports a threshold of 1106 ng/mL with sensitivity of 95%,[13] while another in Paris reports a threshold of 1000 ng/mL with sensitivity of 90%.[34]

To our knowledge, only one other study looked at ED patients with COVID-19 in the US with suspected PE. In their cohort, Bledsoe et al. found a threshold of 1000 ng/mL yielded a sensitivity of 88%.[35] The difference in sensitivity compared to our findings could be due to a lower prevalence of PE in their cohort (4% vs. 13% in our study).[36] Their study included all patients with DD testing up to 48 h after initial ED presentation. According to the 2022 Emergency Department Benchmarking Alliance survey, the median length of stay (LOS) for all patients in the ED was 211 minutes. Thus, including those with testing up to 48 h after arrival (>10× the median LOS) may have inadvertently selected for patients already on inpatient services. In comparison, our study only looked at patients who had DD testing and/or CTPA performed while in the ED. Despite a small sample size, our study may better approximate the population of interest. Our study eliminates any patients who may have developed thromboembolism associated with hospitalization, which could confound results. Further, the study design in Bledsoe et al. allowed for inclusion of patients with evidence of PE up to 30 days after presentation, which may have led to the inclusion of patients who developed thromboembolism related to hospitalization rather than due to COVID-19. Prospective studies are warranted to determine an optimal DD threshold to rule out PE in COVID-19 patients in the ED.

In conclusion, DD performed well as a screening test for PE in our patient population with an AUC of 0.91. Increasing the DD threshold to 1089 ng/mL safely predicted PE in COVID-19 patients presenting to our ED while reducing unnecessary CTPAs by 50% without any missed diagnoses. History of diabetes, elevated glucose, elevated LDH, elevated WBC count, elevated platelets, elevated respiratory rate, and lower temperature were associated with increased risk for PE. Those with PE were significantly more likely to be hospitalized and admitted to the ICU.

AUTHOR CONTRIBUTIONS

Shannon Lovett and George Lew conceived the study. Shannon Lovett, George Lew, Megan A. Rech, and Natalie M. Lemon designed the study. Natalie M. Lemon and Megan A. Rech supervised the conduct of the trial and data collection. Natalie M. Lemon and Luke K. Taylor collected and interpreted the data. Quang Nguyen and Gregory J. Matthews provided statistical advice on study design and analyzed the data. Natalie M. Lemon drafted the manuscript with significant help from Luke K. Taylor, and all authors contributed substantially to its revision. Shannon Lovett takes responsibility for the paper as a whole.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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