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Clinical Paper

Chest computed tomography and plain radiographs demonstrate vascular distribution and characteristics in COVID-19 lung disease – a pulmonary vasculopathy

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ABSTRACT

Introduction

Early in the COVID-19 pandemic, CT was demonstrated as a sensitive tool for diagnosing COVID-19. We undertook a detailed study of CT scans in COVID-19 patients to characterise disease distribution within lung parenchyma, respiratory airways, and pulmonary vasculature, aiming to delineate underlying disease processes.

Methods

We characterised acute phase chest CT of 40 participants with COVID-19 from the REACT study, 31 with CT pulmonary angiography (CTPA), 4 with intravenous contrast enhanced CT and 5 with non-intravenous contrast enhanced CT. Participants had neither been vaccinated nor received systemic steroids. We further correlated the distribution of lung parenchymal damage on CT with contemporaneous chest radiographs.

Results

Parenchymal lung damage was found in all subjects. However, airways inflammation was present in only 23% (9) and limited to small areas. Notably, vascular abnormalities were dominant and characterised by dilated peripheral pulmonary vessels supplying areas of lung damage in a gravity-dependent distribution bilaterally in 95% (38), basally in 90% (36), peripherally in 92.5% (37), and posteriorly in 90% (36). Macrothrombosis was demonstrated in 23% (7) of CTPAs. Wedge-shaped peripheral lung damage, resembling areas of pulmonary vascular congestion, were distinct in 53% (21) with or without visible macrothrombosis. Pleural effusions were seen in 28% (11). Notably, lung opacification distribution in 98% of the plain radiographs matched distribution on CT (39).

Conclusion

Our study frames COVID-19 as a pulmonary vasculopathy rather than a more conventional pneumonia which may be important not only for guiding mechanistic study design but also for the development of novel targeted therapeutics.

Key Words: COVID-19; CT imaging; Chest Radiographs; Vasculopathy; Respiratory Infections

INTRODUCTION

The importance of CT was highlighted early in the pandemic when it was established to be sensitive for diagnosing COVID-19 in the absence of polymerase chain reaction (PCR) testing, even in asymptomatic patients[1,2]. Lung damage with ground glass opacities (GGOs) was quickly identified as a typical diagnostic feature of COVID-19[3-6]. However, at that time the main focus was on making a diagnosis and little consideration was given to the underlying disease processes responsible for the lung damage.

Lung damage with GGOs or consolidation has been widely attributed to alveolar cellular pathology[5] and thromboembolic phenomena were initially considered to be complications of a respiratory tract infection in patients, rather than an intrinsic part of COVID-19 disease itself[4]. The term *COVID-19 pneumonia* is still widely used by many investigators. However, GGOs are a non-specific feature of lung damage and other causes are possible, including vascular phenomena and interstitial oedema[1]. Pulmonary vascular congestion with thrombi of small peripheral vessels can give rise to GGOs on CT, such as is found in peripheral wedge-shaped pulmonary infarcts in the context of conventional pulmonary thromboembolic disease. However, despite emerging histological evidence of vasculopathy being a typical finding at autopsy in the context of COVID-19[7,8], the contribution of vasculopathy to CT and radiographic findings is not fully delineated and COVID-19 is still viewed by some as more similar to a conventional respiratory pneumonia than primarily a pulmonary vasculopathic disease.

Therefore, we undertook a study to deeply characterise CT scans of inpatients with acute COVID-19 to confirm the extent to which disease affects the respiratory airways, the pulmonary vessels, and the lung parenchyma. In doing so,

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we aimed to gain insights into the pathological processes responsible for radiologically visible abnormalities and the nature of mechanistic processes in disease pathogenesis. We further correlated the distribution of lung damage on CT with plain chest radiographs, a more readily available resource in the emergency setting.

METHODS

Study design

Data were collected for COVID-19 positive patients as part of the Research Evaluation Alongside Clinical Treatment in COVID-19 (REACT COVID-19) observational and biobanking study[9-11]. Participants in this present study were admitted to a University Hospital in the UK between 3rd March and 10th November 2020. This was prior to the widespread availability of vaccination. Dexamethasone was introduced into clinical guidance in June 2020, but at the time of imaging participants included within our cohort had not been treated with dexamethasone.

Participants

Participants were included in the study if they tested positive for SARS-CoV-2 on real time reverse transcription PCR from a nasopharyngeal swab and had a chest CT (n=54). All requests for CT stated clinical indications relating to investigating chest symptoms of COVID-19 and no history of other infection to explain symptoms. None of the participants (smokers or non-smokers) were stated to have a history of pre-existing pulmonary vascular disease. Participants with major pre-existing lung or heart disease and those imaged for reasons other than to investigate COVID-19, such as trauma, were excluded (n=13), or those with scans of inadequate diagnostic quality (n=1). A total of 40 participants met the inclusion/exclusion criteria and were included in this study. 31 participants were imaged with CT pulmonary angiography (CTPA), 4 with intravenous contrast enhanced CT (arterial phase), and 5 with non-intravenous contrast enhanced CT.

Variables

Core demographic information (including, age, sex, body mass index, smoking history and COVID-19 symptom onset date) was collected as part of this study, alongside other data collected as part of routine clinical care (**Table 1**). This information, alongside CT scans and radiographs, were compiled into a database. Participant records, including radiological records, were continuously updated during hospital stay and their follow-up period.

CT Analysis

Detailed analysis of CT included the following categories: distribution of lung parenchymal damage; characteristics of parenchymal lung damage; respiratory phenomena (central and distal airways were considered separately); vascular phenomena; non-specific features in the lungs; and other features in the chest associated with pneumonias. All CT and plain radiographic images were analysed independently by two radiologists (one specialist cardiothoracic radiologist and one general radiologist with specialist interest in chest imaging, both with 13 years' experience). Definitions for all radiographic phenomena were agreed prior to the study, except for the 'vascular tree-in-bud' sign (highlighted in the results). CTPAs were assessed to determine the presence of macroscopic pulmonary arterial filling defects. Where there was disagreement, consensus was gained following discussion.

Ethics statement

Ethical approval was obtained from the HRA Specific Review Board for waiver of informed consent for the database-only cohort; the procedures conform with the Declaration of Helsinki. The study design, protocol, and patient-facing documentation for the biobanking arm of the study have been approved by the regional Ethics Committee as an amendment to the University Hospital National Institute for Health Research Clinical Research Facility-managed Research Biorepository.

Outcome Measures

CT lung parenchymal damage characterisation

Areas of lung parenchymal damage were defined by the presence of ground glass opacities (GGOs) or consolidation. If both GGOs and consolidation were present we determined whether they were equal in their contribution to overall lung damage, or which was dominant. Other lung parenchymal changes were also recorded including lobar consolidation, and the reverse-halo sign (atoll sign)[12] which, for the purposes of characterisation, we considered as a non-specific feature of parenchymal damage[13].

Distribution of lung parenchymal damage was recorded as unilateral or bilateral. Bilateral disease was defined as any amount of acute parenchymal damage in both lungs. The predominance of disease distribution was also recorded as upper versus basal, anterior versus posterior, and central versus peripheral. Perihilar lung damage was considered central, and disease distributed in the subpleural areas was considered peripheral. The posterior and peripheral segments of the upper lobes were also considered to contribute to this overall pattern of disease distribution if they were involved predominantly compared to their adjacent more anterior segments.

CT phenomena affecting the respiratory airways

Observations in the central and peripheral airways – bronchial wall thickening centrally (tracheal or bronchial) and peripherally (segmental or subsegmental) – were recorded separately. Mucous secretion plugging was documented to be present if either central or peripheral. Subsegmental and distal bronchioles were also assessed for presence of

the 'respiratory tree-in-bud' sign – a sign of small airways inflammation (bronchiolitis)[14,15].

CT phenomena affecting the pulmonary vessels

We documented the presence of dilated pulmonary vessels, reported to be a key feature of COVID-19[16]. Both arteries and veins were considered dilated if larger than expected for the location in the vascular tree, and their association with areas of lung parenchymal damage was documented. We also documented the presence or absence of the 'vascular tree-in-bud' sign, reported as a specific feature of COVID-19 lung disease[17].

CTPAs were assessed for evidence of macrothrombosis (pulmonary embolus or in situ thrombus), as defined by visible pulmonary arterial filling defects. We also looked for the presence of wedge-shaped areas of sub-pleural parenchymal lung damage resembling areas of pulmonary vascular congestion, analogous to the morphology of pulmonary infarcts found in the context of conventional pulmonary thromboembolic disease, and not thought to be due to a cause other than acute COVID-19, such as fungal infection, bacterial septic emboli or neoplasm.

Other CT features

The presence or absence of pleural effusions (unilateral or bilateral), thoracic lymph node enlargement and any other lung parenchymal or pleural abnormalities were also recorded.

Correlation of CT and chest radiographic findings

CT lung parenchymal disease distribution was subsequently correlated with lung shadowing on plain radiographs, both those most contemporaneous to the CT and, if different from the most contemporaneous, those obtained on presentation to the Emergency Department. Severity and any change in severity was observed in accordance with the standard scoring system in operation clinically (**Box 1**).

Box 1

Chest radiograph severity scoring system

Normal = no abnormality

Mild disease = lung opacification affecting <25% of lung area

Moderate = lung opacification affecting 25-50% of lung area

Severe = lung opacification affecting >50% of lung area

Distribution was assessed as above, with the caveat that frontal plain chest radiographs cannot be used to determine anterior versus posterior distribution of disease.

RESULTS

Cohort characteristics

40 subjects were included within this study (**Table 1**). 23 were male (57%) and the median age was 61 (interquartile range (IQR) 54, 70). The majority were never-smokers (23, 58%). 3 subjects (8%) had been prescribed inhaled corticosteroids prior to scanning, but none had received systemic steroids or a COVID-19 vaccination. 31 participants had a CT pulmonary angiography (CTPA), 4 had a contrast enhanced CT (arterial phase), and 5 had a non-contrast CT. 23/31 of those with a CTPA had already received prophylaxis doses of parenteral anticoagulants (commencing 1-17 days prior to scanning). The majority of subjects had both raised D-dimers (86%) and raised fibrinogen (86%). CRP was raised in 37 participants (92.5%). 33 participants (75%) required oxygen support to maintain oxygen saturations >94%.

CT distribution of lung parenchymal damage

Distribution of lung damage (GGO and/or consolidation) was dominantly bilateral (95%), basal (90%), peripheral (92.5%), and posterior (90%). In the 2 patients who had unilateral disease both had limited lung damage which was confined only to a small area. Where a basal or peripheral dominance was not observed, widespread disease was present throughout both lungs, so no dominance of distribution was distinguishable. 10% of scans (4) in which posterior disease was not dominant showed uniform lung damage, which was both anterior and posterior, so no dominance was distinguishable. No scans demonstrated lung damage dominantly in an upper, central, or anterior distribution.

CT characteristics of lung parenchymal damage

Lung parenchymal damage was present on all CT scans. 15% of scans demonstrated GGOs without consolidation and 5% showed consolidation without GGOs. 80% of CT scans (n=32) showed both GGOs and consolidation **(Fig. 1).** Of those 32 scans, GGOs were dominant over consolidation

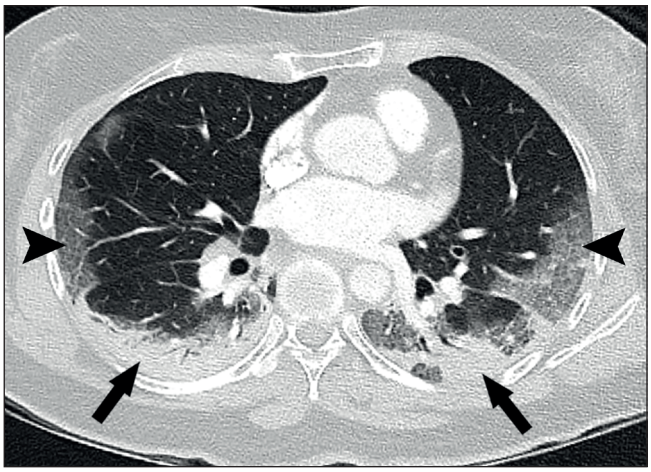

Figure 1
CT chest of a patient with COVID-19 lung disease showing areas of consolidation (arrows) and GGOs (arrowheads) in a peripheral, posterior and basal distribution bilaterally.

Table 1: Patient demographics according to cohort

	Total n = 40
Age, median (IQR)	61 (54, 70)
Male/Female, (% Male)	23/17 (57)
Smoking History, Current/ex/never, n (%)	2/15/23 (5/37.5/57.5)
Hypoxic on air (oxygen saturation of <94%) or requiring oxygen support, n (%)	33 (75)
Number who received prophylactic parental anticoagulation prior to scan, n (%)	24 (60): enoxaparin, 23 (58); apixaban 1 (3)
Use of Inhaled Corticosteroids, n (%)	3 (8)
Median interquartile range (IQR) timeframe (in days) from admission to CT scan	7.4 (1, 14)
CRP mg/L, median (IQR)	129.0 (40, 181)
Creatinine µmol/L, Median (IQR)	75 (64, 101)
D-dimer ng/mL, Median (IQR)	552 (335, 1508)
Fibrinogen g/L, Median (IQR)	7.8 (6, 8)

in 63% (20/32, 50% of total 20/40), dominant consolidation in 19% (6/32, 15% of total 6/40), and equal contributions to parenchymal lung damage due to GGOs and consolidation in 19% (6/32, 15% of total 6/40). Therefore, GGOs were the dominant or only form of lung damage in 65% (26). Consolidation was the dominant or single form of lung damage in 20% (8).

CT phenomena affecting the respiratory airways

Anatomical elements of the macroscopic airways (trachea, major bronchi, lobar bronchi, segmental, subsegmental bronchi, or distal airways) showed abnormality on 23% of scans (9) limited only to small areas. Of these 9 scans the central bronchial walls were thickened in isolation in 3 subjects, the peripheral bronchial walls were thickened in isolation in 1 subject, and both were thickened in 3 subjects. Segmental bronchiectasis was observed in 2 subjects. Neither of these 2 subjects demonstrated signs of acute inflammation within the bronchiectatic airways (no bronchial wall thickening or mucous plugging). Bronchiolectasis with airways traction was also observed in two subjects but without bronchial wall thickening.

Inflammatory phenomena affecting the respiratory airways were not widespread or the dominant pattern of disease in any subject and if present were limited to only a small area of lung (maximum of two lung segments). Significantly, respiratory tree-in-bud phenomenon, a sign usually ascribed to acute small airways inflammation (bronchiolitis) and commonly seen in influenza, was completely absent from any areas of the lungs in all subjects.

CT phenomena affecting the pulmonary vessels

Abnormal blood vessels supplying all areas of lung parenchymal damage were present on 95% (38) of scans, and in all subjects these dilated vessels were observed to be both pulmonary arteries and veins **(Fig. 2)**. In the two subjects in whom dilated vessels were not observed distinctly, one had severe consolidation and the other was considered to have resolving COVID-19 with development of organising pneumonia and early fibrosis, characteristic of intermediate to late phases of disease[18].

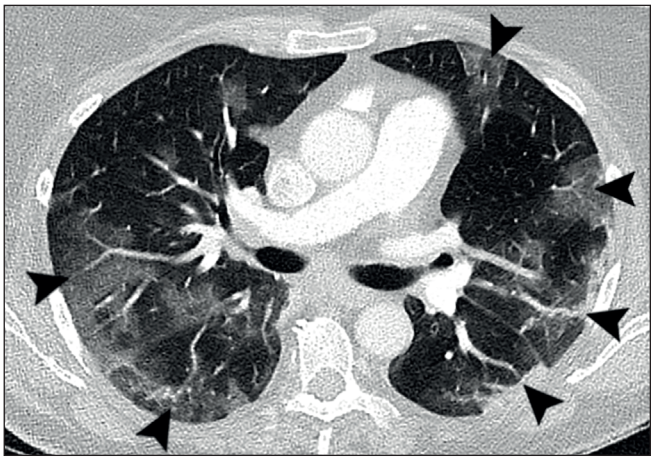

Figure 2
CT chest of a patient with COVID-19 showing areas of lung damage (GGO or consolidation) accompanied by dilated blood vessels (arrowheads). Analysis showed dilatation of both the pulmonary arteries and veins in these areas of lung damage.

We observed vascular tree-in-bud as a distinct phenomenon in

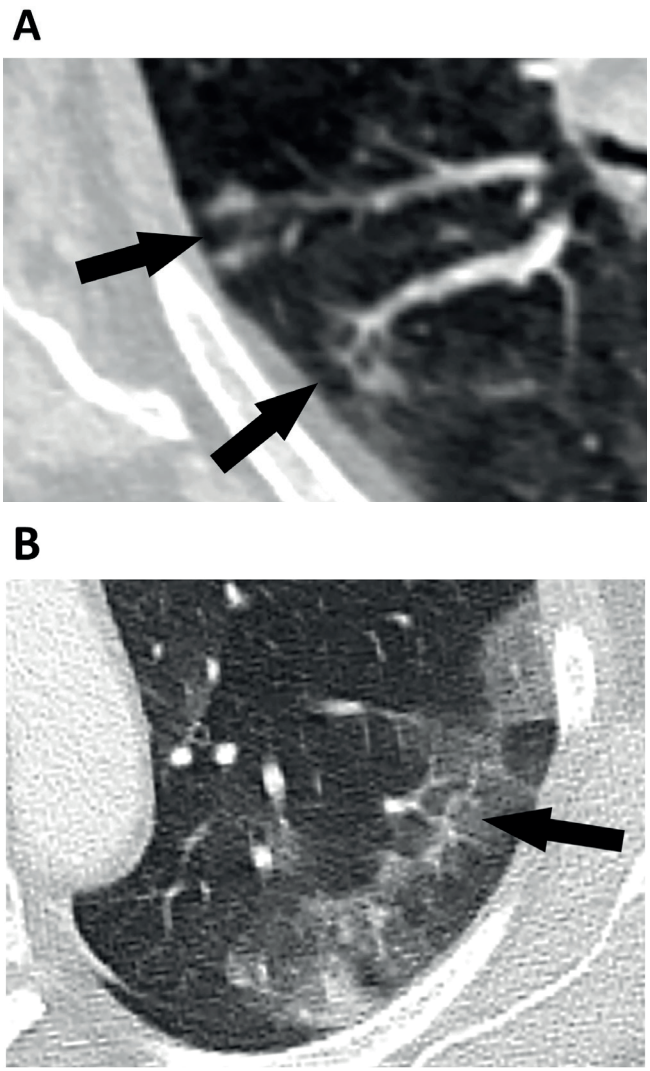

Figure 3
(A) CT chest in a patient with COVID-19 lung disease showing vascular tree-in-bud opacification in isolation of lung damage. **(B)** CT chest in a patient with COVID-19 lung disease showing vascular tree-in-bud opacification in an area of lung damage. This phenomenon was not considered a feature distinct from dilated vessels within GGOs.

areas not affected by lung damage in 5% (2/40) **(Fig. 3a)**. One observer documented its presence also within GGOs in 73% (29/40) **(Fig. 3b)**, but this was not considered to be a feature distinct from dilated vessels within GGOs. As no definition of this phenomenon was agreed prior to engagement in the study, we did not attempt to gain consensus on this feature and present variance in description for discussion below.

Thrombotic and other CT phenomena considered potentially vascular

7 of the 31 CTPA scans (23%) demonstrated macroscopic pulmonary arterial filling defects, indicating macrothrombotic disease. This was observed in 5 subjects who had already received prophylaxis doses of parenteral anticoagulants (commencing 1-17 days prior to scanning). Wedge-shaped areas of subpleural lung damage (GGOs or consolidation) were observed in 53% (21) **(Fig. 4)**. This phenomenon, which is reported elsewhere as representing the presence of microthrombosis in situ, or so-called *infarct pneumonia*[19], was present both with macrothrombosis (77% 16/21) or without visible macrothrombosis (19% 4/21). Macrothrombosis without a pattern of wedge-shaped subpleural lung damage was observed on one CT scan (5% 1/21). We also observed lung parenchymal damage (GGOs or consolidation) in a distinct pattern which spared the immediate subpleural lung in 35% (14), discussed below.

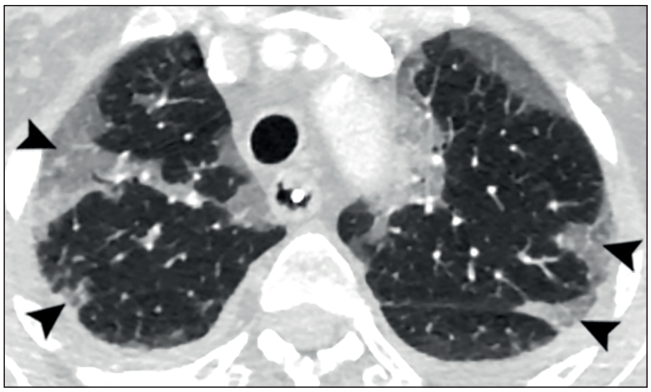

Figure 4
CT chest in a patient with COVID-19 lung disease showing multiple areas of wedge-shaped lung damage in the lung peripheries (analogous to pulmonary infarcts or areas of vascular congestion in the context of conventional pulmonary thromboembolic disease).

Other non-specific CT lung and pleural observations

Lobar consolidation was observed in 5% (2). Pleural effusions were observed in 28% (11) – 10% bilateral (4) and 18% unilateral (7). Enlarged thoracic lymph nodes (hilar and/or mediastinal) were observed in 33% (13) and the reverse halo sign in 5% (2). Other findings included subpleural atelectasis in 13% (5), a lung nodule with benign characteristics 3% (1), minor emphysema 5% (2) and calcified pleural plaque 3% (1). Pericardial effusion was not observed.

Comparison of CT with contemporaneous chest radiographs

To gain insights about COVID-19 processes underpinning lung opacification on chest radiographs, the distribution of disease recorded on the reference CT was compared with distribution of lung opacification observed on the most contemporaneous chest radiograph. Median time between reference CT and contemporaneous chest radiograph was 26.5 hours (IQR 7,69). 95% (38) of contemporaneous chest radiographs were abnormal. Indirect comparison of imaging modalities (CT versus contemporaneous chest radiograph) showed matching bilateral, basal and peripheral distribution of opacification in 98% (39) **(Fig. 5)**. The subject in whom lung damage distribution varied was an outlier with an interval from reference CT to contemporaneous chest radiograph of 360 hours and demonstrated improvement in lung damage.

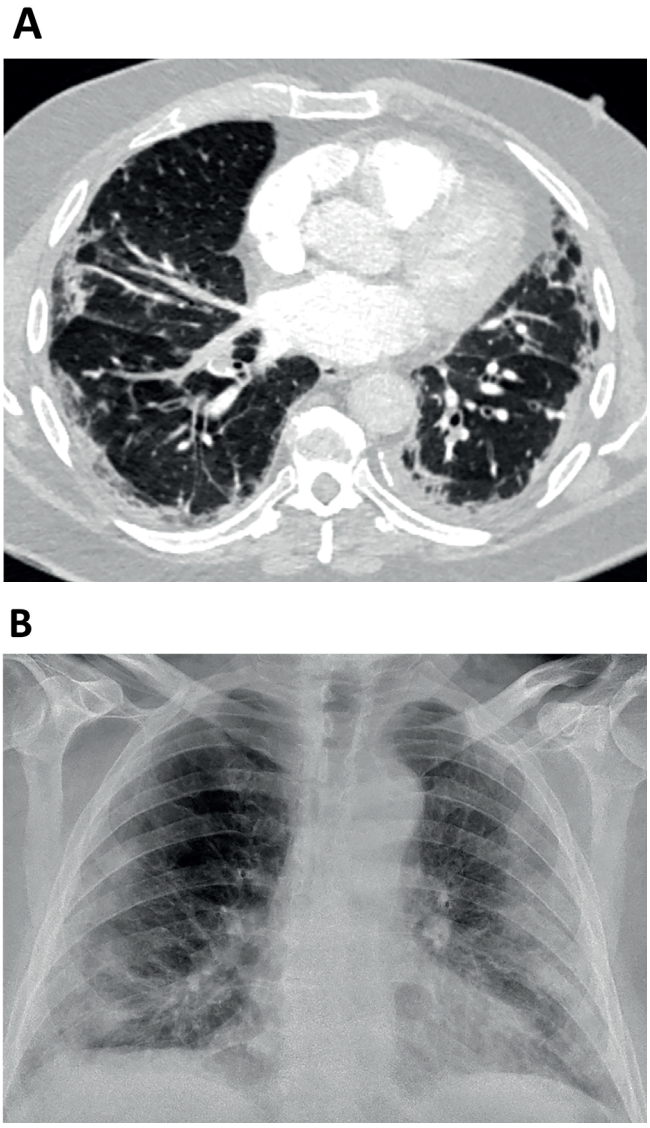

Figure 5
(A) CT and **(B)** contemporaneous chest radiograph in a patient with COVID-19 lung disease. The typical distribution of opacification due to lung damage shown on CT (bilateral, basal, peripheral, and posterior) is matched by bilateral, basal and peripheral distribution of opacification on the contemporaneous radiograph.

If different from the contemporaneous radiograph, the chest radiograph acquired closest to the time of admission to the Emergency Department was also assessed for disease severity. The contemporaneous radiograph was different from the admission radiograph in 23 subjects. Change in severity scoring was documented for these subjects. All but one subject demonstrated no change or worsening of severity scoring during admission until the point of CT scanning. This is predictable as the population studied all had the reference CT – a criterion for inclusion in the study – for the purpose of investigating the cause of worsening or persistence of symptoms. Significantly, although severity changed over time, the pattern of lung shadowing did not change in terms of dominant areas of distribution affected between admission versus contemporaneous radiographs. Below we discuss the significance of this observation in relation to clinical management of COVID-19 in the Emergency Department.

DISCUSSION

We undertook a detailed study to characterise chest CT scans of hospitalized patients with COVID-19 to determine distribution and characteristics of lung disease and involvement of the airways versus pulmonary vessels. We demonstrate that pulmonary vascular processes were dominant, and that lung damage (GGOs or consolidation) was characterised by dilated pulmonary vessels supplying all areas of lung damage in a distinctly vascular distribution. We further demonstrate that distribution of opacification on chest radiographs is analogous to distribution of lung damage visible on CT. Further understanding this correlation could provide insights for chest radiographs use in early clinical decision-making in the Emergency Department.

Within our cohort, we determine the presence of dilated blood vessels within areas of lung parenchymal damage (GGOs or consolidation) to be the hallmark feature of COVID-19 lung disease, rather than GGOs in isolation. These areas of lung damage were dominantly in the most vascularised gravity-dependent regions of the low-pressure pulmonary circulation; basal, peripheral, bilateral and posterior. These findings provide rationale for framing COVID-19 as a vasculopathic disease. It is interesting to note that this vascular distribution of lung damage also represents areas of the lung least accessible to an inhaled pathogen, making it possible to speculate that a vascular delivery of pathological viral components and their endovascular interaction could be contributing to this lung damage[20]. Future mechanistic studies are required to test this hypothesis.

There are various potential mechanistic explanations for our findings. For instance, dilated pulmonary vessels seen in COVID-19 are identical to arteriovenous shunts seen in pulmonary arterial hypertension[21] and could explain the clinical phenomenon of 'silent hypoxia' in COVID-19[22]. Microangiopathic phenomena and subsequent pulmonary vascular congestion could be a key mechanism driving the dilated peripheral vessels and associated lung damage seen in our study. Histopathological studies have demonstrated pulmonary vascular congestion with thrombi of small peripheral vessels to be typical in COVID-19 lungs. Autopsy findings in COVID-19 include microscopic clotting in small peripheral pulmonary vessels[7] (both in arterioles and venules[23]), immunothrombosis[24], endotheliitis[25], and platelet aggregation[26]. These phenomena visible histologically could be responsible for the vasculopathic lung damage demonstrated on imaging. Whichever mechanism is responsible, we consider the dilated pulmonary vessels to be intrinsically linked to underlying pathophysiology in the lung disease of COVID-19 and indicative of vasculocentric processes.

Over half of the cohort within our study had wedge-shaped lung damage in the lung periphery analogous to

pulmonary infarcts, regardless of the presence or absence of macroscopic arterial filling defects. This could be explained by pulmonary vascular congestion following thrombosis, which has a higher propensity to occur within small peripheral vessels rather than central vessels[27]. Ridge et al. identified wedge-shaped perfusion defects analogous of pulmonary infarcts in acute COVID-19 using Dual Energy CT[28]. Other studies compared pre-mortem CT studies with post-mortem histology and highlighted capillary dilatation, congestion and microthrombosis as drivers of lethal disease, and even revealed microvascular damage and thrombosis in areas of the lungs on autopsy which were normal on pre-mortem CT[29,30]. A further recent study using optical coherence tomography demonstrated *in vivo* microscopic distal pulmonary arterial thrombosis, even when CTPA was negative, in patients with acute COVID-19[31]. Therefore, our observations are in accordance with the findings of others that thrombotic phenomena are key in COVID-19 lung disease and differ in distribution compared with conventional thromboembolism[19,32,33] .

Diffuse alveolar damage (DAD), as found in autopsy studies of fatal COVID-19, has previously been taken to indicate that primary alveolar processes are driving disease. However, our study highlights that thrombotic and endothelial cell damage could explain the phenomena visible on imaging. Indeed, alveolar capillary endothelial cell damage is intrinsic to the definition of DAD[34]. Also, DAD is reported to be atypical in COVID-19 with airways containing fibrin[35]. In line with this concept of underlying microscopic thrombotic processes, a post-mortem study using hierarchical phase-contrast tomography (HiP-CT) demonstrated well-preserved alveolar structure with alveolar obstruction reported to be due to the presence of thrombi[36]. This aligns with our study which suggests that alveolar damage is not primarily due to airways inflammation, but rather by vascular-driven pathology in the lung peripheries.

Immunothrombosis (inflammatory-mediated clotting) has been proposed as an underlying mechanism of microthrombosis *in situ* in the context of COVID-19[24,32]. This pathological process could explain the vasculocentric distribution of lung damage and vasculopathic characteristics of disease observed in our study. The phenomenon of vascular tree-in-bud opacification is considered specific to acute COVID-19 and is thought to represent immunothrombosis[37]. Reference Figure 3A, our study identified this finding as a distinct entity separate from areas of lung parenchymal damage in 5% of subjects. Reference Figure 3B, furthermore, one observer considered it also to be present within areas of GGOs in 73%, broadly in line with others who report the finding in 64%[17]. However, when documented in the presence of GGOs, we did not consider vascular tree-in-bud opacification as a distinct phenomenon from dilatation of blood vessels within GGOs. Both phenomena are considered to represent vasculocentric pathology.

The distinct pattern of GGOs which spare the immediate subpleural lung observed in our study could also represent vasculopathic processes. This phenomenon is similar to the pattern seen in pulmonary haemorrhage[38], another feature described on autopsy in fatal COVID-19[23,39]. Nevertheless, we consider this a non-specific CT feature as it is observed in the context of acute respiratory distress syndrome (ARDS) of any cause[40]. We demonstrated a similar incidence of macroscopic pulmonary arterial filling defects relating to thromboembolic disease (23%) compared to some studies (22-37%)[41] but lower than in other studies (44%)[42].

In addition to the vasculocentric distribution and vasculopathic characteristics of lung parenchymal damage, our study demonstrates a striking lack of airways inflammation on CT, as would be expected in influenza or influenza-like pneumonias[43]. This paucity of airways disease confirms the findings of others which have suggested airways inflammation on CT to be inconsistent with the diagnosis of COVID-19[44]. Taken together, our findings challenge the prior notion of COVID-19 being a conventional respiratory pneumonia and highlights that the term *pulmonary vasculopathy* is a more accurate term to describe COVID-19 lung disease in the acute phase[45,46].

Correlation of contemporaneous radiographs with CT provides evidence that radiographic lung opacification is analogous to the lung damage associated with vasculocentric phenomena visible on CT in COVID-19 lung disease. This further highlights that plain chest radiograph opacification in the context of acute COVID-19 should not be considered to be due to a conventional respiratory pneumonia, which may later be complicated by vascular processes, but rather to represent the pulmonary vasculopathy itself. In view of the greater availability of chest radiographs and the lower exposure of radiation, future work elucidating these correlations could potentially inform early clinical decision-making pathways on patient presentation to the Emergency Department.

Our study was a single centre, relatively small study which aimed to deeply characterise CT scans of subjects with acute COVID-19 lung disease to generate insights into disease distribution and characteristics. In accordance with the CT scans studied, the number of matching chest radiographs was also relatively small. Furthermore, due to the broad inclusion criteria of all suitable patients with an appropriate CT scan, CTs were obtained at different disease stages, thus limiting assessment of some CT features. A variety of CT techniques were included in the study, necessitating the caveat that CTPA can occasionally exaggerate GGOs. Our study used participants admitted in 2020, before the widespread use of vaccination and dexamethasone treatment, thus providing insights about the native disease phenomena prior to influence by these interventions. This, and the emergence of later variants, potentially limits the clinical applicability of our findings as Omicron is considered to cause a different phenotype of radiological disease from Delta and pre-Delta variants[47]. However, with the continual emergence

of new COVID-19 strains, and the burden of long COVID, understanding the acute and lasting impact of the pulmonary vasculopathy could be pivotal.

Conclusion

Our study of chest CT findings highlights COVID-19 as a pulmonary vasculopathy, with the distribution and characteristics of COVID-19 lung disease being dominantly vasculopathic. We further show a lack of visible airways inflammation in this cohort, indicating that COVID-19 lung disease is not a conventional respiratory pneumonia.

STATEMENTS

Funding Statement

No funding was received for this work.

Patient and Public Involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research

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