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CORRESPONDENCE

Re: Extent of pulmonary thromboembolic disease in patients with COVID-19 on CT: relationship with pulmonary parenchymal disease

Sir—We recently reported an overall incidence of pulmonary thromboembolism (PTE) of 44% in hospitalised patients with COVID-19 (1). It has been observed that for a significant number of patients, the symptoms of respiratory dysfunction persist beyond the acute phase of the disease (2). The aim of this letter is to report the incidence of PTE in hospitalised patients with severe COVID-19 who have persistent respiratory illness well after their initial presentation. This follow-up project has the same ethics approval as the original study.

We retrospectively reviewed hospitalised COVID-19 patients from our initial cohort (1) who attended a specialist respiratory follow-up clinic 3–6 months after discharge and met the criteria for follow-up clinical assessment (Fig. 1). From the 1,200 patients admitted to our hospital between 23 March to 19 April 2020, 201 patients met the criteria for a follow-up review (Fig. 1). A medical assessment including a standardised symptom questionnaire and 1-minute sit-to-stand exercise desaturation test was performed in order to determine the requirement for further CT imaging (Table 1). Ventilation–perfusion single-photon-emission computed tomography (SPECT) was performed in selected patients with high clinical suspicion for PTE with incongruous imaging findings, who had negative or indeterminate CTPA on follow-up.
One hundred and sixty-six patients attended, including 106 men (64%), with a median age of 57 years (range 25–84 years). Thirty-five patients did not attend. Eighty-nine of the 166 (53.6%) patients (median age: 56 years, range 25–84 years) met the criteria for CT chest imaging (Table 1); 66/89 (74%) of the patients had unenhanced CT chest followed by CTPA, whereas 23/89 (26%) of patients had unenhanced CT chest only.

Thirty-six patients out of 166 (21.7%) had been diagnosed with PTE during the acute phase of their illness. Seventeen of the 36 patients had repeat CTPA during follow-up. Nine of the 17 had complete resolution of PTE and the remaining eight patients all showed reduced clot burden. The study design and outcome are illustrated in Fig. 1. The remaining 19 patients from the 36 patients who had PTE during their initial hospital admission did not meet the criteria for follow-up.

One patient out of the 49 patients not previously diagnosed with PTE was diagnosed with new-onset lobar PTE during the follow-up. The remaining 48 patients had negative CTPA during follow-up; 12/48 (25%) of these patients were referred for SPECT imaging due to high clinical suspicion for PTE. Two of the 12 showed peripheral perfusion defects suggestive of distal PTE and were subsequently treated with anticoagulation therapy. Therefore, the overall incidence of PTE in our cohort of patients who attended follow-up clinic without previously known PTE was 6.1% (3/49).

Pulmonary parenchymal disease was assessed in 89 patients who underwent CT imaging, 13/89 scans (14.6%) were normal, 22/89 scans (24.7%) showed <50%
parenchymal involvement, and 54/89 scans (60.7%) showed ≥50% parenchymal abnormalities.

This observational study confirms that in patients recovering from severe COVID-19 who remain symptomatic on follow-up, the incidence of new PTE was significantly lower at 6.1% compared to 44% reported by this group during the acute phase of the disease. Persistent signs and symptoms of respiratory dysfunction in patients recovering from severe COVID-19 pneumonia are therefore unlikely to be due to PTE, but more likely as a result of persistent lung parenchymal disease with ≥50% disease extent. In those patients with persistent respiratory symptoms where the CT was normal or <50% of lung parenchyma was involved, we postulate the symptoms could be result of pulmonary vasculopathy. Future research in this domain is required to evaluate this hypothesis.

SPECT has been used to diagnose PTE during the COVID-19 pandemic in patients who have had non-diagnostic CTPA or where CTPA is contraindicated (3). To the authors’ knowledge, there are no studies in the current literature assessing the value of SPECT imaging in patients with COVID-19 who have had a negative CTPA. Nevertheless, in the present cohort, two additional cases with potential distal PTE were diagnosed with SPECT imaging. It is worth highlighting that the findings on the SPECT imaging in these two cases may not be new. Both patients received anticoagulation therapy based on a multidisciplinary team decision taking into consideration patients’ clinical presentation and imaging findings. It is of particular interest to repeat SPECT imaging in these patients to assess response to anticoagulation therapy upon completion. Our observations also suggest that
anticoagulation therapy is an effective treatment in COVID-19 patient with PTE given that over half of the patients with known PTE in our cohort showed complete or near-complete resolution of pulmonary thromboembolic disease.

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Figure 1. Consort diagram illustrating the process of selecting patients for the analysis.

Table 1. Indications for CT and CTPA imaging in patients recovering from severe COVID-19

| Indication for CT of the thorax ± CTPA                                                                 |
|---------------------------------------------------------------------------------------------------------|
| • Increased dyspnoea since hospital discharge OR                                                       |
| • Desaturation ≥4% on exercise or persisting dyspnoea resulting in reduced exercise tolerance level compared to pre-COVID level OR |
| • Persisting chest radiography abnormalities at 6 weeks (greater than 1/3 lung involvement) OR         |
| • Chest radiography appearances suggestive of fibrotic lung damage OR                                  |
| • Less than 50% improvement in chest radiography abnormalities at 6 weeks OR                           |
| • Patients already on anticoagulation therapy for PTE during initial hospital admission showing worsening of symptoms warrant repeated imaging to exclude worsening of clot burden |

Indication for CT thorax only (for those who met the above criteria, but CTPA is not required for the following reasons)

|                                                                                                               |
|----------------------------------------------------------------------------------------------------------------|
| • Already on anticoagulation therapy with symptoms suggesting persistent parenchymal disease               |
| • Symptoms predominately suggest parenchymal disease rather than PTE                                       |
| • Contraindication to intravenous iodine contrast medium                                                   |

CT computed tomography; CTPA, CT pulmonary angiography; PTE, pulmonary thromboembolism.
Declaration of interests

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐ The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: