

## SYSTEMATIC REVIEW

Therapy area: Other

# Imaging approach to COVID-19 associated pulmonary embolism

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**Abstract**

The novel coronavirus disease-2019 (COVID-19) illness and deaths, caused by the severe acute respiratory syndrome coronavirus-2, continue to increase. Multiple reports highlight the thromboembolic complications, such as pulmonary embolism (PE), in COVID-19. Imaging plays an essential role in the diagnosis and management of COVID-19 patients with PE. There continues to be a rapid evolution of knowledge related to COVID-19 associated PE. This review summarises the current understanding of prevalence, pathophysiology, role of diagnostic imaging modalities, and management, including catheter-directed therapy for COVID-19 associated PE. It also describes infection control considerations for the radiology department while providing care for patients with COVID-19 associated PE.

## 1 | INTRODUCTION

The novel coronavirus disease-2019 (COVID-19) illness caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a global pandemic, and the number of cases and deaths continue to rise despite extensive measures.<sup>1,2</sup> The most common symptoms at the onset of COVID-19 are respiratory tract infection with fever, cough, fatigue, and dyspnea.<sup>3,4</sup> In a fraction of patients, there is deterioration into a severe systemic illness with multiorgan failure resulting in a hypercoagulable state and thromboembolic complications.<sup>5,6</sup> Pulmonary embolism (PE) is a severe and common sequela of this hypercoagulability in patients with COVID-19.<sup>7</sup>

Our understanding of COVID-19 associated PE continues to evolve. We summarise the current knowledge regarding the prevalence, pathophysiology, diagnosis, and PE management in COVID-19 patients. We also review imaging-based considerations in managing these patients while balancing the challenges of this pandemic.

The overall annual incidence of venous thromboembolism (VTE) in the United States is estimated to be 1-2 per 1000 of the population, with mortality rates ranging between 10% and 30% within 30 days.<sup>8</sup> However, the prevalence of COVID-19 associated PE may be as high as 37.1% (Table 1). The incidence of PE in nonintensive care unit (ICU) patients ranges between 1.6% and 6.4%,<sup>9,10</sup> while ICU

patients have higher rates of 13.6%-26.6%<sup>10-16</sup> (Table 2). Even among the patients managed in the ICU, COVID-19 patients (a study on 107 patients) had an absolute increased risk of PE of 13.1%-14.4% compared with other ICU patients with similar illness severity.<sup>14</sup> It is unclear if patients with COVID-19 illness associated PE have increased mortality. Several studies comparing COVID-19 patients with and without PE found no statistically significant mortality difference between the two groups, although mechanical ventilation and ICU admission rates may be higher in patients who also have COVID-19 associated PE.<sup>9,11,15,17-21</sup> However, variable and small sample sizes, and nonuniform patient diagnostic and management policies, contribute to our limited understanding of the true prevalence and impact of PE in COVID-19 patients.<sup>10-13</sup> Despite this uncertainty, there is understandable concern that COVID-19 illness combined with PE may result in worse outcomes than either entity alone. Future studies on larger and more balanced patient cohorts may clarify this.

### 1.1 | Pathophysiology

The pathophysiology of COVID-19 associated PE may differ from other causes of PE. Studies on COVID-19 patients have demonstrated PE in central pulmonary artery locations (main and lobar

pulmonary arteries)<sup>13,19,21-24</sup> as well as in a peripheral distribution.<sup>9,25-28</sup> Lung autopsies of COVID-19 patients revealed microangiopathy of alveolar capillaries with 69%-91% of thrombi in segmental and subsegmental pulmonary arteries.<sup>9,25-28</sup> Interestingly, in patients with known PE, there is a lower incidence of deep vein thrombosis (DVT) (6.9%-13.6%) in COVID-19 patients<sup>9,14,17</sup> compared to non-COVID-19 patients (45%-70%).<sup>9,14,17,25,26</sup> Also, unlike non-COVID-19 patients, COVID-19 patients often lack many traditional risk factors and comorbidities for PE.<sup>14,17,20</sup> These observations have facilitated the theory that in situ microthrombi in the small peripheral pulmonary vasculature may play an important role in COVID-19 associated PE.<sup>9,27,28</sup> Thrombotic microvascular injuries have also been described in other organs (eg, kidneys and skin) despite adequate anticoagulation in COVID-19 patients.<sup>28-30</sup> In addition, lower extremity DVT was found in 85.4% of COVID-19 patients admitted to the ICU (study of 48 patients) despite prophylactic anticoagulation highlighting the severity of the hypercoagulable state.<sup>31</sup> Hence, researchers currently believe that the combination of microvascular thrombus and SARS-CoV-2 viral-induced endothelial damage leads to a systemic inflammatory reaction and progressive multisystem prothrombotic state, resulting in multiorgan failure and death.<sup>32</sup>

## 1.2 | D-dimer considerations

The root cause of increased D-dimer levels in COVID-19 illness is unclear. Studies have shown that elevated D-dimer levels are sensitive in diagnosing PE in COVID-19 patients.<sup>9,11,19-23,27</sup> Elevated serum D-dimer levels of >4000 ng/mL accurately predicted COVID-19 associated VTE when combined with clinical exam findings (sensitivity of 80% and specificity of 70%) for diagnosing DVT.<sup>33</sup> Similarly, D-dimer cut-off levels of 2660 and 1394 ng/mL were shown to have 100% and 95% sensitivity for diagnosing PE in COVID-19 patients. However, similar to the non-COVID-19 patient population, elevated D-dimer levels lack specificity (67% and 71%) in detecting COVID-19 associated VTE.<sup>20,23</sup> Hence, it is currently not recommended to use D-dimer levels to diagnose COVID-19 associated VTE,<sup>34</sup> or decide which patients should undergo imaging to diagnose PE.<sup>35</sup> However, similar to non-COVID-19 patients, normal D-dimer values can effectively rule out VTE in the context of low pretest probability. Elevated D-dimers may also predict adverse outcomes such as mechanical ventilation, ICU admission, and disease severity in patients with COVID-19.<sup>5,36-38</sup> Studies have also shown high bleeding complications in COVID-19 patients with elevated D-dimer levels (>2500 ng/mL), complicating anticoagulation strategies for these patients.<sup>39,40</sup>

## 2 | IMAGING CONSIDERATIONS

### 2.1 | Chest radiograph

Chest radiographs (CXR) lack accuracy in diagnosing PE and are typically reserved for diagnosing alternative conditions, such as

### How did you gather, select, and analyse the information you considered in your review?

- We searched PubMed using the terms “Pulmonary Embolism” and “COVID-19” or “SARS-CoV-2” or “coronavirus 2019” for studies published in the medical literature without a time limit.
- We manually searched the references of selected papers for additional relevant articles.
- We selected articles that only directly addressed PE in patients with COVID-19. Only articles written in the English language were included.

### Message for the clinic: What is the “take-home” message for the clinician?

- COVID-19 illness is associated with a hypercoagulable state, predisposing patients to thromboembolic complications such as pulmonary embolism.
- CTPA is effective for the diagnosis of COVID-19 associated pulmonary embolism, but attention must be made for appropriate infection control and peripheral thromboemboli, unique to COVID-19.
- Other modalities such as ventilation-scintigraphy, extremity venous Doppler ultrasound, and chest radiographs can be helpful, but only when utilised in the appropriate setting.

pulmonary edema, pneumonia, and pneumothorax that could simulate PE. CXR findings in PE are nonspecific and subtle, such as cardiomegaly, enlarged pulmonary artery size, lung atelectasis, consolidation, and diminished pulmonary vascularity (Figures 1A and 2A).<sup>41-43</sup> Due to this nonspecific nature, CXR is not recommended for the diagnosis of PE in COVID-19 infection. However, the portable, quick, inexpensive, and ubiquitous nature of CXR can help assess disease severity, predict prognosis, and direct management for patients with known COVID-19 pneumonia.<sup>44-46</sup>

### 2.2 | Ventilation perfusion scintigraphy

Ventilation-perfusion (VQ) scintigraphy plays an essential role in the evaluation of PE in patients with contraindications for intravenous contrast administration (advanced renal failure with eGFR under 30 mL/min/1.73 m<sup>2</sup> or severe allergy to iodinated contrast material), young females, or large patients who cannot be scanned with computed tomography (CT).<sup>41</sup> However, in COVID-19 patients, the ventilation portion of the VQ may result in the airborne spread of COVID-19 due to aerosol leakage. Patients' cough may also worsen after inhalation of radiopharmaceuticals, further increasing this risk.<sup>47,48</sup> As a result, multiple authors have suggested performing only a planar perfusion scan, perhaps

**TABLE 1** Summary of retrospective cohort studies of COVID-19 positive patients with PE diagnosed on CTPA

	Bompard et al, France	Fauvel et al, France	Gervaise et al, France	Grillet et al, France	Kamineztky et al, USA
<b>Study</b>	<b>n = 135</b>	<b>n = 1240 (multicentre, 24 hospitals)</b>	<b>n = 72</b>	<b>n = 100</b>	<b>n = 62</b>
<b>Cohort</b>	Two hospitals 47% ED 35% Inpatient 18% ICU patients	Inpatients (patients who got directly admitted under ICU care were excluded)	Single-centre ED	Single-centre Inpatients (not further specified)	Single-centre 50% ED 43.5% Inpatients 6.5% ICU patients
<b>PE prevalence</b>	24%	8.3%	18%	23%	37.1%
<b>PE distribution</b>	31% proximal 56% segmental 13% subsegmental	N/A	38% bilateral 15% main PA 30% lobar 55% segmental	N/A	N/A
<b>Other observations</b>	<ul style="list-style-type: none"> <li>Patients with PE had more ICU care (38%) and intubation (31%) than patients without PE</li> <li>↑ incidence of PE in ICU patients (50%)</li> <li>19% of PE associated with right heart strain</li> <li>No difference of disease extent on CT between PE and non-PE patients</li> </ul>	<ul style="list-style-type: none"> <li>Patients with PE were male sex, ↑ CRP, and longer time from symptom onset to hospitalization</li> <li>11.7% of PE patients had DVT</li> <li>PE protective factors include anticoagulation with therapeutic dose before admission or anticoagulation with prophylaxis dose during hospitalization</li> </ul>	<ul style="list-style-type: none"> <li>38% of PE had a pleural effusion</li> <li>PE patients were older and demonstrated ↑ D-dimer</li> <li>No CT imaging features differentiated between patients with PE and without PE</li> </ul>	<ul style="list-style-type: none"> <li>Patients with PE had more frequently ICU care (74%), intubation (65%), and had an ↑ interval from symptom onset to CTPA (12 days)</li> <li>Degree of pneumonia extent on CT is not associated with PE prevalence</li> <li>No significant difference in comorbidities between patients with PE and without PE</li> </ul>	<ul style="list-style-type: none"> <li>D-dimer value of 1394 ng/mL predicted PE with 95% sensitivity 71% specificity</li> <li>43.5% of PE associated with right heart strain</li> <li>No difference in degree of lung parenchymal involvement between patients with PE and without PE</li> <li>D-dimer correlated with degree of pulmonary artery obstruction</li> </ul>
<b>Study</b>	Leonard-Lorant et al, France <b>n = 106</b> Two hospitals	Mestre-Gomez et al, Spain <b>n = 91</b> Single-centre	Poyiadji et al, USA <b>n = 328</b> Multiple hospitals in a single health system	Whyte et al, UK <b>n = 214</b> Single-centre	
<b>Cohort</b>	Not further specified	Inpatients (noncritically ill)	51% ED	Inpatients	
<b>PE prevalence</b>	30%	31.9%	22%	37%	
<b>PE distribution</b>	22% main PA 34% lobar 28% segmental 16% subsegmental	52% bilateral 31% proximal 69% peripheral	13% central 31% lobar 51% segmental 5% subsegmental	43% bilateral 4% saddle embolus 35% segmental 16% subsegmental	
<b>Other observations</b>	<ul style="list-style-type: none"> <li>D-dimer value of 2660 ng/mL predicted PE with 100% sensitivity 67% specificity</li> <li>Associated with PE were male sex, ↑ interval from symptom onset to CT (14 days), and more frequent ICU care (75%)</li> </ul>	<ul style="list-style-type: none"> <li>No differences in BMI, prior thrombosis, or personal history of thrombophilia/malignancy/lung disease</li> <li>6.9% of PE patients had DVT</li> <li>Cumulative PE incidence of 6.4%</li> <li>No differences in mortality between patients with PE and without PE</li> </ul>	<ul style="list-style-type: none"> <li>Statins ↓ risk for PE</li> <li>↑ D-dimer, CRP, obesity, and a rising D-dimer over time posed ↑ risk for PE</li> <li>11% of PE cases associated with right heart strain</li> </ul>	<ul style="list-style-type: none"> <li>Patients with PE had ↑ D-dimer levels and more frequently had ICU care (45%) than patients without PE</li> <li>11% of PE patients had right heart strain</li> <li>PE is a common complication in COVID-19, even in general medical wards outside the ICU</li> </ul>	

Abbreviations: BMI, body mass index; CRP, C-reactive protein; DVT, deep vein thrombosis; ED, emergency department; ICU, intensive care unit; PA, pulmonary artery; PE, pulmonary embolism.

**TABLE 2** Summary of cohort studies reporting the PE prevalence in COVID-19 positive ICU patients

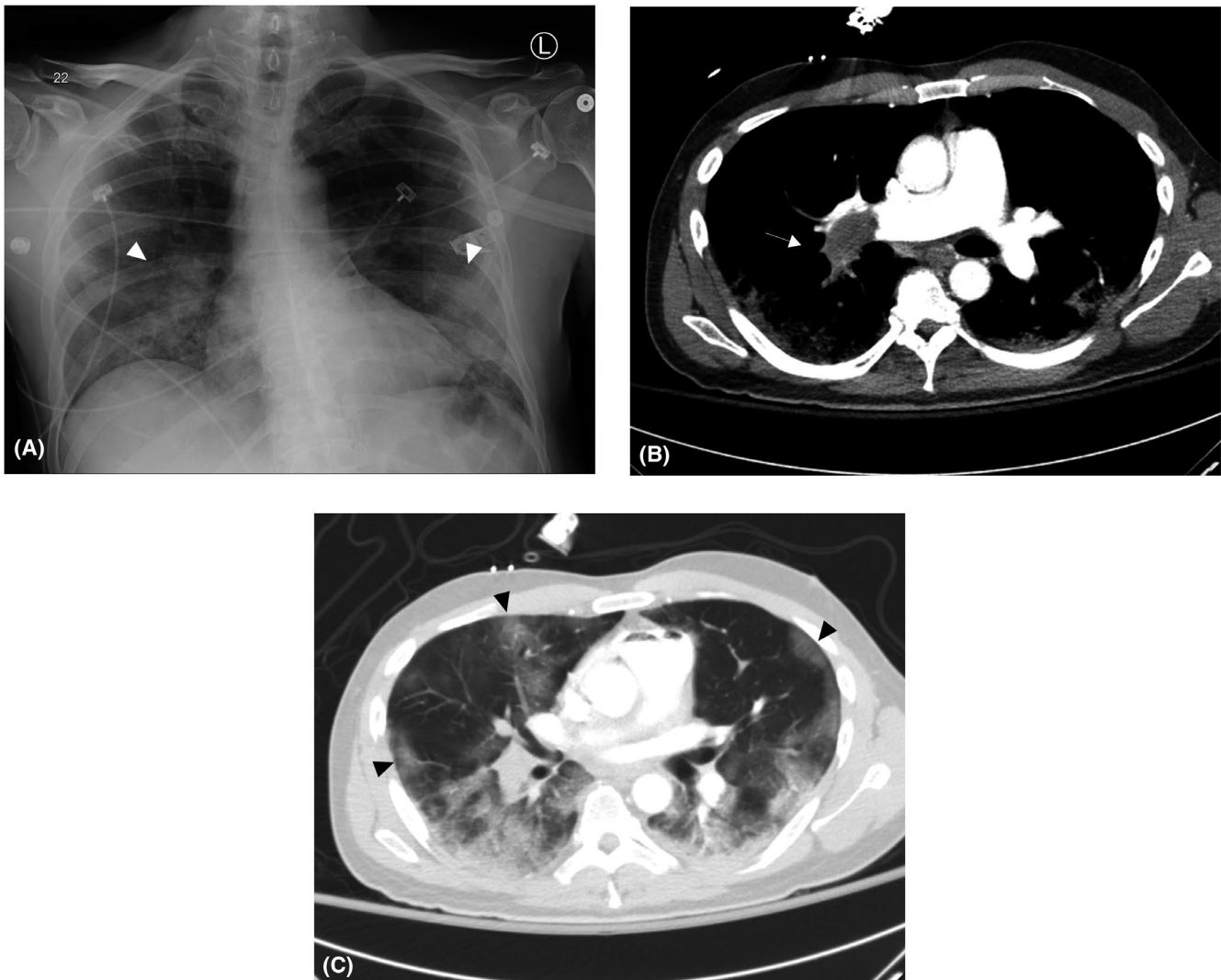
	Beun et al, Netherlands	Fraisse et al, France	Helms et al, France
	<i>n</i> = 75	<i>n</i> = 92	<i>n</i> = 150
<b>Study</b>	Single-centre	Single-centre	Two hospitals (4 ICUs)
Cohort	ICU	ICU	ICU
PE prevalence	26.6%	20.7%	16.7%
PE distribution	80% segmental and subsegmental  20% central	N/A	36% main PA 32% lobar 20% segmental 12% subsegmental
Other observations	<ul style="list-style-type: none"> <li>• Factors VIII was found to be extremely ↑</li> <li>• D-dimer and fibrinogen also ↑</li> <li>• Normal antithrombin levels</li> </ul>	<ul style="list-style-type: none"> <li>• PE as leading cause of thrombotic complications in COVID-19 patients</li> <li>• High rate (21%) of hemorrhagic events</li> </ul>	<ul style="list-style-type: none"> <li>• PE diagnosed in median 5.5 days after ICU admission</li> <li>• Compared to non-COVID-19 ARDS patients, COVID-19 ARDS patients developed significantly more thrombotic complications, primarily PE</li> <li>• 96.6% of patients with renal replacement therapy also experienced dialysis circuit clotting</li> </ul>
<b>Study</b>	Klok et al, Netherlands <i>n</i> = 184 Three hospitals	Middeldorp et al, Netherlands <i>n</i> = 75 Single-centre	Poissy et al, France <i>n</i> = 107 Single-center
Cohort	ICU	ICU	ICU
PE prevalence	13.6% (median follow-up observation duration 7 days)  35.3% (median follow-up observation duration 14 days)	15%	20.6%
PE distribution	71% segmental or more proximal  29% subsegmental	9% central or lobar  82% segmental  9% subsegmental	40% bilateral  10% proximal  55% segmental
Other observations	<ul style="list-style-type: none"> <li>• PE was most frequent thrombotic complication (81%-87%)</li> <li>• Age and coagulopathy were predictors of thrombotic complications</li> <li>• Chronic anticoagulation therapy at admission associated with lower risk</li> </ul>	<ul style="list-style-type: none"> <li>• ICU stay, ↑ WBC, low lymphocytic count, and ↑ D-dimer associated with VTE</li> <li>• Cumulative incidence of any and symptomatic VTE was 59% and 34% at 21 days in ICU patients, respectively</li> </ul>	<ul style="list-style-type: none"> <li>• Compared to control groups (patients with similar severity score due to non-COVID illness and influenza cohort) absolute increased risk prevalence of 14.4% and 13.1%, respectively</li> <li>• 77.3% of patients with PE had ARDS and intubation</li> <li>• 13.6% of patients with PE had DVT</li> </ul>

Abbreviations: ARDS, acute respiratory distress syndrome; DVT, deep vein thrombosis; ICU, intensive care unit; PA, pulmonary artery; PE, pulmonary embolism; VTE, venous thromboembolism; WBC, white blood cell.

at the bedside, or perfusion single-photon emission computed tomography (Q-SPECT), and forgo ventilation scintigraphy in COVID-19 patients.<sup>48-50</sup> Zuckier et al proposed performing the perfusion portion of the scan if a CXR was clear and performing the ventilation portion only if clinically imperative; if perfusion defects are present, the scan should be interpreted as indeterminate, and the patient referred for alternate testing.<sup>48</sup> However, this approach would exclude critically ill COVID-19 patients with extensive pulmonary consolidation and hence incorporating Q-SPECT and low-dose CT may be helpful.<sup>50</sup> Similarly, Lu et al proposed obtaining planar perfusion images first to rule out PE and only if abnormal,

performing Q-SPECT/CT to diagnose PE using the “MSKCC Q-SPECT/CT criteria” ( $\geq 1$  wedge-shaped  $\geq 50\%$  segmental peripheral defect seen on all three orthogonal planes, without corresponding CT image abnormality).<sup>49</sup>

It is unclear if negative perfusion-only scintigraphy can reliably rule out PE in COVID-19 patients.<sup>51</sup> Also, Q-SPECT/CT without ventilation is reported to have high false-positive results that need to be weighed against the risks of anticoagulation.<sup>52</sup> As the COVID-19 pandemic evolves differently across regions, the Society of Nuclear Medicine & Molecular Imaging has recently updated its guidance and recommends performing ventilation scans on a case-by-case basis



**FIGURE 1** 50-year-old man with PCR test positive COVID-19 infection. A, Chest radiograph shows ground-glass opacities (arrowheads) in the lower lungs (right more than left). B, CTPA shows a large filling defect (arrow) in the right main pulmonary artery with dilated right and main pulmonary arteries. C, The lung window shows peripheral bilateral ground-glass opacities (arrowheads) typical of COVID-19

while adhering to the local and institutional COVID-19 policies for aerosol-generating procedures.<sup>48</sup>

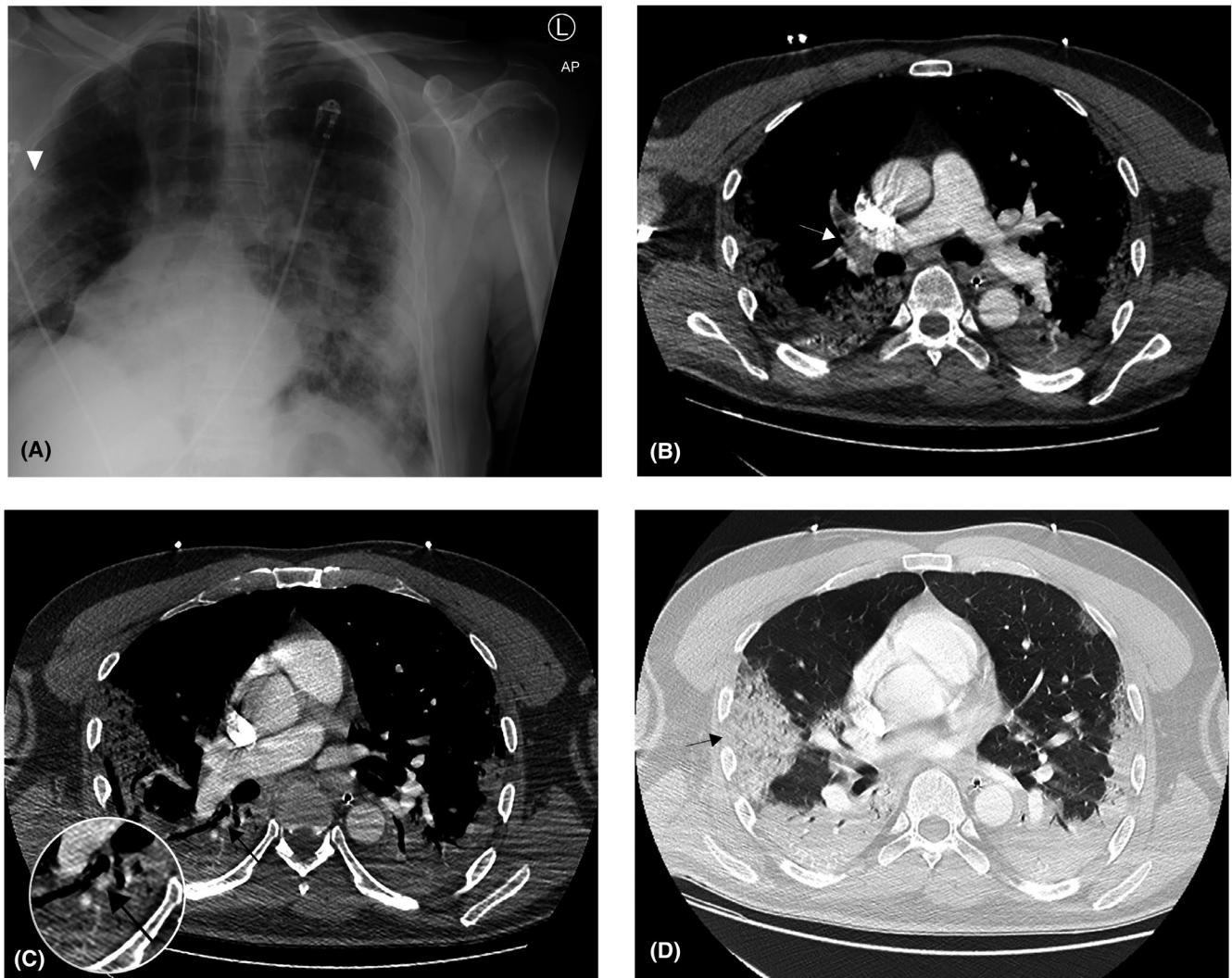
### 2.3 | Chest computed tomography

Chest CT helps evaluate patients with known COVID-19 pneumonia and related thoracic complications.<sup>53,54</sup> Semi-quantitate CT assessment of pneumonia severity and serial lung changes over time may correlate with disease severity and outcomes.<sup>55,56</sup> Typical imaging manifestations of COVID-19 pneumonia are bilateral peripheral ground-glass opacities without pleural effusions (Figure 1).<sup>53,54,57,58</sup> Based on the illness state, consolidation and intralobular reticulations may also be present.<sup>53,57,59</sup> Studies report abnormal pulmonary vascular thickening (“thick vessel sign”) within COVID-19 pneumonia opacities (Figure 2C).<sup>60</sup> Lang et al also observed extensive vascular changes (a study of 48 patients) demonstrating mosaic perfusion (94%), dilated and tortuous distal

vascular enlargement (85%) present either within (79%) or outside (56%) the COVID-19 pneumonia opacities that extend to the pleura (83%) and along the lung fissures (63%).<sup>61</sup> Since these changes are usually not present in patients with non-COVID pneumonia, they hypothesized that abnormal vasoregulation in the lung might play a larger role in COVID-19 illness. However, there are imaging pitfalls with using chest CT. The absence of lung findings does not rule out COVID-19 infection and even the typical COVID-19 lung findings overlap with other conditions.<sup>62</sup> Suboptimal breath-holding during chest CT can also cause artificial diffuse GGOs simulating COVID-19 pneumonia. Also, COVID-19 pneumonia may resemble the ischemia-related lung changes of PE on chest CT (Figure 2C).<sup>17,18,20,21</sup>

Indications for computed tomography pulmonary angiogram (CTPA) in COVID-19 patients include high demand for supplementary oxygen despite limited lung disease, unexplained severe respiratory failure, abnormal coagulation parameters, hemodynamic compromise, and right heart chamber dilation.<sup>11,58,63,64</sup> Care providers should always consider the risks of spreading infection by





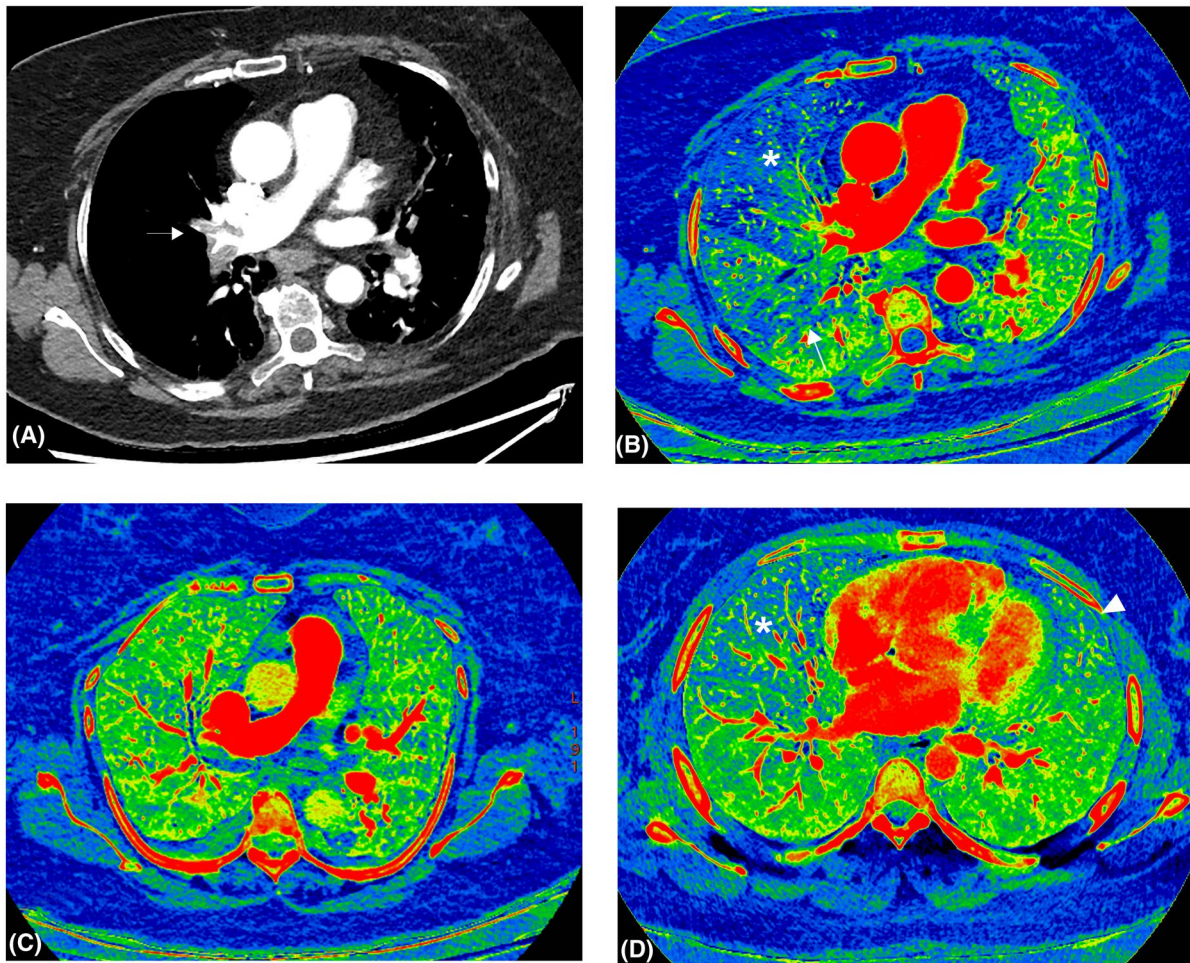
**FIGURE 2** 56-year-old man presented to the hospital approximately two weeks after testing positive for COVID-19. A, Chest radiograph shows peripheral ground-glass opacities as well as a wedge-shaped opacity in the right mid lung (arrowhead). B and C, CTPA shows a right lobar pulmonary embolism (white arrow, B) and peripheral parenchymal opacities with internal dilated small peripheral pulmonary vessels (black arrow, C). D, The lung window shows a peripheral wedge-shaped opacity (black arrow) in the right upper lobe indicating pulmonary infarction

transporting severely ill patients to the CT scanner suite and the renal impairment risks by administering potentially nephrotoxic intravenous contrast material prior to any CTPA.<sup>65</sup> There are also special considerations for CTPA in evaluating for PE in COVID-19 patients. As discussed earlier, small peripheral thrombi may be more prevalent in COVID-19.<sup>9,25-28</sup> Hence, evaluating the subsegmental pulmonary arteries on CTPA is essential using thin-collimation CT images.<sup>66</sup> Dual-energy CT iodine maps may offer incremental benefits by showing lung parenchymal perfusion defects (Figure 3).<sup>67</sup> Even in the absence of PE, dual-energy CT can offer useful information on disease severity. Quantitative perfusion mapping can highlight vasculopathy in COVID-19, and decreased perfused blood volume relative to pulmonary artery enhancement is associated with right ventricular dysfunction.<sup>68</sup> Finally, during a CTPA,

delayed images through the pelvis and lower extremities may be considered to evaluate DVT, thereby avoiding additional studies.<sup>69</sup>

## 2.4 | Ultrasound

In patients with known PE, there is a lower incidence of DVT (6.9%-13.6%) in COVID-19 patients<sup>9,14,17</sup> compared to non-COVID-19 patients (45%-70%).<sup>9,14,17,25,26</sup> This difference may partly be explainable by a lack of universal screening for COVID-19 patients. Clinical DVT prediction scores (CURB-65 score of 3 to 5 or Padua prediction score greater than or equal to 4) and elevated D-dimer levels can help stratify COVID-19 patients at risk for DVT who should undergo diagnostic imaging.<sup>70</sup> Compared to conventional



**FIGURE 3** A and B, 78-year-old woman presented with two days of shortness of breath. A, Dual-energy CTPA shows pulmonary embolism (arrow) in the distal right main extending into lobar pulmonary arteries. B, Colour-iodine map of the dual-energy CTPA shows extensive geographic perfusion defects (blue colour) in the right middle (asterisk) and right lower lobes (arrow). C, Normal colour-iodine map in a different patient without macroscopic filling defects on dual-energy CTPA (not shown) demonstrates no perfusion defects in the lungs. D, Colour-iodine map of a 31-year-old woman with COVID-19 and no macroscopic filling defects on dual-energy CTPA (not shown) shows geographic areas of blue in the right middle lobe (asterisk) and lingular segment (arrowhead), raising the suspicion for possible microscopic thrombi in the absence of macroscopic filling defects. Colour is required for this figure in print

venography, the diagnostic sensitivity and specificity of ultrasound (US) to detect proximal DVT using compression is 90%-100%.<sup>71</sup>

Currently, extremity venous Doppler US for DVT is recommended for symptomatic patients; however, a routine screening examination in asymptomatic patients is not recommended. Only in rare circumstances where a patient has high suspicion for PE but is unable to undergo CTPA should extremity US despite the absence of DVT symptoms be considered.<sup>69</sup> Bedside echocardiography may also help diagnose PE-associated findings such as right ventricular dilatation or dysfunction and intracardiac thrombus, indicating a clot-in-transit.<sup>72</sup>

The risk of spread of infection to sonographers can be minimised with specific changes to extremity venous Doppler US examination.<sup>33</sup> Customising and abbreviating the US scanning protocol for DVT, limiting the use of colour Doppler, avoiding routine scanning of the calf veins, and limiting studies to patients with clinical suspicion for DVT such as elevated D-dimer levels or abnormal dead-space

fraction (a method to measure anatomical and alveolar dead space) indicating PE are helpful. Whenever possible, deferral until the patient is less contagious can be considered.<sup>33,69,73</sup>

### 3 | MANAGEMENT

#### 3.1 | Prophylaxis and medical management

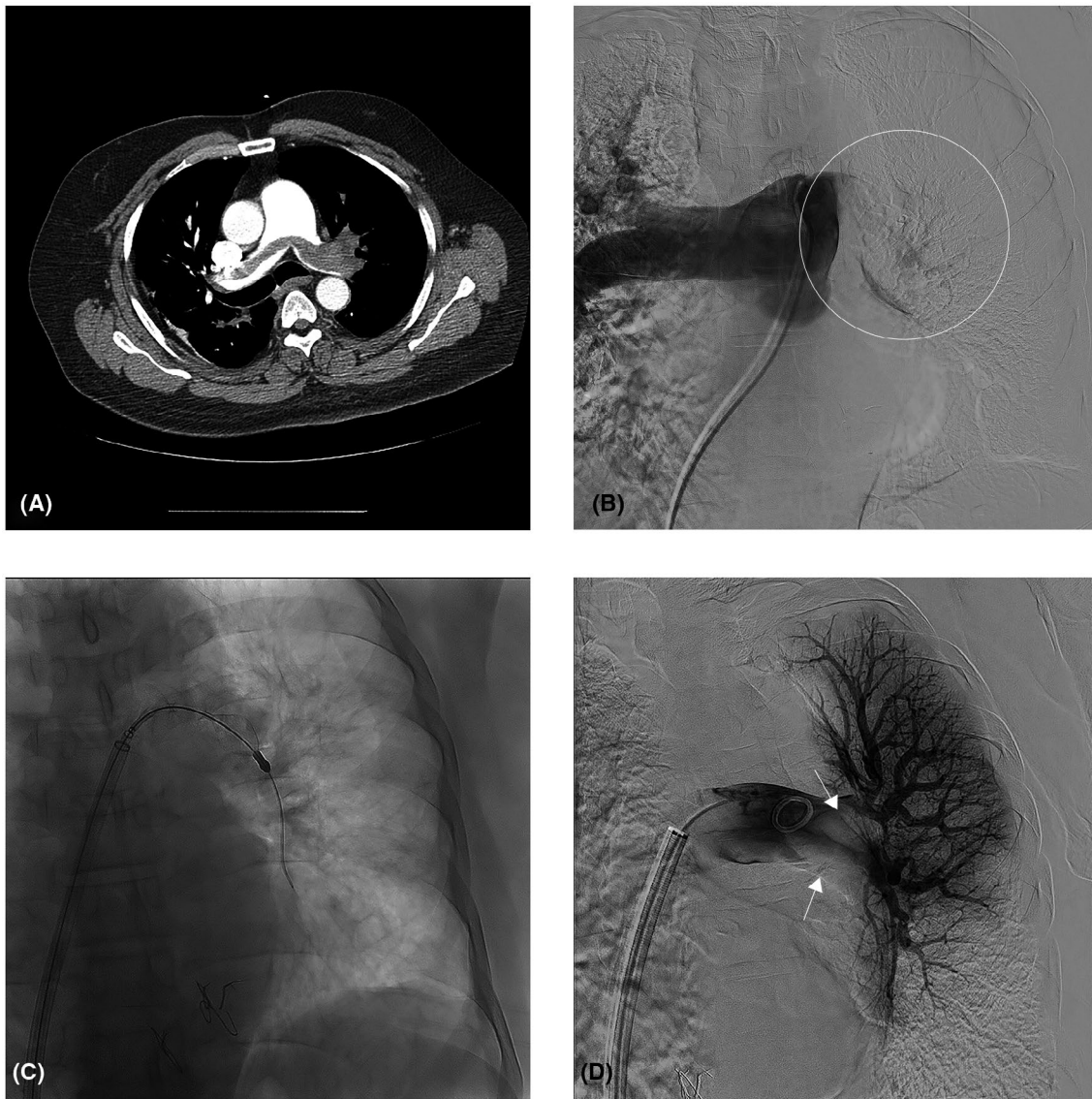
Adequate anticoagulation in COVID-19 patients appears to correlate with better outcomes in severe COVID-19 infections and a lower incidence of PE.<sup>17,74</sup> However, acute PE and breakthrough PEs occur in severely ill hospitalised COVID-19 patients despite prophylactic or therapeutic anticoagulation.<sup>9,13-15,23,75</sup> Recent studies investigating PE in COVID-19 patients indicate that statin therapy may be beneficial in decreasing the risk of PE,<sup>9,19</sup> although definite studies are needed to validate this observation.<sup>76</sup>



The International Society on Thrombosis and Haemostasis and the American Society of Hematology recommend all hospitalised patients with COVID-19 receive pharmacologic thromboprophylaxis, with standard-dose low molecular weight heparin or unfractionated heparin injections and if there are contraindications, using other measures such as pneumatic compression devices.<sup>75</sup> Therapeutic (full-dose) anticoagulation in patients with COVID-19 is reserved for patients with confirmed VTE. The routine use of full-dose prophylaxis for primary prevention in critically ill patients without confirmed or suspected VTE is not recommended as there is no data supporting empiric use. There are currently multiple trials investigating the benefit of varying doses of anticoagulation, and these recommendations may evolve.<sup>77</sup>

### 3.2 | Catheter-directed therapy for patients with COVID-19 associated PE

Catheter-directed therapy (CDT) can play a life-saving role in COVID-19 patients with massive or submassive PE, especially when systemic thrombolysis is contraindicated. The American Heart Association defines massive PE as causing sustained hypotension and submassive PE as causing cardiac dysfunction evidenced on CTPA as right ventricular dilatation (RV/LV ratio greater than 0.9) and/or interventricular septal bowing. The European Society of Cardiology alternatively classifies massive and submassive PE as high and intermediate-risk respectively. CDT generally falls into one



**FIGURE 4** 57-year-old man with PCR test positive COVID-19 infection. A, CTPA shows a large saddle embolus extending into the left lobar pulmonary arteries. B, Initial pulmonary arteriography shows essentially total occlusion of the left main pulmonary artery (circle). C, The T20 FlowTriever mechanical thrombectomy device (Inari Medical, Irvine, Calif) is seen positioned in the left main pulmonary artery. D, After catheter thrombectomy, pulmonary arteriography shows improved perfusion of the left upper lung, but with persistent filling defects in the left main pulmonary artery (arrows). The patient had a significant hemodynamic improvement post-intervention. However, due to concomitant COVID-19 pneumonia and a history of metastatic lung cancer, the patient continued to have worsening hypoxic respiratory failure

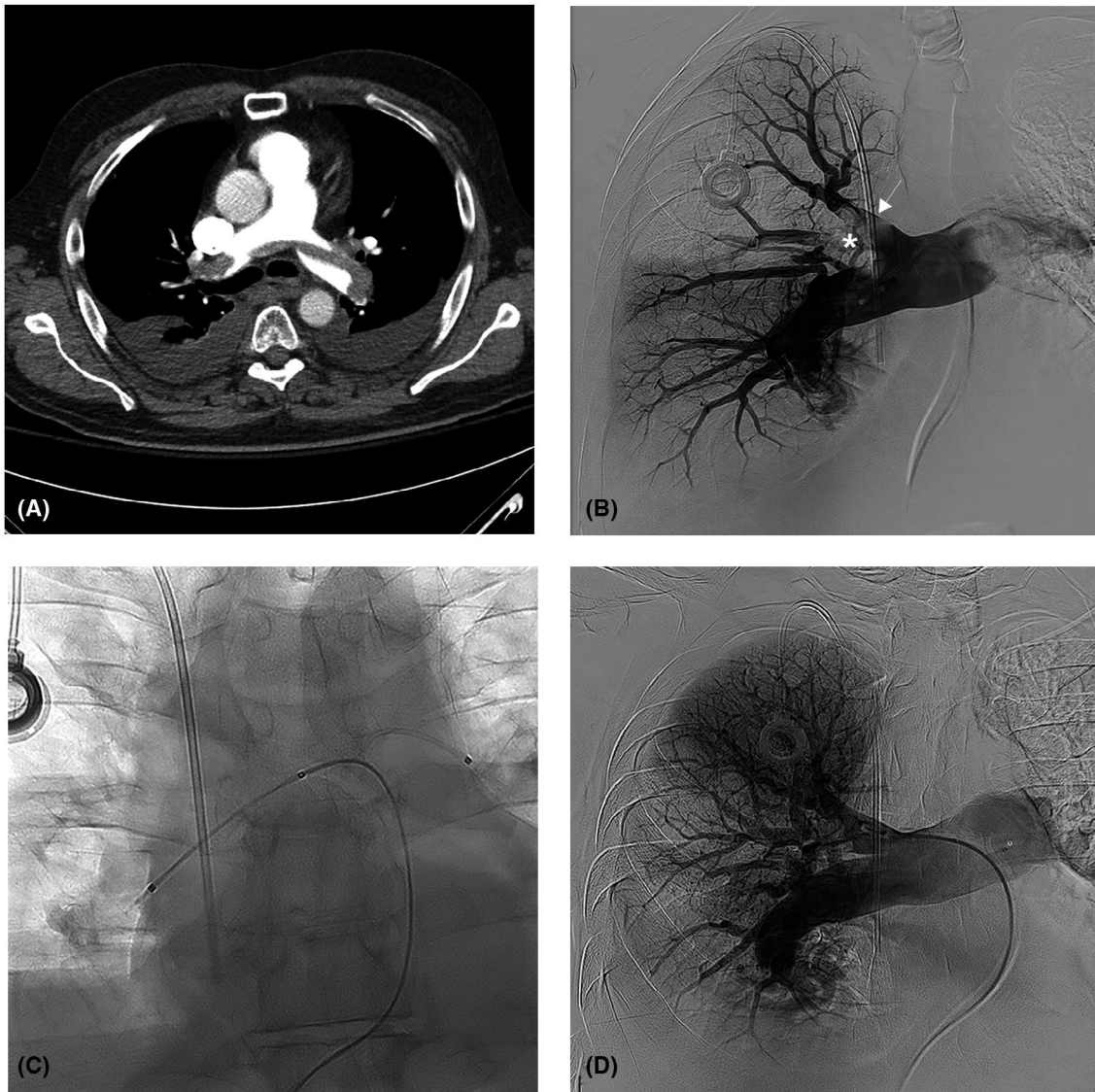


of two categories: mechanical thrombectomy or catheter-directed thrombolysis.

Increased pulmonary artery pressure resulting in cardiac dysfunction is the primary mechanism of morbidity in COVID-19 associated massive or submassive PE.<sup>78</sup> The goal of CDT is to improve cardiac output by reducing thrombus burden and restoring pulmonary perfusion.<sup>79</sup> Proposed algorithms for the treatment of PE in COVID-19 have closely reflected prior consensus guidelines for CDT.<sup>37,78,80-83</sup> However, the multidisciplinary National Pulmonary Embolism Response Team Consortium advises a conservative approach leaning

towards medical management, given the risk of nosocomial spread and uncertain benefits of invasive therapies. Invasive procedures, including CDT, should be considered for massive PE with contraindication to systemic thrombolysis and submassive PE with impending clinical decompensation and contraindication to systemic thrombolysis. Any planned intervention requires multidisciplinary discussion with benefit and risk analysis.<sup>72</sup>

The decision to proceed with thrombectomy or mechanical thrombolysis in COVID-19 patients requires disease-specific considerations. Single session thrombectomy (Figure 4) will reduce the



**FIGURE 5** 55-year-old man with a negative viral test but highly suspicious changes on chest CT for COVID-19 (not shown). A, CTPA shows a large saddle embolus in bilateral main pulmonary arteries. B, Initial pulmonary arteriography shows filling defects in the right lobar arteries and corresponding abnormal perfusion, predominantly involving the right upper lobe (arrow) and right middle lobe (asterisk). C, 5-French Cragg-McNamara infusion catheters positioning within the right and left main pulmonary arteries. D, Completion pulmonary arteriography shows a reduction in thrombus burden and improved lung perfusion, particularly in the upper and middle lobes. Also noted are areas of persistent diminished perfusion in the lower lobe compatible with subsegmental emboli. Postintervention, the patient had a decrease in mean pulmonary arterial pressure consistent with hemodynamic improvement. However, shortly afterward, comfort care was provided due to progressive clinical deterioration due to extensive comorbidities and an unfavourable prognosis

duration of staff exposure and conserve personal protective equipment (PPE) compared to multisession thrombolysis. Pulmonary artery pressure monitoring in the ICU with catheter removal after improvement may eliminate the need for multiple sessions and follow-up angiography. Patient positioning during catheter-directed thrombolysis may present challenges concerning rapid changes in ventilation requirements and positioning in critically ill COVID-19 patients. Furthermore, thrombocytopenia is common in COVID-19, and the administration of thrombolytic agents in this setting increases bleeding risk and can itself worsen the hematologic profile.<sup>82</sup> Mechanical thrombectomy is also favoured over catheter tPA thrombolysis for patients requiring extracorporeal membrane (ECMO) oxygenation due to the increased bleeding risk associated with ECMO.<sup>84</sup> However, the use of smaller catheters for thrombolysis allows access through alternatives sites, such as the popliteal vein, which may be necessary for COVID-19 patients requiring prone positioning for optimal ventilation (Figure 5).

## 4 | INFECTION CONTROL CONSIDERATIONS

Appropriate staff education regarding infection control measures and the centralisation of PPE will help ensure workers are equipped to care for the surge of COVID-19 patients safely.<sup>85,86</sup> Niu et al defined three levels of infection protection measures in a radiology department. Besides strict hand hygiene, basic (Level I) protection for workers in the general areas for individuals without fever includes disposable protective caps, disposable medical surgical masks, working clothes, and disposable latex gloves if necessary. Advanced (Level II) protection for working in the locations of patients with suspected or confirmed COVID-19 infection includes cap, N95 masks or higher-level protective face mask, goggles/protective screen, medical protective clothing, and disposable shoe covers. Finally, higher (Level III) protection includes a protective screen, comprehensive respiratory protector, or positive pressure headgear applied in severe cases when long-term exposure to high aerosol concentrations in a relatively closed environment is expected.<sup>87</sup>

Nosocomial infection is an unfortunate risk when caring for COVID-19 patients. If possible, institutions should try to dedicate specific CT scanners to allow for quick diagnoses, avoid cross infections, and ensure adequate isolation and control of suspected cases.<sup>85,87,88</sup> Deep cleaning of hospital equipment is required after caring for patients with COVID-19. Tables, detectors, and gantries are areas that commonly come into contact with patients and require specific attention. Similarly, gamma-cameras must undergo decontamination, especially if aerosolisation is suspected following VQ scanning.<sup>85,87,88</sup> Modifications in portable chest radiographic techniques, such as acquiring images through a glass window from the hallway outside the patient room, may be necessary.<sup>89</sup> Equipment covers for US machines and probes should be utilised, followed by proper cleaning.<sup>73</sup> Improved indoor air circulation is important for limiting the spread of viral particles and may include the use of

high-efficiency particulate air filters.<sup>85-88</sup> After imaging, approximately 30 min to 1 h should be allowed for room decontamination and passive air exchange.

The American College of Radiology (ACR) provides guidelines regarding the safe resumption of routine radiology care. Overall, the risks of healthcare-acquired COVID-19 must be weighed against the risks of delaying radiology care. Additional safety measurements include screening all patients, workers, and visitors for COVID-19 symptoms; enacting social distancing measures such as limiting the number of patients in waiting rooms with modified scheduling; and creating flags in the electronic medical record with current or recent or suspected COVID-19 illness. The ACR recommends a four-tiered approach for the safe resumption of nonurgent radiology care.<sup>90</sup> The Centers for Disease Control and Prevention (CDC) continually updates safety recommendations for healthcare providers and facilities on their website. Some of these recommendations include implementing telehealth, universal use of PPE, and targeted SARS-CoV-2 testing.<sup>91</sup> Unfortunately, no one-size-fits-all approaches and strict adherence to local and institutional policies aligned with CDC guidelines may further minimise the infection rate in the work environment.<sup>88</sup>

## 5 | CONCLUSION

In summary, PE is a commonly encountered complication in COVID-19 patients, although the exact prevalence and clinical outcomes remain unclear. COVID-19 associated PE may have unique pathophysiology differing from traditional PE. The role of D-dimer levels in the detection and management of these patients is also unclear. Although chest CT is not recommended to screen or diagnose COVID-19 infection, CTPA plays an essential role in the context of suspected COVID-19 associated PE since VQ scintigraphy and ultrasound may not be possible. Appropriate modifications of imaging protocols may be needed while managing patients with COVID-19 associated PE. CDT can play a role in managing patients with COVID-19 associated massive or submassive PE, although currently, medical management is considered first line. Adhering to local and institutional infection control measures and policies aligned with CDC guidelines would help to minimise COVID-19 spread among patients, healthcare providers, and reduce equipment contamination in the radiology department.

## DISCLOSURES

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## DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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