# Evidence Search Service Results of your search request

## Prognostic value of D-dimer for pulmonary embolism in patients with COVID-19

**ID of request:** 25816  
**Date of request:** 28th October, 2020  
**Date of completion:** 30th October, 2020

If you would like to request any articles or any further help, please contact:  Tom Roper at [tom.roper@nhs.net](mailto:tom.roper@nhs.net)

Please acknowledge this work in any resulting paper or presentation as: Evidence search: Prognostic value of D-dimer for pulmonary embolism in patients with COVID-19. Tom Roper. (30th October, 2020). BRIGHTON, UK: Brighton and Sussex Library and Knowledge Service.

**Sources searched**  
EMBASE (9)  
Google Scholar (1)  
MEDLINE (38)  
NICE Evidence Search (1)  
TRIP Database (1)  
UNCOVER (Usher Network for COVid-19 Evidence Reviews) (0)  
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**Date range used** (5 years, 10 years): 2020 onwards   
**Limits used** (gender, article/study type, etc.): None   
**Search terms and notes** (full search strategy for database searches below):

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## A. National and International Guidance

#### British Thoracic Society (BTS)

**BTS Guidance on Venous Thromboembolic Disease in patients with COVID-19** (2020)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=f4e7bab0acabc9eace428652dfc49967)

#### Royal College of Anaesthetists (RCoA);Royal College of Physicians (RCP);Intensive Care Society

**Clinical guide for the prevention, detection and management of thromboembolic disease in patients with COVID-19** (2020)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=142422eeec04cfea6d620af0d63335cb)

## B. Systematic Reviews

#### Cardiology in review

**Elevated D-Dimer Levels Are Associated With Increased Risk of Mortality in Coronavirus Disease 2019: A Systematic Review and Meta-Analysis.** (2020)

Shah S., Shah K., Patel SB, et al.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=52d6bf017d13ea12499f046cdb4e803d)

Our meta-analysis demonstrates that patients with COVID-19 infection presenting with elevated d-dimer levels have an increased risk of severe disease and mortality.

#### ERJ Open Research

**D-dimer as an indicator of prognosis in SARS-CoV-2 infection: a systematic review** (2020)

Vidali S. et al

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=11dec1b89908ce18a4759238cf8472f2)

Correlations exist between COVID-19 infection, severe elevation of D-dimer levels, and increase in the rate of complications and composite end-point. The appropriateness of early and continuous D-dimer monitoring and labelled anticoagulation as management tools for COVID-19 disease deserves accurate investigation, to prevent complications and reduce interventions.

#### medRxiv

**A Systematic Review and Meta-analysis of D-Dimer Levels in Patients Hospitalized with Coronavirus Disease 2019 (COVID-19)** (2020)

Bansal A. et al

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=2d4090a3537a258e7a34cf9a986ee709)

Preprint: not yet peer-reviewed. The results of this concise meta-analysis suggest that d-dimer is significantly increased in patients having a worse clinical outcome (all-cause mortality, ICU admission or ARDS).

## C. Original Research

1. **A higher D-dimer threshold for predicting pulmonary embolism in patients with COVID-19: a retrospective study.**  
   Ventura-Díaz Sofía Emergency radiology 2020;:No page numbers.

PURPOSECOVID-19 raises D-dimer (DD) levels even in the absence of pulmonary embolism (PE), resulting in an increase in computed tomography pulmonary angiogram (CTPA) requests. Our purpose is to determine whether there are differences between DD values in PE-positive and PE-negative COVID-19 patients and, if so, to establish a new cutoff value which accurately determines when a CTPA is needed.METHODSThis study retrospectively analyzed all COVID-19 patients who underwent a CTPA due to suspected PE between March 1 and April 30, 2020, at Ramón y Cajal University Hospital, Madrid (Spain). DD level comparisons between PE-positive and PE-negative groups were made using Student's t test. The optimal DD cutoff value to predict PE risk in COVID-19 patients was calculated in the ROC curve.RESULTSTwo hundred forty-two patients were included in the study. One hundred fifty-one (62%) were men and the median age was 68 years (IQR 55-78). An increase of DD (median 3260; IQR 1203-9625 ng/mL) was detected in 205/242 (96%) patients. 73/242 (30%) of the patients were diagnosed with PE on CTPA. The DD median value was significantly higher (p < .001) in the PE-positive group (7872, IQR 3150-22,494 ng/mL) compared with the PE-negative group (2009, IQR 5675-15,705 ng/mL). The optimal cutoff value for DD to predict PE was 2903 ng/mL (AUC was 0.76 [CI 95% 0.69-0.83], sensitivity 81%). The overall mortality rate was 16% (39/242).CONCLUSIONA higher threshold (2903 ng/mL) for D-dimer could predict the risk of PE in COVID-19 patients with a sensitivity of 81%.

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1. **Acute pulmonary embolism in COVID-19 disease: Preliminary report on seven patients.**  
   Faggiano Pompilio International journal of cardiology 2020;313:129-131.

There is some evidence that Covid 19 pneumonia is associated with prothrombotic status and increased risk of venous thromboembolic events (deep venous thrombosis and pulmonary embolism). Over a two-week period we admitted in our Unit 25 patients with Covid-19 pneumonia, of these pulmonary embolism was diagnosed using computed tomography angiography in 7. We report on clinical and biochemical features of these patients. They were all males, with a mean age of 70.3 years (range 58-84); traditional risk factors for venous thromboembolism were identified in the majority of patients with pulmonary embolism, however not differently from those without pulmonary embolism. Clinical presentation of pulmonary embolism patients was usually characterized by persistence or worsening of respiratory symptoms, with increasing oxygen requirement. D-dimer levels were several fold higher than the upper threshold of normal; in patients in whom PE was recognized during hospital stay, a rapid and relevant increase of D-dimer levels was observed. Computed tomographic findings ranged from massive acute pulmonary embolism to a segmental or sub-segmental pattern; furthermore, thrombosis of sub-segmental pulmonary arteries within lung infiltrates were occasionally seen, suggesting local mechanisms. Six out of 7 patients were treated with unfractionated or low molecular weight heparin with clinical benefit within few days; one patient needed systemic thrombolysis (death from hemorrhagic complication).

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[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=fe8da2bb71bfd31245c514bf3798d785)

1. **Acute pulmonary embolism in non-hospitalized COVID-19 patients referred to CTPA by emergency department.**  
   Gervaise Alban European radiology 2020;30(11):6170-6177.

OBJECTIVESTo evaluate the prevalence of acute pulmonary embolism (APE) in non-hospitalized COVID-19 patients referred to CT pulmonary angiography (CTPA) by the emergency department.METHODSFrom March 14 to April 6, 2020, 72 non-hospitalized patients referred by the emergency department to CTPA for COVID-19 pneumonia were retrospectively identified. Relevant clinical and laboratory data and CT scan findings were collected for each patient. CTPA scans were reviewed by two radiologists to determinate the presence or absence of APE. Clinical classification, lung involvement of COVID-19 pneumonia, and CT total severity score were compared between APE group and non-APE group.RESULTSAPE was identified in 13 (18%) CTPA scans. The mean age and D-dimer of patients from the APE group were higher in comparison with those from the non-APE group (74.4 vs. 59.6 years, p = 0.008, and 7.29 vs. 3.29 μg/ml, p = 0.011). There was no significant difference between APE and non-APE groups concerning clinical type, COVID-19 pneumonia lung lesions (ground-glass opacity: 85% vs. 97%; consolidation: 69% vs. 68%; crazy paving: 38% vs. 37%; linear reticulation: 69% vs. 78%), CT severity score (6.3 vs. 7.1, p = 0.365), quality of CTPA (1.8 vs. 2.0, p = 0.518), and pleural effusion (38% vs. 19%, p = 0.146).CONCLUSIONSNon-hospitalized patients with COVID-19 pneumonia referred to CT scan by the emergency departments are at risk of APE. The presence of APE was not limited to severe or critical clinical type of COVID-19 pneumonia.KEY POINTS• Acute pulmonary embolism was found in 18% of non-hospitalized COVID-19 patients referred by the emergency department to CTPA. Two (15%) patients had main, four (30%) lobar, and seven (55%) segmental acute pulmonary embolism. • Five of 13 (38%) patients with acute pulmonary embolism had a moderate clinical type. • Severity and radiological features of COVID-19 pneumonia showed no significant difference between patients with or without acute pulmonary embolism.

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1. **Acute Pulmonary Embolism in Patients with COVID-19 at CT Angiography and Relationship to d-Dimer Levels.**  
   Léonard-Lorant Ian Radiology 2020;296(3):E189.

Online supplemental material is available for this article.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=290c161cfa2295d5cb5300c5932d30e6)

1. **Anticoagulant interventions in hospitalized patients with COVID-19: A scoping review of randomized controlled trials and call for international collaboration**  
   Tritschler T. Journal of Thrombosis and Haemostasis 2020;:No page numbers.

Introduction: Coronavirus disease (COVID-19) is associated with a high incidence of thrombosis and mortality despite standard anticoagulant thromboprophylaxis. There is equipoise regarding the optimal dose of anticoagulant intervention in hospitalized patients with COVID-19 and consequently, immediate answers from high-quality randomized trials are needed. <br/>Method(s): The World Health Organization's International Clinical Trials Registry Platform was searched on June 17, 2020 for randomized controlled trials comparing increased dose to standard dose anticoagulant interventions in hospitalized COVID-19 patients. Two authors independently screened the full records for eligibility and extracted data in duplicate. <br/>Result(s): A total of 20 trials were included in the review. All trials are open label, 5 trials use an adaptive design, 1 trial uses a factorial design, 2 trials combine multi-arm parallel group and factorial designs in flexible platform trials, and at least 15 trials have multiple study sites. With individual target sample sizes ranging from 30 to 3000 participants, the pooled sample size of all included trials is 12 568 participants. Two trials include only intensive care unit patients, and 10 trials base patient eligibility on elevated D-dimer levels. Therapeutic intensity anticoagulation is evaluated in 14 trials. All-cause mortality is part of the primary outcome in 14 trials. <br/>Discussion(s): Several trials evaluate different dose regimens of anticoagulant interventions in hospitalized patients with COVID-19. Because these trials compete for sites and study participants, a collaborative effort is needed to complete trials faster, conduct pooled analyses and bring effective interventions to patients more quickly.<br/>Copyright &#xa9; 2020 International Society on Thrombosis and Haemostasis

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1. **Anticoagulant therapy in COVID-19 critically ill: Should we go for more?**  
   Vandenbriele C. Journal fur Kardiologie 2020;27(5):156-158.

Critically ill COVID-19 patients often develop a severe pro-thrombotic milieu, as reflected by the markedly increased d-dimer levels. Several cohort studies have reported high rates of thrombotic complications, including deep venous thrombosis (DVT) and pulmonary embolism (PE), myocardial infarction, stroke and microvascular thrombosis. Accordingly, COVID-19 patients who are hospitalized either at a normal, non-intensive care unit (ICU) or at the ICU need to receive appropriate dosages of anticoagulant therapy to prevent or treat these thrombotic complications. This manuscript summarizes the institutional guidance for the antithrombotic prophylaxis and treatment of VTE as outlined by a multidisciplinary team of experts during the first weeks of the COVID-19 pandemic in Europe. Controlled studies are needed to verify the optimal anticoagulation for both prophylaxis and treatment.<br/>Copyright &#xa9; 2020 Krause und Pachernegg GmbH. All rights reserved.

1. **Association of D-dimer and fibrinogen magnitude with hypercoagulability by thromboelastography in severe COVID-19**  
   Chandel A. et al medRxriv 2020;:2020.07.27.20162842.

Preprint: not yet peer-reviewed. In critically ill patients with COVID-19, D-dimer concentration had an inverse relationship with hypercoagulability as measured by TEG MA. D-dimer elevation may reflect severity of COVID-19 related sepsis rather than designate patients likely to benefit from anticoagulation. Fibrinogen concentration may represent a more useful marker of hypercoagulability in this population.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=73e8bfb638178383e771c2e4e3df21d7)

1. **Blue Lungs in Covid-19 Patients: A Step beyond the Diagnosis of Pulmonary Thromboembolism using MDCT with Iodine Mapping.**  
   Pérez Dueñas Virginia Archivos de bronconeumologia 2020;:No page numbers.

OBJECTIVETo evaluate the diagnostic capacity of pulmonary angiography with multidetector computed tomography (MDCT) and iodine mapping in the diagnosis of pulmonary thromboembolism (PTE) in patients with Covid-19 disease.METHODSRetrospective observational study of 81 consecutive patients admitted with Covid-19 respiratory infection who underwent MDCT for clinical suspicion of PTE (sudden dyspnea, chest pain, hemoptysis, severe respiratory failure (SRF) not corrected with high O2 flow) and/or raised D-dimer.RESULTSOf the 81 patients studied [64 (79.01%) men], acute PTE was identified in 22 (27.16%), bilaterally in 13 (59.09%), and 13 (59,09%) showed areas of hypoperfusion. Of the 59 (72.83%) patients without PTE, hypoperfusion was observed in 41 (69.49%) (attributable in one case to pulmonary emphysema). In 18 (22.2%) of the total number of patients, neither PTE nor hypoperfusion were seen. A crazy paving pattern is a risk factor for developing PTE (OR 1.94; 95% CI 0.28-13.57), as are consolidations (OR 1.44; 95% CI 0.24-8.48) and septal thickening/bronchiectasis (OR 1.47; 95% CI 0.12-17.81). Patients with O2-refractory SRF showed a 6.36-fold higher risk for hypoperfusion on the iodine map.CONCLUSIONBy adding the functional image to the anatomical image, pulmonary angiography with MDCT and iodine mapping can demonstrate not only PTE in main, lobar and segmental arteries, but also the presence of hypoperfusion in distal vessels. This makes it a highly useful tool for the accurate diagnosis and therapeutic orientation of patients with Covid-19 lung involvement.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=ca3cf33e50b92b8fa94b2bb3c75d017a)

1. **Characteristics of Acute Pulmonary Embolism in Patients With COVID-19 Associated Pneumonia From the City of Wuhan.**  
   Chen Jianpu Clinical and applied thrombosis/hemostasis : official journal of the International Academy of Clinical and Applied Thrombosis/Hemostasis 2020;26:1076029620936772.

The aim of this study was to describe clinical, imaging, and laboratory features of acute pulmonary embolism (APE) in patients with COVID-19 associated pneumonia. Patients with COVID-19 associated pneumonia who underwent a computed tomography pulmonary artery (CTPA) scan for suspected APE were retrospectively studied. Laboratory data and CTPA images were collected. Imaging characteristics were analyzed descriptively. Laboratory data were analyzed and compared between patients with and without APE. A series of 25 COVID-19 patients who underwent CTPA between January 2020 and February 2020 were enrolled. The median D-dimer level founded in these 25 patients was 6.06 μg/mL (interquartile range [IQR] 1.90-14.31 μg/mL). Ten (40%) patients with APE had a significantly higher level of D-dimer (median, 11.07 μg/mL; IQR, 7.12-21.66 vs median, 2.44 μg/mL; IQR, 1.68-8.34, respectively, P = .003), compared with the 15 (60%) patients without APE. No significant differences in other laboratory data were found between patients with and without APE. Among the 10 patients with APE, 6 (60%) had a bilateral pulmonary embolism, while 4 had a unilateral embolism. The thrombus-prone sites were the right lower lobe (70%), the left upper lobe (60%), both upper lobe (40%) and the right middle lobe (20%). The thrombus was partially or completely absorbed after anticoagulant therapy in 3 patients who underwent a follow-up CTPA. Patients with COVID-19 associated pneumonia have a risk of developing APE during the disease. When the D-dimer level abnormally increases in patients with COVID-19 pneumonia, CTPA should be performed to detect and assess the severity of APE.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=771f8ec32340b9a8ee198f5a97f00bac)

1. **Coagulopathy in COVID-19**  
   Iba T. Journal of Thrombosis and Haemostasis 2020;18(9):2103-2109.

The COVID-19 pandemic has become an urgent issue in every country. Based on recent reports, the most severely ill patients present with coagulopathy, and disseminated intravascular coagulation (DIC)-like massive intravascular clot formation is frequently seen in this cohort. Therefore, coagulation tests may be considered useful to discriminate severe cases of COVID-19. The clinical presentation of COVID-19-associated coagulopathy is organ dysfunction primarily, whereas hemorrhagic events are less frequent. Changes in hemostatic biomarkers represented by increase in D-dimer and fibrin/fibrinogen degradation products indicate the essence of coagulopathy is massive fibrin formation. In comparison with bacterial-sepsis-associated coagulopathy/DIC, prolongation of prothrombin time, and activated partial thromboplastin time, and decrease in antithrombin activity is less frequent and thrombocytopenia is relatively uncommon in COVID-19. The mechanisms of the coagulopathy are not fully elucidated, however. It is speculated that the dysregulated immune responses orchestrated by inflammatory cytokines, lymphocyte cell death, hypoxia, and endothelial damage are involved. Bleeding tendency is uncommon, but the incidence of thrombosis in COVID-19 and the adequacy of current recommendations regarding standard venous thromboembolic dosing are uncertain.<br/>Copyright &#xa9; 2020 International Society on Thrombosis and Haemostasis

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[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=e93f2a51bd4583c40f04bf76e145cd42)

1. **Coagulopathy of Coronavirus Disease 2019.**  
   Iba Toshiaki Critical care medicine 2020;48(9):1358-1364.

OBJECTIVESRecent studies have reported a high prevalence of thrombotic events in coronavirus disease 2019. However, the significance of thromboembolic complications has not been widely appreciated. The purpose of this review is to provide current knowledge of this serious problem.DESIGNNarrative review.DATA SOURCESOnline search of published medical literature through PubMed using the term "COVID-19," "SARS," "acute respiratory distress syndrome," "coronavirus," "coagulopathy," "thrombus," and "anticoagulants."STUDY SELECTION AND DATA EXTRACTIONArticles were chosen for inclusion based on their relevance to coagulopathy and thrombosis in coronavirus disease 2019, and anticoagulant therapy. Reference lists were reviewed to identify additional relevant articles.DATA SYNTHESISCoronavirus disease 2019 is associated with a strikingly high prevalence of coagulopathy and venous thromboembolism that may contribute to respiratory deterioration. Monitoring coagulation variables is important, as abnormal coagulation tests are related to adverse outcomes and may necessitate adjuvant antithrombotic interventions. In the initial phase of the infection, D-dimer and fibrinogen levels are increased, while activated partial prothrombin time, prothrombin time, and platelet counts are often relatively normal. Increased D-dimer levels three times the upper limit of normal may trigger screening for venous thromboembolism. In all hospitalized patients, thromboprophylaxis using low-molecular-weight heparin is currently recommended. The etiology of the procoagulant responses is complex and thought to be a result of specific interactions between host defense mechanisms and the coagulation system. Although the coagulopathy is reminiscent of disseminated intravascular coagulation and thrombotic microangiopathy, it has features that are markedly distinct from these entities.CONCLUSIONSSevere acute respiratory syndrome coronavirus 2/coronavirus disease 2019 frequently induces hypercoagulability with both microangiopathy and local thrombus formation, and a systemic coagulation defect that leads to large vessel thrombosis and major thromboembolic complications, including pulmonary embolism in critically ill hospitalized patients. D-dimers and fibrinogen levels should be monitored, and all hospitalized patients should undergo thromboembolism prophylaxis with an increase in therapeutic anticoagulation in certain clinical situations.

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[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=9b475b0dc71f21bf8138688eb2653be2)

1. **COVID-19 and Pulmonary Emboli: A Case Series and Literature Review.**  
   Greenan-Barrett James Clinical practice and cases in emergency medicine 2020;4(3):299-303.

INTRODUCTIONThere is recent evidence that coronavirus disease 2019 (COVID-19) infection results in a prothrombotic state that may increase the risk of venous thromboembolism. Both COVID-19 infection and pulmonary emboli can present with dyspnoea, tachypnoea, hypoxaemia and an elevated D-dimer. Identifying a pulmonary embolus in a patient with COVID-19 and differentiating it from the typical clinical and biochemical features of COVID-19 is challenging.CASE REPORTSWe report four cases, and reviewed two further cases in the literature, of a pulmonary embolus in patients who presented to the emergency department with COVID-19 and no other risk factor for a pulmonary embolus.CONCLUSIONWe identified a series of atypical features that should raise suspicion for a pulmonary embolus: pleuritic chest pain; haemoptysis; atrial fibrillation; tachycardia; hypotension; late onset deterioration; evidence of right heart strain; or a disproportionally elevated D-dimer in comparison to ferritin.

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1. **Covid-19 pneumonia and pulmonary embolism: Presentation of four cases**  
   Alikhani F. Indian Journal of Critical Care Medicine 2020;24(9):873-876.

Since the beginning of the COVID-19 outbreak, elevated D-dimer levels as an acute-phase reactant have been reported in some patients. Additionally, the patients with pneumonia are at increased risk of developing thromboembolic events. Diagnosing acute pulmonary embolism and deep vein thrombosis can be challenging in SARS-CoV2-positive patients. Here, we report four patients with COVID-19 pneumonia to highlight the possibility of acute thromboembolism in these patients. The physicians should be aware of this complication and even consider prophylactic anticoagulant therapy in proper clinical settings.<br/>Copyright &#xa9; The Author(s). 2020.

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1. **COVID-19 Presenting as Acute Bilateral Submassive Pulmonary Embolism in a Young Healthy Female.**  
   Fransawy Alkomos Mina Cureus 2020;12(7):e9266.

Similar symptoms, signs, and laboratory abnormalities between coronavirus disease 2019 (COVID-19) and pulmonary embolism (PE) creates a diagnostic challenge to every physician, and emerging data show an association between COVID-19, hypercoagulable state, and venous thromboembolism. We present a rare case of COVID-19 presented as bilateral sub-massive PE. A 28-year-old COVID-19 positive female with no significant past medical history presented with a dry cough and shortness of breath for three days. Initial laboratory test showed elevated D-dimer, electrocardiogram (EKG) showed right axis deviation, right ventricular strain pattern, and SI QIII TIII pattern, and echocardiogram (ECHO) showed right ventricular dysfunction. Those two bedside tests directed the urgency of chest CT angiography that showed bilateral sub-massive PE. Since EKG finding of SI QIII TIII pattern and right ventricular strain, and ECHO finding of right ventricular dysfunction are well described in PE but not in COVID-19, these bedside diagnostic tools can help identify COVID-19 patients with underlining PEs.

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1. **COVID-19 versus HIT hypercoagulability.**  
   Warkentin Theodore E. Thrombosis research 2020;196:38-51.

A striking feature of COVID-19 is the high frequency of thrombosis, particularly in patients who require admission to intensive care unit because of respiratory complications (pneumonia/adult respiratory distress syndrome). The spectrum of thrombotic events is wide, including in situ pulmonary thrombosis, deep-vein thrombosis and associated pulmonary embolism, as well as arterial thrombotic events (stroke, myocardial infarction, limb artery thrombosis). Unusual thrombotic events have also been reported, e.g., cerebral venous sinus thrombosis, mesenteric artery and vein thrombosis. Several hematology abnormalities have been observed in COVID-19 patients, including lymphopenia, neutrophilia, thrombocytopenia (usually mild), thrombocytosis, elevated prothrombin time and partial thromboplastin times (the latter abnormality often indicating lupus anticoagulant phenomenon), hyperfibrinogenemia, elevated von Willebrand factor levels, and elevated fibrin d-dimer. Many of these abnormal hematologic parameters-even as early as the time of initial hospital admission-indicate adverse prognosis, including greater frequency of progression to severe respiratory illness and death. Progression to overt disseminated intravascular coagulation in fatal COVID-19 has been reported in some studies, but not observed in others. We compare and contrast COVID-19 hypercoagulability, and associated increased risk of venous and arterial thrombosis, from the perspective of heparin-induced thrombocytopenia (HIT), including the dilemma of providing thromboprophylaxis and treatment recommendations when available data are limited to observational studies. The frequent use of heparin-both low-molecular-weight and unfractionated-in preventing and treating COVID-19 thrombosis, means that vigilance for HIT occurrence is required in this patient population.

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1. **COVID-19: Coagulopathy, Risk of Thrombosis, and the Rationale for Anticoagulation.**  
   Miesbach Wolfgang Clinical and applied thrombosis/hemostasis : official journal of the International Academy of Clinical and Applied Thrombosis/Hemostasis 2020;26:1076029620938149.

The novel coronavirus infection (COVID-19) is caused by the new coronavirus SARS-CoV-2 and is characterized by an exaggerated inflammatory response that can lead to severe manifestations such as adult respiratory syndrome, sepsis, coagulopathy, and death in a proportion of patients. Among other factors and direct viral effects, the increase in the vasoconstrictor angiotensin II, the decrease in the vasodilator angiotensin, and the sepsis-induced release of cytokines can trigger a coagulopathy in COVID-19. A coagulopathy has been reported in up to 50% of patients with severe COVID-19 manifestations. An increase in d-dimer is the most significant change in coagulation parameters in severe COVID-19 patients, and progressively increasing values can be used as a prognostic parameter indicating a worse outcome. Limited data suggest a high incidence of deep vein thrombosis and pulmonary embolism in up to 40% of patients, despite the use of a standard dose of low-molecular-weight heparin (LMWH) in most cases. In addition, pulmonary microvascular thrombosis has been reported and may play a role in progressive lung failure. Prophylactic LMWH has been recommended by the International Society on Thrombosis and Haemostasis (ISTH) and the American Society of Hematology (ASH), but the best effective dosage is uncertain. Adapted to the individual risk of thrombosis and the d-dimer value, higher doses can be considered, especially since bleeding events in COVID-19 are rare. Besides the anticoagulant effect of LMWH, nonanticoagulant properties such as the reduction in interleukin 6 release have been shown to improve the complex picture of coagulopathy in patients with COVID-19.

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1. **CT imaging of pulmonary embolism in patients with COVID-19 pneumonia: a retrospective analysis.**  
   Espallargas Irene European radiology 2020;:No page numbers.

OBJECTIVESTo describe imaging and laboratory findings of confirmed PE diagnosed in COVID-19 patients and to evaluate the characteristics of COVID-19 patients with clinical PE suspicion. Characteristics of patients with COVID-19 and PE suspicion who required admission to the intensive care unit (ICU) were also analysed.METHODSA retrospective study from March 18, 2020, until April 11, 2020. Inclusion criteria were patients with suspected PE and positive real-time reverse-transcription polymerase chain reaction (RT-PCR) for SARS-CoV-2. Exclusion criteria were negative or inconclusive RT-PCR and other chest CT indications. CTPA features were evaluated and severity scores, presence, and localisation of PE were reported. D-dimer and IL-6 determinations, ICU admission, and previous antithrombotic treatment were registered.RESULTSForty-seven PE suspicions with confirmed COVID-19 underwent CTPA. Sixteen patients were diagnosed with PE with a predominant segmental distribution. Statistically significant differences were found in the highest D-dimer determination in patients with PE and ICU admission regarding elevated IL-6 values.CONCLUSIONPE in COVID-19 patients in our series might predominantly affect segmental arteries and the right lung. Results suggest that the higher the D-dimer concentration, the greater the likelihood of PE. Both assumptions should be assessed in future studies with a larger sample size.KEY POINTS• On CT pulmonary angiography, pulmonary embolism in COVID-19 patients seems to be predominantly distributed in segmental arteries of the right lung, an assumption that needs to be approached in future research. • Only the highest intraindividual determination of d-dimer from admission to CT scan seems to differentiate patients with pulmonary embolism from patients with a negative CTPA. However, interindividual variability calls for future studies to establish cut-off values in COVID-19 patients. • Further studies with larger sample sizes are needed to determine whether the presence of PE could increase the risk of intensive care unit (ICU) admission in COVID-19 patients.

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1. **D-dimer and C-reactive Protein Blood Levels Over Time Used to Predict Pulmonary Embolism in Two COVID-19 Patients.**  
   Becher Yael European journal of case reports in internal medicine 2020;7(6):001725.

The diagnosis of pulmonary embolism is challenging in symptomatic COVID-19 patients since shortness of breath, chest pain, tachycardia, tachypnoea, fever, oxygen desaturation and high D-dimer blood levels might be features of both diseases. We present two COVID-19 patients in whom pulmonary embolism was suspected (and diagnosed) due to a discrepancy between an increase in D-dimer blood levels and a decrease in C-reactive protein blood levels over time. We believe that an opposite change in the blood levels of both biomarkers over time may be used as a novel method to predict pulmonary embolism in COVID-19 patients.LEARNING POINTSThe diagnosis of pulmonary embolism is challenging in COVID-19 patients since symptoms, signs and high D-dimer blood levels might be similar in both diseases.An increase in D-dimer blood levels and a decrease in C-reactive protein blood levels over time may be used as a novel method to predict pulmonary embolism in COVID-19 patients.

1. **D-dimer and mortality in COVID-19: a self-fulfilling prophecy or a pathophysiological clue?**  
   Breakey Neal Swiss medical weekly 2020;150:w20293.

The emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) as a global phenomenon has presented clinicians around the world with multiple challenges. Thromboembolic events are recognised complications of viral infection, but the diagnosis of an acute pulmonary thrombotic complication in the context of coronavirus disease 2019 (COVID-19) can be challenging because of the similarities of presentation, logistical considerations of diagnosis in a patient isolated for infection control reasons and the effects of cognitive errors in diagnostic reasoning. We present the case of a patient who was diagnosed with a pulmonary thrombotic complication during inpatient care for COVID-19. The haemostasis parameters we observed, including increased levels of von Willebrand factor and factor VIII, point towards a relevant involvement of endothelial cells in patients with severe COVID-19. We suggest that it is possible to hypothesise a spectrum of secondarily acquired, prothrombotic coagulopathy mediated by the endothelial interaction with SARS-CoV-2 as a cause of mortality in a subset of patients with a complicated clinical course of COVID-19. We support the recommendation of thromboembolic chemoprophylaxis for inpatients with COVID-19 as a very minimum in the absence of strict contraindications, while recognising that pulmonary thrombotic complications can occur under standard thromboprophylaxis. We suggest that higher, possibly therapeutic levels of anticoagulation might be mandatory for a further subset of patients with COVID-19 where a discrepant evolution of C-reactive protein and D-dimer is observed. Therapeutic levels of anticoagulation are obligatory where new evidence of a macrovascular thrombotic complication has been documented. More research to delineate the macro- and microvascular thrombotic complications of COVID-19, and the therapeutic implications for this patient group is required.

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1. **D-dimer as a biomarker for disease severity and mortality in COVID-19 patients: a case control study.**  
   Yao Yumeng Journal of intensive care 2020;8:49.

BackgroundOver 5,488,000 cases of coronavirus disease-19 (COVID-19) have been reported since December 2019. We aim to explore risk factors associated with mortality in COVID-19 patients and assess the use of D-dimer as a biomarker for disease severity and clinical outcome.MethodsWe retrospectively analyzed the clinical, laboratory, and radiological characteristics of 248 consecutive cases of COVID-19 in Renmin Hospital of Wuhan University, Wuhan, China from January 28 to March 08, 2020. Univariable and multivariable logistic regression methods were used to explore risk factors associated with in-hospital mortality. Correlations of D-dimer upon admission with disease severity and in-hospital mortality were analyzed. Receiver operating characteristic curve was used to determine the optimal cutoff level for D-dimer that discriminated those survivors versus non-survivors during hospitalization.ResultsMultivariable regression that showed D-dimer > 2.0 mg/L at admission was the only variable associated with increased odds of mortality [OR 10.17 (95% CI 1.10-94.38), P = 0.041]. D-dimer elevation (≥ 0.50 mg/L) was seen in 74.6% (185/248) of the patients. Pulmonary embolism and deep vein thrombosis were ruled out in patients with high probability of thrombosis. D-dimer levels significantly increased with increasing severity of COVID-19 as determined by clinical staging (Kendall's tau-b = 0.374, P = 0.000) and chest CT staging (Kendall's tau-b = 0.378, P = 0.000). In-hospital mortality rate was 6.9%. Median D-dimer level in non-survivors (n = 17) was significantly higher than in survivors (n = 231) [6.21 (3.79-16.01) mg/L versus 1.02 (0.47-2.66) mg/L, P = 0.000]. D-dimer level of > 2.14 mg/L predicted in-hospital mortality with a sensitivity of 88.2% and specificity of 71.3% (AUC 0.85; 95% CI = 0.77-0.92).ConclusionsD-dimer is commonly elevated in patients with COVID-19. D-dimer levels correlate with disease severity and are a reliable prognostic marker for in-hospital mortality in patients admitted for COVID-19.

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1. **D-dimer in patients infected with COVID-19 and suspected pulmonary embolism.**  
   Garcia-Olivé Ignasi Respiratory medicine 2020;169:106023.

OBJECTIVETo analyze the risk factors for pulmonary embolism (PE) in patients infected with COVID-19.METHODSWe conducted an observational, retrospective study. Patients with severe infection with COVID-19 and suspected PE were included.RESULTSPatients with higher levels of D-dimer and those requiring intubation were at a higher risk of developing PE. Higher D-dimer levels were associated with a greater probability of PE 3, 6, 9 and 12 days after determining D-dimer levels with an OR of 1.7, 2.0, 2.4 and 2.4, respectively.CONCLUSIONIn conclusion, patients infected with COVID-19 requiring OTI with higher levels of D-dimer have an increased risk of developing PE.

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1. **Detection of Pulmonary Embolism in Returning Travelers with Hypoxemic Pneumonia due to COVID-19 in Reunion Island.**  
   Larsen Kevin The American journal of tropical medicine and hygiene 2020;103(2):844-846.

The aim of this study was to evaluate the occurrence of pulmonary embolism in returning travelers with hypoxemic pneumonia due to COVID-19. All returning travelers to Reunion Island with hypoxemic pneumonia due to COVID-19 underwent computed tomography pulmonary angiography (CTPA) and were included in the cohort. Thirty-five patients were returning travelers with hypoxemic pneumonia due to COVID-19 and had recently returned from one of the countries most affected by the COVID-19 outbreak (mainly from France and Comoros archipelago). Five patients (14.3%) were found to have pulmonary embolism and two (5.9%) were incidentally found to have deep vein thrombosis on CTPA. Patients with pulmonary embolism or deep vein thrombosis had higher D-dimer levels than those without pulmonary embolism or deep vein thrombosis (P = 0.04). Returning travelers with hypoxemic pneumonia due to COVID-19 should be systematically screened for pulmonary embolism.

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1. **Diagnosis, management, and outcomes of venous thromboembolism in COVID-19 positive patients: a role for direct anticoagulants?**  
   Kartsios C. Journal of Thrombosis and Thrombolysis 2020;:No page numbers.

Coronavirus disease 2019 (COVID-19) has been associated with an increased risk of thromboembolic complications due to systemic coagulation activation. Little is known about the role of direct anticoagulants (DOACs) in COVID-19 related thrombosis. In this audit we sought to distinguish COVID-19 hospitalised patients with a diagnosis of venous thromboembolism (VTE) and record their outcomes over a period of 3 months (01/02/2020-30/04/2020). A total of 1583 patients were diagnosed with laboratory proven COVID-19 disease. Amongst them, 38 patients (0.82%) suffered VTE (median age 68 years, male/female: 20/18). VTE was the presenting symptom on admission in 71%. Pulmonary embolism was diagnosed in 92% of patients; 5 patients required intensive care and 3 underwent thrombolysis. 27 patients received initial treatment with unfractionated heparin/low molecular weight heparin (LMWH) while 10 were treated with direct anticoagulants (DOACs). After a median follow up of 25 days, 29 (76%) patients were alive while 5 were still hospitalised. Most patients (83%) were discharged on DOACs, no VTE recurrence or bleeding was recorded post-discharge. Our results suggest that direct anticoagulants could be a safe and effective treatment option in selected COVID-19 positive patients who have suffered venous thromboembolism.<br/>Copyright &#xa9; 2020, Springer Science+Business Media, LLC, part of Springer Nature.

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1. **Elevated D-dimers and lack of anticoagulation predict PE in severe COVID-19 patients.**  
   Mouhat Basile The European respiratory journal 2020;56(4):No page numbers.

BACKGROUNDCoronavirus disease 2019 (COVID-19) may predispose to venous thromboembolism. We determined factors independently associated with computed tomography pulmonary angiography (CTPA)-confirmed pulmonary embolism (PE) in hospitalised severe COVID-19 patients.METHODSAmong all (n=349) patients hospitalised for COVID-19 in a university hospital in a French region with a high rate of COVID-19, we analysed patients who underwent CTPA for clinical signs of severe disease (oxygen saturation measured by pulse oximetry ≤93% or breathing rate ≥30 breaths·min-1) or rapid clinical worsening. Multivariable analysis was performed using Firth penalised maximum likelihood estimates.RESULTS162 (46.4%) patients underwent CTPA (mean±sd age 65.6±13.0 years; 67.3% male (95% CI 59.5-75.5%). PE was diagnosed in 44 (27.2%) patients. Most PEs were segmental and the rate of PE-related right ventricular dysfunction was 15.9%. By multivariable analysis, the only two significant predictors of CTPA-confirmed PE were D-dimer level and the lack of any anticoagulant therapy (OR 4.0 (95% CI 2.4-6.7) per additional quartile and OR 4.5 (95% CI 1.1-7.4), respectively). Receiver operating characteristic curve analysis identified a D-dimer cut-off value of 2590 ng·mL-1 to best predict occurrence of PE (area under the curve 0.88, p<0.001, sensitivity 83.3%, specificity 83.8%). D-dimer level >2590 ng·mL-1 was associated with a 17-fold increase in the adjusted risk of PE.CONCLUSIONElevated D-dimers (>2590 ng·mL-1) and absence of anticoagulant therapy predict PE in hospitalised COVID-19 patients with clinical signs of severity. These data strengthen the evidence base in favour of systematic anticoagulation, and suggest wider use of D-dimer guided CTPA to screen for PE in acutely ill hospitalised patients with COVID-19.

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1. **Imbalance between procoagulant factors and natural coagulation inhibitors contributes to hypercoagulability in the critically ill COVID-19 patient: clinical implications.**  
   Voicu S. European review for medical and pharmacological sciences 2020;24(17):9161-9168.

OBJECTIVECoronavirus Disease-2019 (COVID-19) predisposes patients to thrombosis which underlying mechanisms are still incompletely understood. We sought to investigate the balance between procoagulant factors and natural coagulation inhibitors in the critically ill COVID-19 patient and to evaluate the usefulness of hemostasis parameters to identify patients at risk of venous thromboembolic event (VTE).PATIENTS AND METHODSWe conducted an observational study recording VTEs defined as deep vein thrombosis or pulmonary embolism using lower limb ultrasound (92% of the patients), computed tomography pulmonary angiography (6%) and both tests (2%). We developed a comprehensive analysis of hemostasis.RESULTSNinety-two consecutive mechanically ventilated COVID-19 patients (age, 62 years [53-69] (median [25th-75th percentiles]); M/F sex ratio, 2.5; body-mass index, 28 kg/m2 [25-32]; past hypertension (52%) and diabetes mellitus (30%)) admitted to the Intensive Care Unit (ICU) from 03/11/2020 to 5/05/2020, were included. When tested, patients were receiving prophylactic (74%) or therapeutic (26%) anticoagulation. Forty patients (43%) were diagnosed with VTE. Patients displayed inflammatory and prothrombotic profile including markedly elevated plasma fibrinogen (7.7 g/L [6.1-8.6]), D-dimer (3,360 ng/mL [1668-7575]), factor V (166 IU/dL [136-195]) and factor VIII activities (294 IU/dL [223-362]). We evidenced significant discrepant protein C anticoagulant and chromogenic activities, combined with slightly decreased protein S activity. Plasma D-dimer >3,300 ng/mL predicted VTE presence with 78% (95%-confidence interval (95% CI), 62-89) sensitivity, 69% (95% CI, 55-81) specificity, 66% (95% CI, 51-79) positive predictive value and 80% (95% CI, 65-90) negative predictive value [area under the ROC curve, 0.779 (95%CI, 0.681-0.859), p=0.0001].CONCLUSIONSMechanically ventilated COVID-19 patients present with an imbalance between markedly increased factor V/VIII activity and overwhelmed protein C/S pathway. Plasma D-dimer may be a useful biomarker at the bedside for suspicion of VTE.

1. **Incidence of pulmonary embolism in non-critically ill COVID-19 patients. Predicting factors for a challenging diagnosis.**  
   Mestre-Gómez B. Journal of thrombosis and thrombolysis 2020;:No page numbers.

Recent studies suggest that thrombotic complications are a common phenomenon in the novel SARS-CoV-2 infection. The main objective of our study is to assess cumulative incidence of pulmonary embolism (PE) in non critically ill COVID-19 patients and to identify its predicting factors associated to the diagnosis of pulmonary embolism. We retrospectevely reviewed 452 electronic medical records of patients admitted to Internal Medicine Department of a secondary hospital in Madrid during Covid 19 pandemic outbreak. We included 91 patients who underwent a multidetector Computed Tomography pulmonary angiography(CTPA) during conventional hospitalization. The cumulative incidence of PE was assessed ant the clinical, analytical and radiological characteristics were compared between patients with and without PE. PE incidence was 6.4% (29/452 patients). Most patients with a confirmed diagnosed with PE recieved low molecular weight heparin (LMWH): 79.3% (23/29). D-dimer peak was significatly elevated in PE vs non PE patients (14,480 vs 7230 mcg/dL, p = 0.03). In multivariate analysis of patients who underwent a CTPA we found that plasma D-dimer peak was an independen predictor of PE with a best cut off point of > 5000 µg/dl (OR 3.77; IC95% (1.18-12.16), p = 0.03). We found ninefold increased risk of PE patients not suffering from dyslipidemia (OR 9.06; IC95% (1.88-43.60). Predictive value of AUC for ROC is 75.5%. We found a high incidence of PE in non critically ill hospitalized COVID 19 patients despite standard thromboprophylaxis. An increase in D-dimer levels is an independent predictor for PE, with a best cut-off point of > 5000 µg/ dl.

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1. **Is COVID Evolution Due to Occurrence of Pulmonary Vascular Thrombosis?**  
   Saba Luca Journal of thoracic imaging 2020;:No page numbers.

In this hypothesis paper, we suggest that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) may induce intravascular pulmonary thrombosis, which may result in the rapid worsening of clinical conditions and, eventually, exitus. Previously published papers have demonstrated that increased levels of D-dimer at hospital admission correlate with a more severe disease (0.5 mg/L) or occurrence of death (1 mg/L). The potential prothrombotic action of the SARS-CoV-2 is supported by the topographical involvement of the lung regions with a predilection for the lower lobe with peripheral involvement. If this hypothesis is demonstrated, this could suggest the benefit of using antithrombotic/coagulation regimens for SARS-CoV-2 and, at the same time, the urgency to identify drugs that could alter the inflammatory storm, thus protecting the vessel wall.

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1. **Left ventricular thrombus and pulmonary embolism: A case series of thrombosis in COVID-19 in Thai patients**  
   Nanthatanti N. Research and Practice in Thrombosis and Haemostasis 2020;:No page numbers.

Thrombosis in COVID-19 is increasingly recognized and is generally associated with a high mortality rate. The key clinical question of this report was whether COVID-19 could be complicated with cardiac thrombus and pulmonary embolism in Asian population. We demonstrated the case series of thrombosis in Thai patients with confirmed severe acute respiratory syndrome coronavirus 2 infection. One patient had the first case of a large left ventricular thrombus, and three other patients had pulmonary embolism. All patients were male and had low absolute lymphocyte count, while lactate dehydrogenase level and d-dimer were markedly elevated, especially at the time when the thrombosis was diagnosed. All patients had severe COVID-19 with pneumonia. Two patients who needed mechanical ventilation were successfully extubated. After hospitalization for 13-49 days, pneumonia and thrombosis improved and all of them could be discharged from the hospital. Thrombosis is common in COVID-19 and could present in both arterial and venous sites even in Asian populations. d-dimer is a strong marker to predict thrombosis and could be a prognostic predictor for severity of COVID-19.<br/>Copyright &#xa9; 2020 The Authors. Research and Practice in Thrombosis and Haemostasis published by Wiley Periodicals LLC on behalf of International Society on Thrombosis and Haemostasis (ISTH).

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1. **Opportunistic Diagnosis of Extensive Pulmonary Embolus Following "COVID-19 Blood Battery" in Very Frail Older Patients**  
   O'Brien M.M.C. Journal of Nutrition, Health and Aging 2020;:No page numbers.

D-dimer is routinely measured to exclude the diagnosis of venous thromboembolism and is its main biomarker. Appropriate age-adjusted D-dimer testing improves D-dimer specificity, could decrease inappropriate CT pulmonary angiograms in the older person, and prevent unnecessary radiation exposure. A "COVID-19 blood battery", designed to increase the efficiency of evaluation of COVID-19 suspected patients is used in our institution. It includes D-dimers which are elevated in COVID-19 infections and potentially an index of severe infection. These 3 very frail patients presented late to the emergency department, all acutely and non-specifically unwell, with high prevalence of comorbidities and were transferred in by ambulance. They were triaged to the COVID-19 pathway of our hospital, and subsequently had negative COVID-19 swabs. All had an incidental finding of markedly elevated D-dimers, with potential causes of their symptoms other than pulmonary embolus. They were transferred to an acute geriatric ward specifically designated to manage older patients (&gt;75years) who had negative nasopharyngeal swab results. They were all ultimately diagnosed with extensive pulmonary emboli with evidence of raised pulmonary pressures on CTPA and/or echocardiogram. It is possible that these patients had false negative COVID-19 swabs. Allowing for the novel nature of COVID-19, prospective evaluation for new symptoms and complications such as thromboembolic disease in those affected by milder symptoms should be considered. In the absence of clinical improvement following treatment of other conditions in frail older patients, D-dimer testing could be indicated with pursuit of specific diagnostic evaluation for venous thromboembolism when significantly elevated.<br/>Copyright &#xa9; 2020, Serdi and Springer-Verlag International SAS, part of Springer Nature.

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1. **Prevalence of pulmonary embolism in patients with COVID-19 pneumonia and high D-dimer values: A prospective study.**  
   Alonso-Fernández Alberto PloS one 2020;15(8):e0238216.

INTRODUCTIONCoronavirus disease 2019 (COVID-19) pneumonia is associated to systemic hyper-inflammation and abnormal coagulation profile. D-dimer elevation is particularly frequent, and values higher than 1μg/mL have been associated with disease severity and in-hospital mortality. Previous retrospective studies found a high pulmonary embolism (PE) prevalence, however, it should be highlighted that diagnoses were only completed when PE was clinically suspected.MATERIAL AND METHODSSingle-center prospective cohort study. Between April 6th and April 17th 2020, consecutive confirmed cases of COVID-19 pneumonia with D-dimer >1 μg/mL underwent computed tomography pulmonary angiography (CTPA) to investigate the presence and magnitude of PE. Demographic and laboratory data, comorbidities, CTPA scores, administered treatments, and, clinical outcomes were analysed and compared between patients with and without PE.RESULTSThirty consecutive patients (11 women) were included. PE was diagnosed in 15 patients (50%). In patients with PE, emboli were located mainly in segmental arteries (86%) and bilaterally (60%). Patients with PE were significantly older (median age 67.0 (IQR 63.0-73.0) vs. 57.0 (IQR 48.0-69.0) years, p = .048) and did not differ in sex or risk factors for thromboembolic disease from the non-PE group. D-dimer, platelet count, and, C reactive protein values were significantly higher among PE patients. D-dimer values correlated with the radiologic magnitude of PE (p<0.001).CONCLUSIONSPatients with COVID-19 pneumonia and D-dimer values higher than 1 μg/mL presented a high prevalence of PE, regardless of clinical suspicion. We consider that these findings could contribute to improve the prognosis of patients with COVID-19 pneumonia, by initiating anticoagulant therapy when a PE is found.

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1. **Pulmonary Embolism and Increased Levels of D-Dimer in Patients with Coronavirus Disease.**  
   Chan Kok Hoe Emerging infectious diseases 2020;26(10):2522-2533.

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1. **Pulmonary embolism in COVID-19 pneumonia: An overlapping diagnosis or a misdiagnosis?**  
   Secco E. Journal of Cardiovascular Echography 2020;30(2):110-112.

Coronavirus pneumonia (COVID-19) is a novel infectious disease with a high mortality rate due to severe acute respiratory syndrome. A 57-year-old woman was admitted to the emergency department (ED) with fever, cough, atypical chest pain, and dyspnea. She remained in the ED for about 48 h while waiting for the result of the COVID-19 oropharyngeal swab. Once she tested positive, she was hospitalized in the pneumological department with a diagnosis of pneumonia based on a chest X-ray and biochemical tests. Although azithromycin and hydroxychloroquine were promptly administered, she had a worsening of dyspnea even with a high-flow oxygen mask. D-dimer was increased, and a computed tomography scan with pulmonary and leg angiogram was positive for bilateral pulmonary embolism, deep-venous thrombosis, and multiple consolidated opacities in the lung parenchyma. This case highlights the fact that, in a pandemic situation, there is a potentially fatal risk of overlooking an alternative diagnosis in a COVID-19 patient who is generally considered as suffering only from pneumonia.<br/>Copyright &#xa9; 2020 Wolters Kluwer Medknow Publications. All rights reserved.

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1. **Pulmonary Embolism in COVID-19 Pneumonia: Random Association or Causality?**  
   Fortuzi Ked Cureus 2020;12(6):e8900.

Coronavirus disease 2019 (COVID-19) is an ongoing pandemic. COVID-19 leads to a plethora of clinical syndromes, most commonly affecting the pulmonary system but also the cardiovascular, hematologic, and gastrointestinal systems. There is emerging evidence of an association between COVID-19 and venous thromboembolism (VTE). In this report, we have discussed three cases with a COVID-19 infection, whose clinical course was complicated by the presence of pulmonary embolism (PE) without evident risk factors for VTE. All three patients presented with hypoxia and were found to have elevated D-dimer levels. Subsequently, the patients underwent computed tomography (CT) angiography of the chest, which confirmed the presence of pulmonary embolism. Anticoagulation was initiated per guidelines. There is a need to have a low threshold for suspecting pulmonary embolism in patients with COVID-19 infection who present with a sudden onset of severe hypoxia. There is a dire need to increase awareness among health care providers regarding this manifestation of the virus.

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1. **Pulmonary embolism in COVID-19: Clinical characteristics and cardiac implications.**  
   Kho Jason The American journal of emergency medicine 2020;:No page numbers.

BACKGROUNDThe thrombogenic potential of Covid-19 is increasingly recognised. We aim to assess the characteristics of COVID-19 patients diagnosed with pulmonary embolism (PE).METHODSWe conducted a single centre, retrospective observational cohort study of COVID-19 patients admitted between 1st March and 30th April 2020 subsequently diagnosed with PE following computed tomography pulmonary angiogram (CTPA). Patient demographics, comorbidities, presenting complaints and inpatient investigations were recorded.RESULTSWe identified 15 COVID-19 patients diagnosed with PE (median age = 58 years [IQR = 23], 87% male). 2 died (13%), both male patients >70 years. Most common symptoms were dyspnoea (N = 10, 67%) and fever (N = 7, 47%). 12 (80%) reported 7 days or more of non-resolving symptoms prior to admission. 7 (47%) required continuous positive airway pressure (CPAP), 2 (13%) of which were subsequently intubated. All patients had significantly raised D-dimer levels, lactate dehydrogenase (LDH), C-reactive protein (CRP), ferritin and prothrombin times. The distribution of PEs correlated with the pattern of consolidation observed on CTPA in 9 (60%) patients; the majority being peripheral or subsegmental (N = 14, 93%) and only 1 central PE. 10 (67%) had an abnormal resting electrocardiogram (ECG), the commonest finding being sinus tachycardia. 6 (40%) who underwent transthoracic echocardiography (TTE) had structurally and functionally normal right hearts.CONCLUSIONOur study suggests that patients who demonstrate acute deterioration, a protracted course of illness with non-resolving symptoms, worsening dyspnoea, persistent oxygen requirements or significantly raised D-dimer levels should be investigated for PE, particularly in the context of COVID-19 infection. TTE and to a lesser degree the ECG are unreliable predictors of PE within this context.

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1. **Pulmonary embolism in hospitalised patients with COVID-19.**  
   Whyte Martin B. Thrombosis research 2020;195:95-99.

BACKGROUNDCoronavirus disease 2019 (COVID-19) is characterised by dyspnoea and abnormal coagulation parameters, including raised D-dimer. Data suggests a high incidence of pulmonary embolism (PE) in ventilated patients with COVID-19.OBJECTIVESTo determine the incidence of PE in hospitalised patients with COVID-19 and the diagnostic yield of Computer Tomography Pulmonary Angiography (CTPA) for PE. We also examined the utility of D-dimer and conventional pre-test probability for diagnosis of PE in COVID-19.PATIENTS/METHODSRetrospective review of single-centre data of all CTPA studies in patients with suspected or confirmed COVID-19 identified from Electronic Patient Records (EPR).RESULTSThere were 1477 patients admitted with COVID-19 and 214 CTPA scans performed, of which n = 180 (84%) were requested outside of critical care. The diagnostic yield for PE was 37%. The overall proportion of PE in patients with COVID-19 was 5.4%. The proportions with Wells score of ≥4 ('PE likely') was 33/134 (25%) without PE vs 20/80 (25%) with PE (P = 0.951). The median National Early Warning-2 (NEWS2) score (illness severity) was 5 (interquartile range [IQR] 3-9) in PE group vs 4 (IQR 2-7) in those without PE (P = 0.133). D-dimer was higher in PE (median 8000 ng/mL; IQR 4665-8000 ng/mL) than non-PE (2060 ng/mL, IQR 1210-4410 ng/mL, P < 0.001). In the 'low probability' group, D-dimer was higher (P < 0.001) in those with PE but had a limited role in excluding PE.CONCLUSIONSEven outside of the critical care environment, PE in hospitalised patients with COVID-19 is common. Of note, approaching half of PE events were diagnosed on hospital admission. More data are needed to identify an optimal diagnostic pathway in patients with COVID-19. Randomised controlled trials of intensified thromboprophylaxis are urgently needed.

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1. **Pulmonary Embolism in Patients Hospitalized With COVID-19 (From a New York Health System).**  
   Xu Hai The American journal of cardiology 2020;133:148-153.

Pulmonary embolisms (PEs) in coronavirus disease 2019 (COVID-19) have increasingly been reported in observational studies. However, limited information describing their clinical characteristics and outcomes exists. Our study aims to describe clinical features and risk stratification strategies of hospitalized COVID-19 patients with PE. We retrospectively analyzed 101 hospitalized patients with COVID-19 infection and acute PE. Clinical outcomes measured were intensive care unit admission, mechanical ventilation, bleeding and transfusion events, acute kidney injury (AKI) and mortality. Pulmonary severity index (PESI) scores were used for risk stratification. The most common comorbidities were hypertension (50%), obesity (27%) and hyperlipidemia (32%) among this cohort. Baseline D-dimer abnormalities (4,647.0 ± 8,281.8) were noted on admission with a 3-fold increase at the time of PE diagnosis (13,288.4 ± 14,917.9; p <0.05). Five (5%) patients required systemic thrombolysis and 12 (12%) patients experienced moderate to severe bleeding. Thirty-one (31%) patients developed AKI and 1 (1%) patient required renal replacement therapy. Twenty-three (23%) patients were admitted to intensive care unit, of which 20 (20%) patients received mechanical ventilation. The mortality rate was 20%. Most patients (65%) had Intermediate to high risk PESI scores (>85), which portended a worse prognosis with higher mortality rate and length of stay. In conclusion, this study provides characteristics and early outcomes for hospitalized patients with COVID-19 and acute pulmonary embolism. PESI scores were utilized for risk stratifying clinical outcomes. Our results should serve to alert the medical community to heighted vigilance of this VTE complication associated with COVID-19 infection.

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1. **Pulmonary Embolism in Patients With Covid-19 Pneumonia: The Utility of D-dimer.**  
   Rodriguez-Sevilla Juanjo Archivos de bronconeumologia 2020;:No page numbers.

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1. **Pulmonary thromboembolic disease in COVID-19 patients on CT pulmonary angiography - Prevalence, pattern of disease and relationship to D-dimer.**  
   Ooi M. W X. European journal of radiology 2020;132:109336.

OBJECTIVESTo define the prevalence of pulmonary thromboembolic (PTE) disease diagnosed on CT pulmonary angiography (CTPA) in COVID-19 patients. To assess distribution of PTE and to evaluate for association between severity of COVID-19 disease, D-dimer values and incidence of PTE.METHODSPatients with diagnosis of COVID-19 presenting to 5 different hospitals across Greater Manchester between 1st March 2020 and 30th April 2020 who had CTPA were included. CTPA images were evaluated for presence of PTE, distribution of PTE (in small and/or large vessels) and distribution of PTE within lungs with or without COVID-19 CT changes. Severity of COVID lung changes were graded. D-dimer values within 72 h of CTPA were obtained. Statistical analyses were performed to evaluate for any significant association between variables. p values of ≤0.05 were regarded as statistically significant.RESULTSA total of 974 patients presented across five hospital sites with COVID-19 infection. Eighty-four (n = 84) COVID-19 patients underwent CTPA. Of these, 38 % (32/84) had PTE. PTE was seen in small vessels in 75 % (24/32) and in lungs demonstrating COVID-19 changes in 72 % (23/32). 84 % (27/32) of PTE positive patients had disease severity of moderate or higher score (p = 0.005). D-dimer values were significantly higher (p ≤ 0.001) in PTE patients, median value in PTE group was 6441mcg/L (range 219-90925). A D-dimer cut off value of 2247mcg/L provides sensitivity of 0.72 and specificity of 0.74.CONCLUSIONThere is increased prevalence of PTE in patients with moderate to severe COVID-19 disease. D-dimer values may have potential in guiding anticoagulation therapy and prognostication.

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1. **Pulmonary thromboembolism in COVID-19: Evaluating the role of D-dimer and computed tomography pulmonary angiography results**  
   Ramadan L. The American journal of emergency medicine 2020;:No page numbers.

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1. **Systematic assessment of venous thromboembolism in COVID-19 patients receiving thromboprophylaxis: incidence and role of D-dimer as predictive factors.**  
   Artifoni Mathieu Journal of thrombosis and thrombolysis 2020;50(1):211-216.

Coagulopathy in COVID-19 is a burning issue and strategies to prevent thromboembolic events are debated and highly heterogeneous. The objective was to determine incidence and risk factors of venous thromboembolism (VTE) in COVID-19 inpatients receiving thromboprophylaxis. In this retrospective French cohort study, patients hospitalized in medical wards non-ICU with confirmed COVID-19 and adequate thromboprophylaxis were included. A systematic low limb venous duplex ultrasonography was performed at hospital discharge or earlier if deep venous thrombosis (DVT) was clinically suspected. Chest angio-CT scan was performed when pulmonary embolism (PE) was suspected. Of 71 patients, 16 developed VTE (22.5%) and 7 PE (10%) despite adequate thromboprophylaxis. D-dimers at baseline were significantly higher in patients with DVT (p < 0.001). Demographics, comorbidities, disease manifestations, severity score, and other biological parameters, including inflammatory markers, were similar in patients with and without VTE. The negative predictive value of a baseline D-dimer level < 1.0 µg/ml was 90% for VTE and 98% for PE. The positive predictive value for VTE was 44% and 67% for D-dimer level ≥ 1.0 µg/ml and ≥ 3 µg/ml, respectively. The association between D-dimer level and VTE risk increased by taking into account the latest available D-dimer level prior to venous duplex ultrasonography for the patients with monitoring of D-dimer. Despite thromboprophylaxis, the risk of VTE is high in COVID-19 non-ICU inpatients. Increased D-dimer concentrations of more than 1.0 μg/ml predict the risk of venous thromboembolism. D-dimer level-guided aggressive thromboprophylaxis regimens using higher doses of heparin should be evaluated in prospective studies.

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1. **The clinical spectrum of pulmonary thromboembolism in patients with coronavirus disease-2019 (COVID-19) pneumonia: A European case series.**  
   Sakr Yasser Journal of critical care 2020;61:39-44.

PURPOSETo describe the clinical characteristics and outcomes of coronavirus disease-2019 (COVID-19)-associated pulmonary thromboembolism (PTE).MATERIALS AND METHODSA case series of five patients, representing the clinical spectrum of COVID-19 associated PTE. Patients were admitted to four hospitals in Germany, Italy, and France. Infection with Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) was confirmed using a real-time reverse transcription polymerase chain reaction test.RESULTSThe onset of PTE varied from 2 to 4 weeks after the occurrence of the initial symptoms of SARS-CoV-2 infection and led to deterioration of the clinical picture in all cases. PTE was the primary reason for hospital admission after a 2-week period of self-isolation at home (1 patient) and hospital readmission after initial uncomplicated hospital discharge (2 patients). Three of the patients had no past history of clinically relevant risk factors for venous thromboembolism (VTE). Severe disease progression was associated with concomitant increases in IL-6, ferritin, and D-Dimer levels. The outcome from PTE was related to the extent of vascular involvement, and associated complications.CONCLUSIONPTE is a potential life-threatening complication, which occurs frequently in patients with COVID-19. Intermediate therapeutic dose of anticoagulants and extend thromboprophylaxis are necessary after meticulous risk-benefit assessment.

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1. **Thrombolysis in severe COVID-19 pneumonia with massive pulmonary embolism.**  
   Alharthy Abdulrahman The American journal of emergency medicine 2020;:No page numbers.

OBJECTIVENo guidelines exist for the management of massive pulmonary embolism (PE) in COVID-19. We present a COVID-19 patient with refractory acute respiratory syndrome (ARDS), and life-threatening PE who underwent successful thrombolysis.CASE PRESENTATIONA previously healthy 47 year old male was admitted to our hospital due to severe COVID-19 pneumonia [confirmed by Real-Time-Polymerase-Chain-Reaction (RT-PCR)]. He had rapidly evolving ARDS [partial arterial pressure of oxygen to fractional inspired concentration of oxygen ratio: 175], and sepsis. Laboratory results showed lymphocytopenia, and increased D-dimer levels (7.7 μg/ml; normal: 0-0.5 μg/ml). The patient was treated in the intensive care unit. On day-1, ARDS-net/prone positioning ventilation, and empiric anti-COVID treatment integrating prophylactic anticoagulation was administered. On hospital day-2, the patient developed shock with worsening oxygenation. Point-of-care-ultrasound depicted a large thrombus migrating from the right atrium to the pulmonary circulation. Intravenous alteplase (100 mg over 2 h) was administered as rescue therapy. The patient made an uneventful recovery, and was discharged to home isolation (day-20) on oral rivaroxaban.CONCLUSIONThrombolysis may have a critical therapeutic role for massive PE in COVID-19; however the risk of potential bleeding should not be underestimated. Point-of-care ultrasound has a pivotal role in the management of refractory ARDS in COVID-19.

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1. **Thrombosis risk associated with COVID-19 infection. A scoping review.**  
   Al-Ani Fatimah Thrombosis research 2020;192:152-160.

BACKGROUNDInfection by the 2019 novel coronavirus (COVID-19) has been reportedly associated with a high risk of thrombotic complications. So far information is scarce and rapidly emerging.METHODSWe conducted a scoping review using a single engine search for studies assessing thrombosis and coagulopathy in COVID-19 patients. Additional studies were identified by secondary review and alert services.RESULTSStudies reported the occurrence of venous thromboembolism and stroke in approximately 20% and 3% of patients, respectively. A higher frequency seems to be present in severely ill patients, in particular those admitted to intensive care units. The thrombotic risk is elevated despite the use of anticoagulant prophylaxis but optimal doses of anticoagulation are not yet defined. Although an increase of biomarkers such as D-dimer has been consistently reported in severely ill COVID-19, the optimal cut-off level and prognostic value are not known.DISCUSSIONA number of pressing issues were identified by this review, including defining the true incidence of VTE in COVID patients, developing algorithms to identify those susceptible to develop thrombotic complications and severe disease, determining the role of biomarkers and/or scoring systems to stratify patients' risk, designing adequate and feasible diagnostic protocols for PE, establishing the optimal thromboprophylaxis strategy, and developing uniform diagnostic and reporting criteria.

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1. **Thrombotic and haemorrhagic complications in critically ill patients with COVID-19: a multicentre observational study.**  
   Shah Akshay Critical care (London, England) 2020;24(1):561.

BACKGROUNDOptimal prophylactic and therapeutic management of thromboembolic disease in patients with COVID-19 remains a major challenge for clinicians. The aim of this study was to define the incidence of thrombotic and haemorrhagic complications in critically ill patients with COVID-19. In addition, we sought to characterise coagulation profiles using thromboelastography and explore possible biological differences between patients with and without thrombotic complications.METHODSWe conducted a multicentre retrospective observational study evaluating all the COVID-19 patients received in four intensive care units (ICUs) of four tertiary hospitals in the UK between March 15, 2020, and May 05, 2020. Clinical characteristics, laboratory data, thromboelastography profiles and clinical outcome data were evaluated between patients with and without thrombotic complications.RESULTSA total of 187 patients were included. Their median (interquartile (IQR)) age was 57 (49-64) years and 124 (66.3%) patients were male. Eighty-one (43.3%) patients experienced one or more clinically relevant thrombotic complications, which were mainly pulmonary emboli (n = 42 (22.5%)). Arterial embolic complications were reported in 25 (13.3%) patients. ICU length of stay was longer in patients with thrombotic complications when compared with those without. Fifteen (8.0%) patients experienced haemorrhagic complications, of which nine (4.8%) were classified as major bleeding. Thromboelastography demonstrated a hypercoagulable profile in patients tested but lacked discriminatory value between those with and without thrombotic complications. Patients who experienced thrombotic complications had higher D-dimer, ferritin, troponin and white cell count levels at ICU admission compared with those that did not.CONCLUSIONCritically ill patients with COVID-19 experience high rates of venous and arterial thrombotic complications. The rates of bleeding may be higher than previously reported and re-iterate the need for randomised trials to better understand the risk-benefit ratio of different anticoagulation strategies.

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1. **Thrombotic Complications of COVID-19 Infection: A Review.**  
   Castro Rebecca Cardiology in review 2020;:No page numbers.

The novel coronavirus (COVID-19 or SARS-CoV-2) is a single-stranded, enveloped RNA virus that created a Public Health Emergency of International Concern in January 2020, with a global case burden of over 15 million in just seven months. Infected patients develop a wide range of clinical manifestations - typically presenting with fever, cough, myalgia, and fatigue. Severely-ill patients may fall victim to acute respiratory distress syndrome, acute heart injuries, neurological manifestations, or complications due to secondary infections. These critically-ill patients are also found to have disrupted coagulation function, predisposing them to consumptive coagulopathies, and both venous and thromboembolic complications. Common laboratory findings include thrombocytopenia, elevated D-dimer, fibrin degradation products, and fibrinogen, all of which have been associated with greater disease severity. Many cases of pulmonary embolism have been noted, along with deep vein thrombosis, ischemic stroke, myocardial infarction and systemic arterial embolism. The pathogenesis of COVID-19 has not been completely elucidated, but the virus is known to cause excessive inflammation, endothelial injury, hypoxia, and disseminated intravascular coagulation, all of which contribute to thrombosis formation. These patients are also faced with prolonged immobilization while staying in the hospital or intensive care unit. It is important to have a high degree of suspicion for thrombotic complications as patients may rapidly deteriorate in severe cases. Evidence suggests that prophylaxis with anticoagulation may lead to a lower risk of mortality, although it does not eliminate the possibility. The risks and benefits of anticoagulation treatment should be considered in each case. Patients should be regularly evaluated for bleeding risks and thrombotic complications.

1. **[Late occurrence of pulmonary embolsim in SARS-CoV-2 pneumonia: a case series].**  
   Halasz Geza Giornale italiano di cardiologia (2006) 2020;21(7):523-525.

Several studies suggested that the acute phase of SARS-CoV-2 infection may be associated with a hypercoagulable state and increased risk for venous thromboembolism but the incidence of thrombotic complications in the late phase of the disease is currently unknown. The present article describes three cases of patients with SARS-CoV-2 pneumonia and late occurrence of pulmonary embolism. Case 1: a 57-year-old man diagnosed with pulmonary embolism and type B aortic dissection after 12 days from SARS-CoV-2 pneumonia. Laboratory panel at the time of pulmonary embolism showed no signs of ongoing inflammation but only an elevated D-dimer. Case 2: a 76-year-old man with a diagnosis of SARS-CoV-2 pneumonia followed by pulmonary embolism 20 days later, high-resolution computed tomography on that time showed a partial resolution of crazy paving consolidation. Case 3: a 77-year-old man with SARS-CoV-2 pneumonia who developed a venous thromboembolic event despite thromboprophylaxis with low molecular weight heparin. Also in this patients no markers of inflammation were present at the time of complication.The present cases raise the possibility that in SARS-CoV-2 infection the hypercoagulable state may persist over the active inflammation phase and cytokine storm. These findings suggest a role for medium-long term therapeutic anticoagulation started at the time of SARS-CoV-2 pneumonia diagnosis.

1. **[The keypoints in treatment of the critical coronavirus disease 2019 patient(2)].**  
   Li X. Y Zhonghua jie he he hu xi za zhi = Zhonghua jiehe he huxi zazhi = Chinese journal of tuberculosis and respiratory diseases 2020;43(4):277-281.

The treatment of critically ill patients with coronavirus disease 2019(COVID-19) faces compelling challenges. In this issue, we'd like to share our first-line treatment experience in treating COVID-19. Hemodynamics need be closely monitored and different types of shock should be distinguished. Vasoconstrictor drugs should be used rationally and alerting of complications is of the same importance. The risk of venous thromboembolism (VTE) needs to be assessed, and effective prevention should be carried out for high-risk patients. It is necessary to consider the possibility of pulmonary thromboembolism (PTE) in patients with sudden onset of oxygenation deterioration, respiratory distress, reduced blood pressure. However, comprehensive analysis of disease state should be taken into the interpretation of abnormally elevated D-Dimer. Nutritional support is the basis of treatment. It's important to establish individual therapy regimens and to evaluate, monitor and adjust dynamically. Under the current epidemic situation, convalescent plasma can only be used empirically, indications need to be strictly screened, the blood transfusion process should be closely monitored and the curative effect should be dynamically evaluated.

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Select Edit from the menu, the Find and type in your term in the search box which is presented. The search function will locate the first use of the term in the document. By pressing 'next' you will jump to further references.

## D. Search History

|  | **Source** | **Criteria** | **Results** |
| --- | --- | --- | --- |
| 1. | Medline | exp \*PULMONARY EMBOLISM/ | 28780 |
| 2. | Medline | ((lung OR pulmonary) ADJ (embol\* OR thrombo\*)).ti,ab | 38602 |
| 3. | Medline | (PE OR PTE).ti,ab | 43314 |
| 4. | Medline | (1 OR 2 OR 3) | 83355 |
| 5. | Medline | \*"FIBRIN FIBRINOGEN DEGRADATION PRODUCTS"/an,me | 3302 |
| 6. | Medline | \*BIOMARKERS/an,bl,me | 32239 |
| 7. | Medline | \*"ENZYME-LINKED IMMUNOSORBENT ASSAY"/ | 15735 |
| 8. | Medline | \*"NEPHELOMETRY AND TURBIDIMETRY"/ | 1752 |
| 9. | Medline | (d-dimer).ti,ab | 10526 |
| 10. | Medline | (fibrin ADJ2 d).ti,ab | 1037 |
| 11. | Medline | ("dimeri?ed plasmin").ti,ab | 15 |
| 12. | Medline | (elisa\* OR elfa\*).ti,ab | 174137 |
| 13. | Medline | ("enzyme linked").ti,ab | 102266 |
| 14. | Medline | ((blood OR latex) ADJ agglutination).ti,ab | 3601 |
| 15. | Medline | (latex ADJ3 assay\*).ti,ab | 878 |
| 16. | Medline | (immunoturbidimetr\* OR turbidimetr\*).ti,ab | 4923 |
| 17. | Medline | (SimpliRed OR Minutex OR NycoCard OR "Instant IA" OR Vidas OR LIATEST OR "IL test" OR "IL‐DD" OR Turbiquant OR Asserachrom OR Enzygnost OR Fibrinostika OR "BC DD" OR Tinaquant OR "Tina‐quant" OR TriniLIZE OR biopool OR TintElize OR HemosIL OR "Innovance‐DD" OR stratus OR FDP OR Dimertest OR LPIA OR EIA).ti,ab | 15861 |
| 18. | Medline | (5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17) | 293169 |
| 19. | Medline | exp CORONAVIRUS/ | 11558 |
| 20. | Medline | ((corona\* OR corono\*) ADJ1 (virus\* OR viral\* OR virinae\*)).ti,ab | 632 |
| 21. | Medline | (coronavirus\* OR coronovirus\* OR coronavirinae\* OR Coronavirus\* OR Coronovirus\* OR Wuhan\* OR Hubei\* OR Huanan OR "2019-nCoV" OR 2019nCoV OR nCoV2019 OR "nCoV-2019" OR "COVID-19" OR COVID19 OR "CORVID-19" OR CORVID19 OR "WN-CoV" OR WNCoV OR "HCoV-19" OR HCoV19 OR CoV OR "2019 novel\*" OR Ncov OR "n-cov" OR "SARS-CoV-2" OR "SARSCoV-2" OR "SARSCoV2" OR "SARS-CoV2" OR SARSCov19 OR "SARS-Cov19" OR "SARSCov-19" OR "SARS-Cov-19" OR Ncovor OR Ncorona\* OR Ncorono\* OR NcovWuhan\* OR NcovHubei\* OR NcovChina\* OR NcovChinese\*).ti,ab | 18512 |
| 22. | Medline | (respiratory\* ADJ2 (symptom\* OR disease\* OR illness\* OR condition\*)).ti,ab | 65062 |
| 23. | Medline | (("seafood market\*" OR "food market\*") ADJ10 (Wuhan\* OR Hubei\* OR China\* OR Chinese\* OR Huanan\*)).ti,ab | 51 |
| 24. | Medline | ((outbreak\* OR wildlife\* OR pandemic\* OR epidemic\*) ADJ1 (China\* OR Chinese\* OR Huanan\*)).ti,ab | 855 |
| 25. | Medline | ("severe acute respiratory syndrome\*").ti,ab | 4761 |
| 26. | Medline | (19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25) | 156532 |
| 27. | Medline | (4 AND 18 AND 26) | 106 |
| 28. | Medline | 4 AND 18 AND 26 [DT FROM 2020] | 85 |
| 29. | EMBASE | \*LUNG EMBOLISM/ | 33415 |
| 30. | EMBASE | ((lung OR pulmonary) ADJ (embol\* OR thrombo\*)).ti,ab | 64984 |
| 31. | EMBASE | (PE OR PTE).ti,ab | 68599 |
| 32. | EMBASE | (29 OR 30 OR 31) | 122512 |
| 33. | EMBASE | \*D DIMER/ | 4031 |
| 34. | EMBASE | BIOLOGICAL MARKER/cr | 18 |
| 35. | EMBASE | FIBRIN DEGRADATION PRODUCT/cr | 1 |
| 36. | EMBASE | \*ENZYME LINKED IMMUNOSORBENT ASSAY/ | 18802 |
| 37. | EMBASE | \*TURBIDIMETRY/ | 534 |
| 38. | EMBASE | (d-dimer).ti,ab | 17438 |
| 39. | EMBASE | (fibrin ADJ2 d).ti,ab | 795 |
| 40. | EMBASE | ("dimeri?ed plasmin").ti,ab | 18 |
| 41. | EMBASE | (elisa\* OR elfa\*).ti,ab | 279499 |
| 42. | EMBASE | ("enzyme linked").ti,ab | 119154 |
| 43. | EMBASE | ((blood OR latex) ADJ agglutination).ti,ab | 4177 |
| 44. | EMBASE | (latex ADJ3 assay\*).ti,ab | 1098 |
| 45. | EMBASE | (immunoturbidimetr\* OR turbidimetr\*).ti,ab | 7738 |
| 46. | EMBASE | (SimpliRed OR Minutex OR NycoCard OR "Instant IA" OR Vidas OR LIATEST OR "IL test" OR "IL‐DD" OR Turbiquant OR Asserachrom OR Enzygnost OR Fibrinostika OR "BC DD" OR Tinaquant OR "Tina‐quant" OR TriniLIZE OR biopool OR TintElize OR HemosIL OR "Innovance‐DD" OR stratus OR FDP OR Dimertest OR LPIA OR EIA).ti,ab | 21194 |
| 47. | EMBASE | (33 OR 34 OR 35 OR 36 OR 37 OR 38 OR 39 OR 40 OR 41 OR 42 OR 43 OR 44 OR 45 OR 46) | 387703 |
| 48. | EMBASE | exp \*CORONAVIRINAE/ | 10040 |
| 49. | EMBASE | exp \*CORONAVIRUS INFECTION/ | 9740 |
| 50. | EMBASE | ((corona\* OR corono\*) ADJ1 (virus\* OR viral\* OR virinae\*)).ti,ab | 1471 |
| 51. | EMBASE | (coronavirus\* OR coronovirus\* OR coronavirinae\* OR Coronavirus\* OR Coronovirus\* OR Wuhan\* OR Hubei\* OR Huanan OR "2019-nCoV" OR 2019nCoV OR nCoV2019 OR "nCoV-2019" OR "COVID-19" OR COVID19 OR "CORVID-19" OR CORVID19 OR "WN-CoV" OR WNCoV OR "HCoV-19" OR HCoV19 OR CoV OR "2019 novel\*" OR Ncov OR "n-cov" OR "SARS-CoV-2" OR "SARSCoV-2" OR "SARSCoV2" OR "SARS-CoV2" OR SARSCov19 OR "SARS-Cov19" OR "SARSCov-19" OR "SARS-Cov-19" OR Ncovor OR Ncorona\* OR Ncorono\* OR NcovWuhan\* OR NcovHubei\* OR NcovChina\* OR NcovChinese\*).ti,ab | 85176 |
| 52. | EMBASE | (respiratory\* ADJ2 (symptom\* OR disease\* OR illness\* OR condition\*)).ti,ab | 87284 |
| 53. | EMBASE | (("seafood market\*" OR "food market\*") ADJ10 (Wuhan\* OR Hubei\* OR China\* OR Chinese\* OR Huanan\*)).ti,ab | 93 |
| 54. | EMBASE | ((outbreak\* OR wildlife\* OR pandemic\* OR epidemic\*) ADJ1 (China\* OR Chinese\* OR Huanan\*)).ti,ab | 123 |
| 55. | EMBASE | ("severe acute respiratory syndrome\*").ti,ab | 12097 |
| 56. | EMBASE | (48 OR 49 OR 50 OR 51 OR 52 OR 53 OR 54 OR 55) | 175577 |
| 57. | EMBASE | (32 AND 47 AND 56) | 161 |
| 58. | EMBASE | 32 AND 47 AND 56 [DT FROM 2020] | 115 |

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