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Utility of D-dimer for diagnosis of deep vein thrombosis in coronavirus disease-19 infection

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ABSTRACT

Objective: The objective of this study was to investigate the clinical usefulness of D-dimer in excluding a diagnosis of deep vein thrombosis (DVT) in patients with coronavirus disease (COVID-19) infection, potentially limiting the need for venous duplex ultrasound examination.

Methods: We retrospectively reviewed consecutive patients admitted to our institution with confirmed COVID-19 status by polymerase chain reaction between March 1, 2020, and May 13, 2020, and selected those who underwent both p-dimer and venous duplex ultrasound examination. This cohort was divided into two groups, those with and without DVT based on duplex ultrasound examination. These groups were then compared to determine the value of p-dimer in establishing this diagnosis.

Results: A total of 1170 patients were admitted with COVID-19, of which 158 were selected for this study. Of the 158, there were 52 patients with DVT and 106 without DVT. There were no differences in sex, age, race, or ethnicity between groups. Diabetes and routine hemodialysis were less commonly seen in the group with DVT. More than 90% of patients in both groups received prophylactic anticoagulation, but the use of low-molecular-weight heparin or subcutaneous heparin prophylaxis was not predictive of DVT. All patients had elevated acute-phase D-dimer levels using conventional criteria, and 154 of the 158 (97.5%) had elevated levels with age-adjusted criteria (mean D-dimer 16,163 \pm 5395 ng/mL). Those with DVT had higher acute-phase D-dimer levels than those without DVT (median, 13,602 [interquartile range, 6616-36,543 ng/mL] vs 2880 [interquartile range, 1030-9126 ng/mL], P < .001). An optimal D-dimer cutoff of 6494 ng/mL was determined to differentiate those with and without DVT (sensitivity 80.8%, specificity 68.9%, negative predictive value 88.0%). Wells DVT criteria was not found to be a significant predictor of DVT. Elevated D-dimer as defined by our optimal metric was a statistically significant predictor of DVT in both univariate and multivariable analyses when adjusting for other factors (odds ratio, 6.12; 95% confidence interval, 2.79-13.39; P < .001).

Conclusions: D-dimer levels are uniformly elevated in patients with COVID-19. Although standard predictive criteria failed to predict DVT, our analysis showed a D-dimer of less than 6494 ng/mL may exclude DVT, potentially limiting the need for venous duplex ultrasound examination. (J Vasc Surg: Venous and Lym Dis 2021;9:47-53.)

Keywords: D-dimer; Deep vein thrombosis; Wells DVT criteria; COVID-19

The coronavirus disease-19 (COVID-19) pandemic has infected more than 3 million people in the United States, resulting in more than 132,000 deaths.¹ It is reported that health care workers are at high risk of contracting this disease owing to increased, prolonged exposure to the virus that causes COVID-19.² As a result, there has been an effort to limit the exposure of health care personnel by restricting the use of diagnostic tests, including venous duplex ultrasound examination, with the intent of limiting the spread of disease. At our institution, a

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policy was implemented restricting venous duplex ultrasound examination to select patients at high risk for DVT based on clinical criteria, including the Wells DVT criteria; high clinical suspicion for pulmonary embolism (PE); and those who were not receiving full systemic anticoagulation. This resulted in fewer venous duplex ultrasound examination studies, despite an increased demand for such studies in patients with COVID-19 who are often critically ill and in need of diagnosis.

D-Dimer is a product of fibrinolysis and has shown a high sensitivity but low specificity for the diagnosis of venous thromboembolism (VTE).³ Elevated D-dimer levels are nonspecific and can also be seen in pregnancy, heart disease, and recent surgery as well as inflammatory conditions.⁴ Owing to their high sensitivity but low specificity, D-dimer levels are most often used along with the Wells DVT criteria to exclude DVT in patients with a low clinical probability. Venous duplex ultrasound examination remains necessary in those patients with a high clinical suspicion by Wells DVT criteria and elevated D-dimer levels.^{3,5} However, the use of Wells DVT criteria and D-dimer levels have not been validated in COVID-19 infection.

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COVID-19-positive patients are considered to have a hypercoagulable state and at increased risk for DVT.⁶ Although it is well-documented that these patients are at high risk for DVT, little is known about the usefulness of p-dimer in patients with COVID-19, and p-dimers are generally elevated in this patient population.^{7,8} Recently, a committee of vascular thrombosis experts proposed guidelines for the diagnosis and treatment of VTE in patients with COVID-19 based on clinical probability of VTE, p-dimer, venous duplex ultrasound examination, and a computed tomography scan for PE protocol, acknowledging that such guidelines may change as further information becomes available.⁹

The purpose of our study was to investigate the usefulness of D-dimer in excluding a diagnosis of DVT in patients with COVID-19 and potentially limit the need for venous duplex ultrasound examination. We theorized that although all patients with COVID-19 admitted to our hospital would have an elevated D-dimer level, those with DVT would have a more pronounced elevation in the acute-phase D-dimer level. Furthermore, we wanted to investigate the value of the Wells DVT criteria in aiding the diagnosis of DVT.

METHODS

Study design. This is a single-center retrospective cohort study composed of consecutive patients with confirmed COVID-19 status, with positive polymerase chain reaction results for severe acute respiratory syndrome coronavirus-2 by nasopharyngeal swab, between March 1, 2020, and May 13, 2020. Patients under the age of 18 were excluded from this analysis, as were those with a known DVT or PE before admission. Patients symptomatic with confirmed COVID-19 status admitted to our hospital all had D-dimer levels measured, and those considered at high risk for DVT based on clinical criteria underwent venous duplex ultrasound examination, forming our study population. Venous duplex ultrasound examination was performed for a variety of indications, including changes in clinical examination, significantly elevated D-dimer levels in critically ill patients, and changes in respiratory status. Ultimately, venous duplex ultrasound examinations were ordered based on the discretion of the attending physician after discussion with a vascular surgeon.

All patients had at least one D-dimer measurement taken during their hospital course. D-Dimer measurements were recorded sequentially for all patients throughout their hospital course. Acute-phase D-dimer values, defined as the highest D-dimer level before obtaining venous duplex ultrasound examination, were used to compare with the presence of confirmed DVT. During the study, venous duplex ultrasound examination protocols differed from our usual standard. All venous duplex ultrasound examinations were performed at bedside rather than in our vascular laboratory owing to

ARTICLE HIGHLIGHTS

- **Type of Research:** Single-center, retrospective cohort study
- **Key Findings:** In 158 coronavirus disease-19-positive patients who underwent both D-dimer and venous duplex ultrasound examination, a D-dimer cutoff level of 6494 ng/mL had a sensitivity of 80.8% and a negative predictive value of 88.0% in excluding the diagnosis of deep vein thrombosis.
- **Take Home Message:** A p-dimer level of less than 6494 ng/mL excluded deep vein thrombosis in most coronavirus disease-19 patients, potentially limiting the need for venous duplex ultrasound examination.

the contact and droplet isolation precautions of each patient with COVID-19. Venous duplex ultrasound examination was limited to the femoral and popliteal veins and did not include the tibial veins. Also, once a diagnosis of DVT was made, the study was terminated, such that not all studies included bilateral extremities. These changes were implemented to limit COVID-19 exposure among our sonographers. Distal DVT and tibial vein DVT were not included in this analysis. All venous duplex studies were done by a registered vascular technologist.

Data collection. Internal institutional review board approval was obtained before collection of patient data (ID# 1595707). Patient consent was not required for our study by our institutional review board because this was a retrospective study and data were deidentified. Variables collected fell into three major categories: patient demographics, prehospital medical conditions active on presentation, and variables associated with a diagnosis of DVT. All data were manually extracted utilizing the hospital electronic medical record, de-identified and aggregated within spreadsheet software (Libre-Office Calc, v6.4.1.2, The Document Foundation, Berlin, Germany) on a password-protected computer with an encrypted hard drive.

Patient demographic factors recorded for study included sex, age, race, ethnicity, height, and weight, as well as date of admission. Patient medical history variables active on presentation that were extracted from the electronic medical record were diabetes mellitus, smoking history (within 30 days), functional status on presentation (independent, partially dependent, or completely dependent), history of chronic obstructive pulmonary diseases, ascites, congestive heart failure, hypertension requiring medication, acute kidney injury, a history of requiring dialysis, active malignancy, metastatic cancer, wound infection or chronic steroid use, active pregnancy, active DVT, PE or disseminated intravascular coagulopathy, any recent trauma (<30 days), any recent surgeries (<30 days), history of coagulopathic or hypercoagulable disorders (such as factor V Leiden, systemic lupus erythematosus, antithrombin III deficiency, prothrombin deficiency), and sepsis or septic shock on presentation (based on systemic inflammatory response syndrome criteria). The use of anticoagulation, either as prophylaxis or therapeutic, was recorded, as was patient intubation during hospital admission. The Wells criteria for DVT were calculated for all patients.

Patients who received a venous duplex ultrasound examination positive for DVT subsequently were initiated on therapeutic anticoagulation with either a parenteral unfractionated heparin infusion with a goal partial thromboplastin time of 60 to 90 seconds or lowmolecular-weight heparin dosed at 1 mg/kg unless a contraindication was present. Those with negative venous duplex ultrasound examination continued to receive DVT thromboprophylaxis as long as no contraindications to do so were observed. None of the patients in our study received thromboprophylaxis higher than the standard dose.

Statistical analysis. Continuous variables were described as means (standard deviation) or medians (interguartile range [IQR]). Categorical values were described as proportions (percentages). Associations between continuous variables were determined using two-sided t-tests or Wilcoxon rank-sum tests where appropriate. Comparisons between categorical variables were made via Pearson χ^2 test. Univariate logistic regression analysis was performed on all of our variables. Statistically significant variables with a P value of less than .05 on our univariate analysis subsequently underwent multivariable analysis. Optimal cutoff values for diagnostic tests were determined by receiver operating characteristic curves and Youden index calculation. A P value of .05 or less was considered significant. R statistical programming language (v3.6.3, R Foundation for Statistical Computing, Vienna, Austria) was used for statistical analysis.

RESULTS

Demographics and comorbidities. A total of 158 patients with COVID-19-positive status who had both a Ddimer level and venous duplex ultrasound examinations during their admission were included in the study. Patients with DVT were more commonly male, although this finding was not significant (61.5% vs 50.0%; P = .17). There were no significant differences in race and ethnicity between patients with and without DVT. Similarly, comorbidities were roughly equally distributed between the two cohorts (Table I). Notable exceptions included diabetes mellitus and routine hemodialysis, which were more common in patients without DVT (49.1% vs 30.8% [P = .03] and 8.5% vs 0.0% [P = .031], respectively). DVT thromboprophylaxis (either

unfractionated subcutaneous heparin 5000 units every 8 hours or low-molecular-weight heparin 40 mg/d) was given to 144 of the 158 patients (90.1%), with proportionally fewer patients in the DVT cohort receiving lowmolecular-weight heparin (21.2% vs 50.0%; P = .002). Patients who presented with acute kidney injury and without a contraindication to thromboprophylaxis were placed on unfractionated subcutaneous heparin, whereas patients without acute kidney injury and a contraindication to thromboprophylaxis were placed on low-molecular-weight heparin. Moreover, patients with DVT were more likely to be intubated during their hospitalization than those without (73.1% vs 51.4%; P = .01).

Adjuncts for diagnosis of DVT. All patients had elevated acute-phase p-dimer levels using the conventional reference range of 230 ng/mL or less p-dimer unit (DDU). Similarly, when adjusting for age, all patients except four (2.5%) had an elevated acute-phase p-dimer levels. Patients with DVT had significantly higher acutephase p-dimer levels than those who did not (median, 13,602 [IQR, 6616-36,543 ng/mL] vs 2879 [IQR, 1030-9126 ng/mL]; P < .001; Fig 1). A Wells DVT Criteria score of greater than 2 (likely DVT) was more common among patients with confirmed DVT, although this difference was not significant (44.2% vs 31.1%; P = .106).

Using the Youden index calculation, an optimal cutoff of 6494 ng/mL DDU was calculated to differentiate between those with and without DVT. By this new metric, 42 of 52 patients (80.8%) with DVT had a D-dimer above this level, whereas 33 of 106 patients (31.1%) without DVT had an elevated D-dimer (P < .001; Table II). Calculated sensitivity and specificity for this new cutoff were 80.8% and 68.9%, respectively. Negative predictive value was 88.0%. The C-statistic (area under the curve) was 0.802 (Fig 2).

Predictors of DVT. In univariate logistic regression analysis, patients with diabetes mellitus were found to have lower risk of DVT (odds ratio [OR], 0.46; 95% confidence interval [CI], 0.23-0.93; P = .03), whereas patients who were intubated (OR, 2.56; 95% CI, 1.24-5.27; P = .01) and patients with a D-dimer level of more than 6494 ng/mL DDU DVT (OR, 9.29; 95% CI, 4.16-20.7; P < .001) were found to have a higher risk of DVT. When adjusting for other significant variables in multivariate analysis, only an elevated D-dimer level was significant (OR, 7.59; 95% CI, 3.34-17.3; P < .001; Table III). In this group of critically ill patients, the Wells DVT criteria (likely DVT classification) was not a significant predictor of DVT (OR, 1.75; 95% CI, 0.89-3.48; P = .107). Similarly, the use of prophylactic agents was not in itself a predictor of DVT, regardless of the agent used.

DISCUSSION

Historically, clinical criteria in addition with a D-dimer level have been useful in determining the probability of DVT.^{3,5} On this basis, those with a high probability

Table I. Comparison of select of	demographics and c	comorbidities a	of patients with	n and without de	ep venous thrombosis
(DVT)					

Variable	Total (n = 158)	Without DVT (n = 106)	With DVT ($n = 52$)	P value
Sex, male	85 (53.8)	53 (50.0)	32 (61.5)	.17
Age, years	67.4 ± 14.6	67.9 ± 15.1	66.4 ± 13.6	.56
Race				.34
Other	22 (13.9)	13 (12.3)	9 (17.3)	
White or Caucasian	52 (32.9)	38 (35.8)	14 (26.9)	
Black or African American	77 (48.7)	52 (49.1)	25 (48.1)	
East Asian or Pacific Islander	7 (4.4)	3 (2.8)	4 (7.7)	
Ethnicity				.60
Non-Hispanic	115 (81.6)	77 (82.8)	38 (79.2)	
Hispanic	26 (18.4)	16 (17.2)	10 (20.8)	
BMI, kg/m ²	29.5 ± 7.5	29.2 ± 6.5	30.1 ± 9.4	.49
Diabetes mellitus	68 (43.0)	52 (49.1)	16 (30.8)	.03
Smoking history	17 (10.8)	13 (12.3)	4 (7.7)	.38
Functional status				.13
Independent	98 (62.0)	60 (56.6)	38 (73.1)	
Partially dependent	41 (25.9)	31 (29.2)	10 (19.2)	
Totally dependent	19 (12.0)	15 (14.2)	4 (7.7)	
Chronic obstructive pulmonary disease	13 (8.2)	10 (9.4)	3 (5.8)	.43
Congestive heart failure	11 (7.0)	9 (8.5)	2 (3.8)	.28
Hypertension	113 (71.5)	80 (75.5)	33 (63.5)	.12
Acute kidney injury	85 (53.8)	60 (56.6)	25 (48.1)	.31
Routine hemodialysis	9 (5.7)	9 (8.5)	0 (0.0)	.03
Active malignancy	11 (7.0)	9 (8.5)	2 (3.8)	.28
Disseminated cancer	7 (4.4)	6 (5.7)	1 (1.9)	.28
Immobilization	23 (14.6)	18 (17.0)	5 (9.6)	.22
Intubation	92 (58.6)	54 (51.4)	38 (73.1)	.01
Sepsis	51 (32.3)	34 (32.1)	17 (32.7)	.94
Septic shock	12 (7.6)	10 (9.4)	2 (3.8)	.21

Values are number (%) or mean \pm standard deviation.

of DVT or an elevated D-dimer level should subsequently undergo venous duplex ultrasound examination.¹⁰ Although venous duplex ultrasound examination has previously been a readily available resource, its use has become increasingly limited owing to the current COVID-19 pandemic. Logistic constraints such as the availability of registered vascular technologists and ultrasound examination machines, or the need for routine decontamination after exposure to COVID-19-positive environments has restricted the ability to obtain venous duplex ultrasound examinations on a regular basis. In addition, limiting the exposure of our registered vascular technologists has become increasingly important, creating the need to determine which patients should be prioritized when obtaining venous duplex ultrasound examinations.

When associated with a low clinical probability for VTE, age-adjusted D-dimer cutoff has been shown to be associated with a decreased incidence of VTE.¹¹ All patients in our study had an increased D-dimer according to the conventional cutoff of 230 ng/mL, along with 97.5% of patients when an age-adjusted D-dimer cutoff was used. Our results correspond with those from Zhou et al.¹² which showed that D-dimer levels were generally elevated in patients with COVID-19 infection. Owing to an elevated D-dimer level according to both conventional and age-adjusted cutoffs in almost all patients, D-dimer would lose its predictive value according to such cutoffs.

Although D-dimer has previously been seen as a relatively nonspecific test, our analysis showed that D-dimer levels were significantly elevated in patients who were confirmed to have a DVT on venous duplex ultrasound examination. An optimal D-dimer cutoff of 6494 ng/mL 100.000



Fig 1. Tukey box-and-whisker comparison of acute-phase D-dimer levels between those with and without deep vein thrombosis (DVT). Horizontal bars represent medians, whereas diamond points represent means. Boxes represent the range between the first and third quartiles, and whiskers represent 1.5 times the interquartile range appended to these quartiles. Extraneous points represent outliers.

was determined to differentiate those with and without DVT with a sensitivity of 80.8%, a specificity of 68.9%, and a negative predictive value of 88.0%. This new cutoff was validated with good predictive merit in both our univariate and multivariate logistic regressions.

As venous duplex ultrasound examination becomes increasingly difficult to obtain owing to increasing demand and limited resources, the need for D-dimer in increased p-dimer level in patients with COVID-19. a new cutoff value should be set. D-Dimer levels have typically shown high sensitivity and negative predictive value (>95%).¹³ Although this new level will have a lower sensitivity and negative predictive value than in patients without COVID-19. creating a new cutoff increases the clinical usefulness of the D-dimer test within patients with COVID-19.

Several institutions have used point-of-care ultrasound examinations to assist in the diagnosis of DVT.¹⁴ Although it would be useful in the appropriate clinical environment and with well-trained personnel, this resource may not be widely available. If available, registered vascular technologists could be equipped with pointof-care ultrasound equipment to assist in providing a diagnosis in a variety of clinical settings, including the emergency room, intensive care unit, and clinic. At the same time, D-dimer levels are likely to be accessible at the majority of hospitals. Similar to patients without COVID-19, the use of D-dimer levels does not replace the need for venous duplex ultrasound examination in patients with a high clinical suspicion for DVT, and these patients should undergo further diagnostic imaging. Instead, the D-dimer is useful in determining which patients may not benefit from venous duplex ultrasound examination and help to determine which studies should be prioritized.

Recent autopsy reports have shown that COVID-19 causes a procoagulant state that involves inflammation to the endothelial system leading to pulmonary vasculature endothelialitis, microthrombosis, and angiogenesis.¹⁵ Owing to this procoagulant state, patients are at increased risk for venous thromboembolic events, and guidelines recommend use of thromboprophylaxis for all patients with COVID-19. At this time, there is a lack of evidence regarding anticoagulation strategies for

Table	II. Acute-phase	e factors of patients	s with and without dee	p vein thrombosis (<i>DVT</i>) be	efore diagnosis

		Without DVT	With DVT		
Variable	Total (n = 158)	(n = 106)	(n = 52)	P value	
DVT prophylaxis				.002	
None	14 (8.9)	9 (8.5)	5 (9.6)		
Subcutaneous heparin	80 (50.6)	44 (41.5)	36 (69.2)		
Low-molecular-weight heparin	64 (40.5)	53 (50.0)	11 (21.2)		
Wells DVT criteria, likely (\geq 2)	56 (35.4)	33 (31.1)	23 (44.2)	.11	
Acute-phase D-dimer	13,736.4 ± 19,939.8	7,152.1 ± 11,027.9	27,158.2 ± 26,453.9	<.001	
Acute-phase D-dimer	5394.5 [1848.5-14668.2]	2879.7 [1030.3-9126.0]	13602.5 [6616.2-36543.0]	<.001	
Age-adjusted acute-phase D-dimer status, elevated	154 (97.5)	102 (96.2)	52 (100.0)	.16	
Custom acute-phase ⊳-dimer status (≥6494 ng/mL DDU), elevated	75 (47.5)	33 (31.1)	42 (80.8)	<.001	
DDU, p-dimer unit. Values are number (%), mean ± standard deviation, or median [interquartile range].					

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Fig 2. Receiver operating characteristic curve demonstrating optimal D-dimer cutoff of 6494 ng/mL for determining the presence of deep vein thrombosis (DVT) in coronavirus disease-19 (COVID-19)-positive patients.

patients with COVID-19.^{9,16} The vast majority of our patient population (91.1%) received thromboprophylaxis in the form of either low-molecular-weight heparin or unfractionated heparin. Our patients in the intensive care unit who had D-dimer levels above our cutoff of 6494 ng/mL were continued on standard dose

thromboprophylaxis, unless a diagnosis of DVT was established. This procedure is in accordance with recently published CHEST guidelines regarding anticoagulation in patients with COVID-19.¹⁶ CHEST guidelines also recommend against increased doses of thromboprophylaxis, even in critically ill patients, and anticoagulation therapy for a minimum of three months after obtaining a diagnosis of DVT with therapeutic weightadjusted low-molecular-weight heparin or parenteral unfractionated heparin as the initial drug of choice. With these recommendations, by obtaining a verified diagnosis of DVT, the intensity of anticoagulation would change from the standard dose of thromboprophylaxis to therapeutic anticoagulation. Establishing a diagnosis of DVT can therefore lead to changes in patient management, such as initiating therapeutic anticoagulation, caval interruption, or catheter-based or systemic thrombolysis. Patients with a positive result would also warrant a minimum of 3 months of therapeutic anticoagulation.

Current recommendations from Obi et al⁹ are to obtain a venous duplex ultrasound examination in patients at high risk for DVT and bleeding, in which the results will change management, and patients with a high clinical suspicion of PE or DVT when a computed tomography scan for PE cannot be obtained. In those COVID-19positive patients with a low risk of bleeding, patients with a high clinical suspicion of DVT can be treated with full therapeutic anticoagulation. In those with a low clinical suspicion for DVT, venous duplex ultrasound examination may be avoided in patients with a D-dimer below our proposed cutoff.

Table III. Regression analysis of select variables for prediction of deep vein thrombosis (DVT)

Variable	Univariate OR (95% CI)	Univariate <i>P</i> value	Multivariable OR (95% CI)	Multivariable <i>P</i> value
Sex, male	1.60 (0.81-3.15)	.17	-	_
Age, years	0.99 (0.97-1.02)	.56	-	-
Diabetes mellitus	0.46 (0.23-0.93)	.03	0.51 (0.23-1.14)	.10
Smoking history	0.60 (0.18-1.93)	.39	-	—
Hypertension	0.56 (0.28-1.16)	.12	-	—
Disseminated cancer	0.33 (0.04-2.79)	.31	-	—
Immobilization	0.52 (0.18-1.49)	.23	-	—
Sepsis	1.03 (0.51-2.09)	.94	-	—
Septic shock	0.38 (0.08-1.82)	.23	-	—
DVT prophylaxis				
None	Reference	Reference	-	—
Subcutaneous heparin	1.47 (0.45-4.79)	.52	-	—
Low-molecular-weight heparin	0.37 (0.11-1.33)	.13	-	—
Intubation	2.56 (1.24-5.27)	.01	1.98 (0.87-4.51)	.10
Wells DVT criteria, likely (≥2)	1.75 (0.89-3.48)	.11	-	-
Custom acute-phase D-dimer status (>6494 ng/mL DDU), elevated	9.29 (4.16-20.7)	<.001	7.59 (3.34-17.3)	<.001

CI, Confidence interval; DDU, D-dimer unit; OR, odds ratio.

This study has several important limitations. First, this study was performed retrospectively, which created difficulty in obtaining important clinical data, including the Wells score. These data were primarily obtained through assessing clinical notes that led up to the decision to perform a venous duplex ultrasound examination and relied on accurate documentation of the patient's clinical condition and medical decision making. Second, owing to the recent onset of the COVID-19 pandemic, our sample size is relatively small compared with prior studies regarding D-dimer and DVT.^{3,5,11,17} As the pandemic progresses, additional patients may also be evaluated. Prospective studies with a larger patient population may help to validate our results. Also, we did not include patients with a diagnosis of pulmonary embolus, and the use of D-dimer in this patient population remains questionable.

CONCLUSIONS

Imaging with the use of noninvasive vascular studies has been limited during the current COVID-19 pandemic. With an increasing scarcity of resources despite a growing demand, utilization of additional tools to aid in diagnosis are necessary. Because D-dimer levels are universally elevated in patients with COVID-19, conventional and age-adjusted use of this marker has become impractical. In our analysis, a D-dimer level of less than 6494 ng/mL excluded DVT, limiting the need for duplex ultrasound examinations.

AUTHOR CONTRIBUTIONS

Conception and design: EC, PM, MZ, MD Analysis and interpretation: EC, PM, MZ, MD Data collection: EC, PM, OC, YK, JH, MD Writing the article: EC, PM, OC, MD Critical revision of the article: EC, PM, OC, YK, JH, MZ, MD Final approval of the article: EC, PM, OC, YK, JH, MZ, MD Statistical analysis: EC, PM, MD Obtained funding: Not applicable Overall responsibility: MD

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