



Deposited via The University of Sheffield.

White Rose Research Online URL for this paper:

<https://eprints.whiterose.ac.uk/id/eprint/170935/>

Version: Published Version

Article:

Shahin, Y., Rajaram, S., Parkash, V. et al. (2021) Patterns of thromboembolic pulmonary vascular disease in COVID-19. *Pulmonary Circulation*, 11 (1). ISSN: 2045-8940

<https://doi.org/10.1177/2045894020979198>

Reuse

This article is distributed under the terms of the Creative Commons Attribution (CC BY) licence. This licence allows you to distribute, remix, tweak, and build upon the work, even commercially, as long as you credit the authors for the original work. More information and the full terms of the licence here:

<https://creativecommons.org/licenses/>

Takedown

If you consider content in White Rose Research Online to be in breach of UK law, please notify us by emailing eprints@whiterose.ac.uk including the URL of the record and the reason for the withdrawal request.

Patterns of thromboembolic pulmonary vascular disease in COVID-19

Yousef Shahin^{1,2} , Smitha Rajaram², Vivak Parkash¹, James M Wild^{1,3}, David G Kiely^{1,4} and Andrew J Swift^{1,2,3}

¹Department of Infection, Immunity and Cardiovascular Disease, University of Sheffield, Sheffield, UK; ²Department of Clinical Radiology, Sheffield Teaching Hospitals, Sheffield, UK; ³INSIGNEO, Institute for In Silico Medicine, University of Sheffield, UK; ⁴Sheffield Pulmonary Vascular Disease Unit, Royal Hallamshire Hospital, Sheffield, UK

Abstract

SARS-CoV-2 (COVID-19) is associated with increased thrombosis. Here, we demonstrate patterns of pulmonary vascular disease in COVID-19 including classical acute pulmonary embolism and subsegmental perfusion defects in the absence of acute pulmonary embolism suggestive of microvascular thrombosis.

Keywords

coronavirus, CT-LSIM, iodine subtraction mapping, pulmonary embolism, microvascular thrombosis

Date received: 29 June 2020; accepted: 13 November 2020

Pulmonary Circulation 2021; 11(1) 1–3

DOI: 10.1177/2045894020979198

Introduction

Severe acute respiratory syndrome (SARS) caused by the coronavirus SARS-CoV-2 (COVID-19) has a high mortality due primarily to respiratory failure. Recent studies have highlighted increased thrombosis in COVID-19.¹ Extensive microvascular thrombosis has been noted at post-mortem and high rates of pulmonary embolism (PE) diagnosed using computed tomography pulmonary angiography (CTPA),² alongside lung parenchymal changes.³ There has been increasing interest in the patterns of pulmonary vascular involvement due to COVID-19 and concern that perfusion abnormalities may represent in-situ thrombosis that may not be appreciated on standard CTPA. The British Thoracic Imaging Society Guidelines recommend unenhanced pulmonary angiography and CTPA. This protocol facilitates lung subtraction iodine mapping (CT-LSIM) for lung perfusion, a clinically sensitive tool in PE. We report the first CT-LSIM images in COVID-19.

Materials and methods

At our institution, 10 patients (mean age (SD) 70 (16), 40% female) with COVID-19, confirmed on reverse transcription polymerase chain reaction (RT-PCR), underwent CTPA and CT-LSIM for suspected acute PE based on clinical

assessment and elevated d-dimer levels (Table 1). Analysis of CT images was approved by our institution review board.

Results

Three patients had confirmed PE on CTPA and CT-LSIM (one case is shown in Fig. 1 (1a, 1b, 1c)). Another patient had perfusion defects on CT-LSIM without visible PE where CT-LSIM showed subsegmental perfusion defects without visible PE (Fig. 1 (2a, 2b, 2c)). Six patients did not have perfusion defects on CT-LSIM.

Discussion

Distinct from classical thromboembolic PE, a high proportion of in situ pulmonary arterial thrombosis exists in COVID-19, and the pathophysiology is not fully understood.⁴ Here, we demonstrate patterns of pulmonary vascular disease in COVID-19 including (i) classical acute PE with central clot associated with lung infarction and (ii)

Corresponding author:

Yousef Shahin, Department of Infection, Immunity and Cardiovascular Disease, University of Sheffield, Glossop Road, Sheffield S10 2JF, UK.

Email: y.shahin@sheffield.ac.uk



Table 1. Patients' characteristics.

Characteristic	Total (n = 10)	No pulmonary vascular changes CTPA/CT-LSIM (n = 6)	Pulmonary vascular changes CTPA/CT-LSIM (n = 4)
Age, years	70 (16)	73 (17)	68 (18)
Female, n	4	3	1
Race or ethnic group, n			
White	8	4	4
Black	1	1	0
Other ethnicity	1	1	0
Comorbidities, n			
Obesity	2	1	1
Smoker	3	2	1
Immunosuppression	2	1	1
Malignancy	1	0	1
Chronic obstructive pulmonary disease	1	1	0
Asthma	2	1	1
Ischaemic heart disease	1	0	1
Hypertension	5	2	3
Diabetes mellitus	2	1	1
Chronic kidney disease	1	0	1
Symptoms and signs around time for CTPA, n			
Tachycardia	4	2	2
Chest pain	2	1	1
Hypoxia	8	4	4
Intubation	2	1	1
Length of hospital stay, days	23 (13)	17 (16)	27 (15)
Critical care admission, n	5	2	3
Peak d-dimer 30 days prior to CTPA, ng/ml ^a	1637 (1075–18,902)	1160 (870–15,240)	8130 (2339–23,317)
Peak c-reactive protein 7 days prior to CTPA, mg/L	192 (127)	204 (84)	181 (170)
Peak Ferritin 30 days prior to CTPA, µg/L ^a	1036 (347–1928)	1089 (218–1360)	982 (342–1801)

Data are presented as mean (SD) or numbers. CTPA: computed tomography pulmonary angiography; CT-LSIM: computed tomography lung subtraction iodine mapping.

^aMedian (interquartile range).

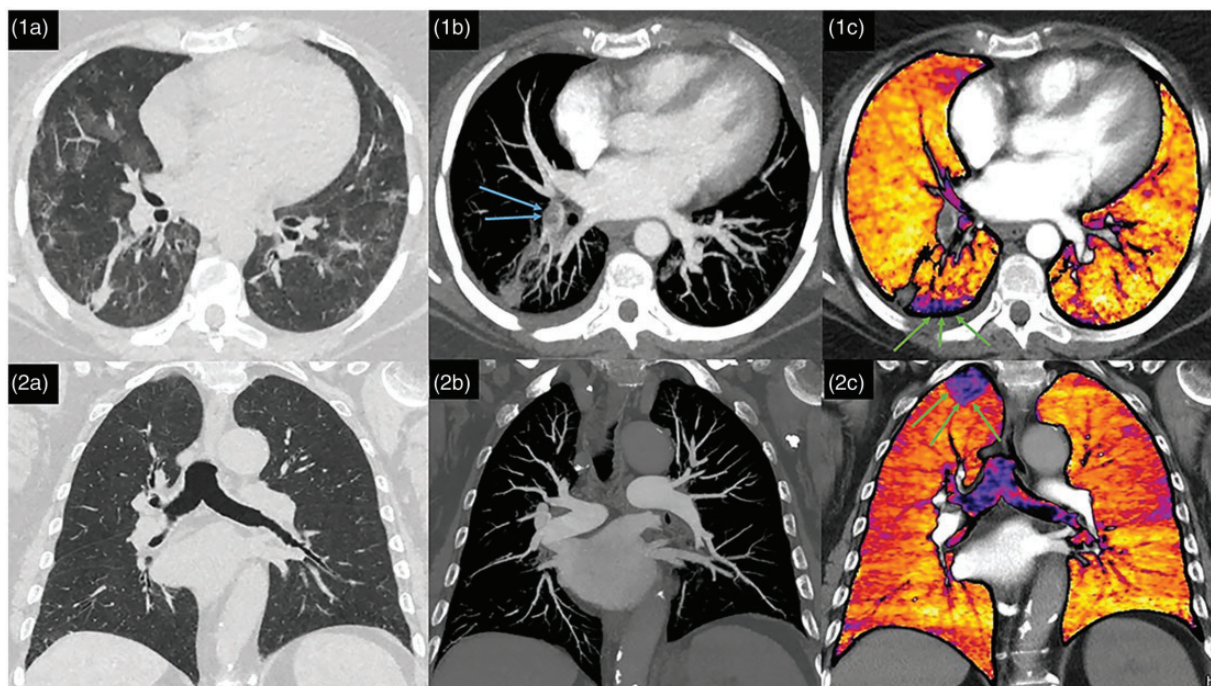


Figure 1. Patterns of parenchymal, vascular, and perfusion abnormalities in COVID-19. Patient 1: (a) Peripheral wedge-shaped abnormality in the right lower lobe associated with a segmental filling defect (blue arrows) on CTPA (b) corresponding to a perfusion defect (green arrows) on CT-LSIM (c). Patient 2: (a) Absence of lung parenchymal involvement and normal pulmonary vasculature on CTPA (b) with a perfusion defect in the right upper lobe on CT-LSIM (c, green arrows).

subsegmental perfusion defects in the absence of acute PE which is perhaps suggestive of microvascular thrombosis.

CT-LSIM is potentially widely available for the assessment of lung perfusion in COVID-19. Further studies to understand the pathophysiology of pulmonary thrombotic disease in COVID-19 are required.

Author contributions

YS: analysed the data and wrote the manuscript; SR and AJS analysed the CT scans and collected the data; VP; collected the clinical data; DGK and JMW reviewed the images and final manuscript.

Conflict of interest

The author(s) declare that there is no conflict of interest.

Ethical approval

Imaging analysis was approved by our institutional review board.

Funding

This study received funding from the Wellcome Trust, UK to AJS. Grant ID: 205188/Z/16/Z.

Guarantor

YS and AJS.

ORCID iD

Yousef Shahin  <https://orcid.org/0000-0001-7425-7798>

References

1. Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 2020; 382: 1708–1720.
2. Bompard F, Monnier H, Saab I, et al. Pulmonary embolism in patients with Covid-19 pneumonia. *Eur Resp J* 2020; 56: 2001365.
3. Salehi S, Abedi A, Balakrishnan S, et al. Coronavirus disease 2019 (COVID-19): a systematic review of imaging findings in 919 patients. *AJR Am J Roentgenol*. Epub ahead of print, 14 March 2020. DOI: 10.2214/AJR.20.23034.
4. Lodigiani C, Iapichino G, Carenzo L, et al. Venous and arterial thromboembolic complications in COVID-19 patients admitted to an academic hospital in Milan, Italy. *Thromb Res* 2020; 191: 9–14.