Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Annals of Medicine and Surgery 84 (2022) 104835

Contents lists available at ScienceDirect

Annals of Medicine and Surgery

journal homepage: www.elsevier.com/locate/amsu

Case Series

Chest CT in covid-19 pneumonia's follow-up: A 30 patients case series

Hanae Ramdani *, Khadija Benelhosni, Nabil Moatassim Billah, Ittimade Nassar

Radiology Department, Ibn Sina University Hospital Center, Lamfadel Cherkaoui Street, Rabat, MA, 10170, Morocco

ARTICLE INFO

Keywords:
Covid-19
Chest-CT
Follow-up
Case series
Pneumonia

ABSTRACT

Background: Lung abnormalities do not fully resolve in all Covid-19 survivors and may progress to fibrosis. Understanding post-COVID lung changes helps identify patients susceptible of post-COVID-19 sequelae. We analyzed scannographic residual lung abnormalities and the full resolution percentage on intermediate- and long-term follow-up (3 months or more).

Methods: Data from 30 RT-PCR positive COVID-19 patients undergoing at least one follow-up chest CT at Ibn Sina Hospital, with a minimal time interval of 3 months between the RT-PCR and the CT performance were gathered retrospectively. The following elements were analyzed: (1) lung opacities, (2) distribution, (3) dominant lung opacity, (4) Sub-pleural bands, (5) Interlobular septal thickening, (6) Vascular dilatation, (7) Bronchiectasis, (8) Honey combing, (9) Architectural distortion, (10) mosaic attenuation, and (11) Additional findings: Enlarged lymph nodes, Pleural and Pericardial fluid. To evaluate the degree of lung opacification, a score founded on visual evaluation of the lung involvement's percentage was employed. Patients were then subdivided into two categories: (1) no residual opacities and (2) remaining pulmonary opacities.

Outcomes: 30 patients were enrolled. The age ranged between 40 and 87 years. CT was indicated for symptoms or functional impairment. The time range between the positive RT-PCR and Follow-up CT varied between 3 and 12 months. CT severity score ranged between o and 23. Residual lung opacities were present in 24 cases (80%). The dominant lung opacities were Ground glass (46.7%), and linear/curvilinear opacities (23.3%). Signs of fibrosis were present in 9 patients (30%).

Conclusion: CT abnormalities following Covid-19 pneumonia's prevalence varies based on the extent of the original lung affection and the time gap since the acute phase. Residual anomalies' effects on respiratory physiology, symptoms, and quality of living are unknown. Maintained monitoring of COVID-19 survivors with clinical examination, iterative pulmonary function tests, and HRCT is advised.

1. Introduction

On March 11, 2020 the World Health Organization (WHO) proclaimed Coronavirus disease 19 (COVID-19) as a pandemic. It generated a critical planetary health crisis, and contaminated almost 277.6 million until December 23, 2021. It has caused over 5.3 million deaths across the world [1]. The infection also severely affected the global economy, as a result of decreased productivity, fatalities, business closing, commerce interruption, and decline of the tourism [2]. Its diagnosis relies on reverse transcriptase polymerase chain reaction (RT-PCR)'s detection of viral nucleic acid in the respiratory discharges. Using chest-computed tomography (CT) as a standard COVID-19 diagnostic tool is not advised by radiological societies. Nonetheless, CT performance is necessary in severe presentations and patients with respiratory degradation throughout the disease evolution. CT monitors the disease evolution and therapeutic response as well [3–5]. COVID-19 survivors present diverse clinical courses. Some recover fully while some experience residual symptoms or functional impairment [6].

As COVID-19's long-term effects are not entirely elucidated yet, the informations from former coronavirus infections could offer valuable understandings. In a study of SARS patients, 36% presented remaining chest X-ray (CXR) lung anomalies at 3 months that lowered to 30% at 6 months. At 6 months, 16% of survivors suffered from diminished diffusion capacity of lungs (DLco), indicating that remaining imaging anomalies had significant physiological repercussions [7]. Likewise, 36% of MERS survivors had remaining radiographic anomalies after a 1–8 months follow-up [8].

The initial data indicate that lung abnormalities do not fully clear-up

* Corresponding author.
E-mail addresses: hanaeramdani@hotmail.fr (H. Ramdani), khadija.benelhosni@gmail.com (K. Benelhosni), moatassimbillah.nabil@gmail.com (N.M. Billah), nassarittimade@yahoo.fr (I. Nassar).

https://doi.org/10.1016/j.amsu.2022.104835
Received 7 August 2022; Received in revised form 29 September 2022; Accepted 30 October 2022
Available online 7 November 2022

in each Covid-19 survivor and in some progress to pulmonary fibrosis [6]. Some published reports have evaluated longitudinal variations of post-COVID lung parenchyma anomalies, however they primarily concentrated on short-term modifications [9–12].

Understanding post-COVID lung changes on CT could help identify risk factors for lasting COVID-19-provoked pulmonary sequelae, and thus precipitate the introduction of suitable treatment. It might help select patients for antifibrotic drugs trials' enrollment.

This study aims to report residual radiological lung findings, and identify the percentage of full radiographic resolution on intermediate- and long-term follow-up (3 months or more).

2. Materials and methods

2.1. Study design

We carried out a retrospective, mono-centric, consecutive case series study at Ibn Sina University Hospital, Rabat-Morocco, from January 2022 to April 2022, registered under the UIN: researchregistry8187 [13].

Ethical approval was not required, and informed consent was waived due to the study's retrospective design.

30 RT-PCR positive COVID-19 patients with no less than one follow-up CT and a time interval of at least 3 months separating the RT-PCR and the CT performance were enrolled.

Follow-up CT's major indications were residual symptoms or functional deterioration.

We gathered and studied the pertinent demographic, clinical, and scannographic features retrospectively.

2.2. CT protocol and interpretation

We carried-out all CTs on a 16-Slice Siemens Multidetector scanner without administration of intravenous contrast medium. In cases of pulmonary embolism suspicion, CT pulmonary angiography was carried-out.

The patient was set up in a supine head-first position.

The used voltage was 100–120 kVp, and current 90–130 mAs. Images reconstruction into a 1.5 mm slice thickness was obtained. The images were analyzed in lung window (Width: 1500 HU; Level: 600 HU) and mediastinal window (Width: 350 HU; Level: 50 HU).

A senior radiology resident with specific training in image interpretation of COVID-19 on chest CT scans, and the use of standardized report templates, analyzed the following elements: (1) existence or not of lung opacities; (2) distribution: one vs two-sided; (3) dominant lung opacity: ground glass opacity (GGO), consolidation, GGO and consolidation, and linear/curvilinear opacities, (4) Sub-pleural bands, (5) Interlobular septal thickening, (6) Vascular dilatation, (7) Bronchiectasis, (8) Honey combing, (9) Architectural distortion, (10) mosaic attenuation, and (11) Additional findings: Enlarged lymph nodes, Pleural fluid, and Pericardial fluid.

To evaluate the degree of lung opacification, a score built on the visual appraisal of the percentage of lung involvement was employed [14]. Every lobe was graded from 0 to 5: no involvement (0), <5% (1), 5–25% (2), 26–50% (3), 51–75% (4) and 76–100% (5). The five lobes scores were totaled to get a whole CT severity score extending from 0 (no participation) to 25 (maximal participation).

Patients were then classified in two sets: (1) full resolution and (2) remaining pulmonary opacities.

This case series has been reported in line with the PROCESS Guideline [15].

3. Results

3.1. Demographic characteristics

3.1.1. Age

The age varied between 40 and 87 years with an average of 53.4 years.

3.1.2. Gender

There were 16 males (53.3%) and 14 females (46.7%).

3.1.3. Respiratory comorbidities

4 patients had chronic obstructive pulmonary diseases. 2 patients had pulmonary tuberculosis. 1 patient had recently diagnosed interstitial lung disease with indeterminate usual interstitial pneumonia pattern (UIP), and 2 patients had a pulmonary embolism.

3.2. Follow-up CT indications

CT was indicated for symptoms or functional impairment on follow-up in all cases.

3.3. Time interval between positive RT-PCR and follow-up CT

The time range between the positive RT-PCR and Follow-up CT varied between 3 and 12 months, with an average of 6 months.

3.4. Clinical manifestations

The major symptoms were Cough in 10 patients (33.3% of cases), and dyspnea in 20 patients (66.7% of cases).

3.5. Follow-up chest CT features

3.5.1. CT severity score

CT severity score ranged between o and 23 (Fig. 1). The mean score was 6.48.

3.5.2. Distribution

Lesions' distribution was bilateral in 22 cases (73.3%)(Fig. 2), unilateral in 2 cases (6.7%). No pulmonary opacities were detected in 6 cases (20%).

3.5.3. Imaging findings

Lung opacities were present in 24 cases (80%).

The dominant lung opacities were Ground glass in 14 cases (46.7%) (Fig. 3), Consolidations in 1 case (3.3%), GGO + Consolidations in 2 cases (6.7%) (Fig. 4), and linear/curvilinear opacities in 7 cases (23.3%) (Fig. 5).

12 patients (40%) presented sub-pleural bands, and 13 patients (43.3%) presented vascular dilatation. Interlobular septal thickening was detected in 13 cases (43.3%), bronchiectasis in 12 cases (40%), honey combing in 2 cases (6.7%), mosaic attenuation in 3 cases (10%), and architectural distortion in 3 cases (10%) (Fig. 6).

The additional findings detected were enlarged lymph nodes in 11 cases (36.7%), Pleural fluid in 2 cases (6.7%), and Pericardial fluid in 4 cases (13.3%).

6 patients (20%) presented no lung opacities whereas 24 patients (80%) had residual pulmonary opacities. Fibrosis signs (Traction bronchiectasis, interlobular septal thickening, honeycombing and/or architectural distortion) were noted in 9 patients (30%).

4. Discussion

Considering the recognized link between viral pneumonias and fibrosis, and the frequency of lung lesions during acute COVID-19 and

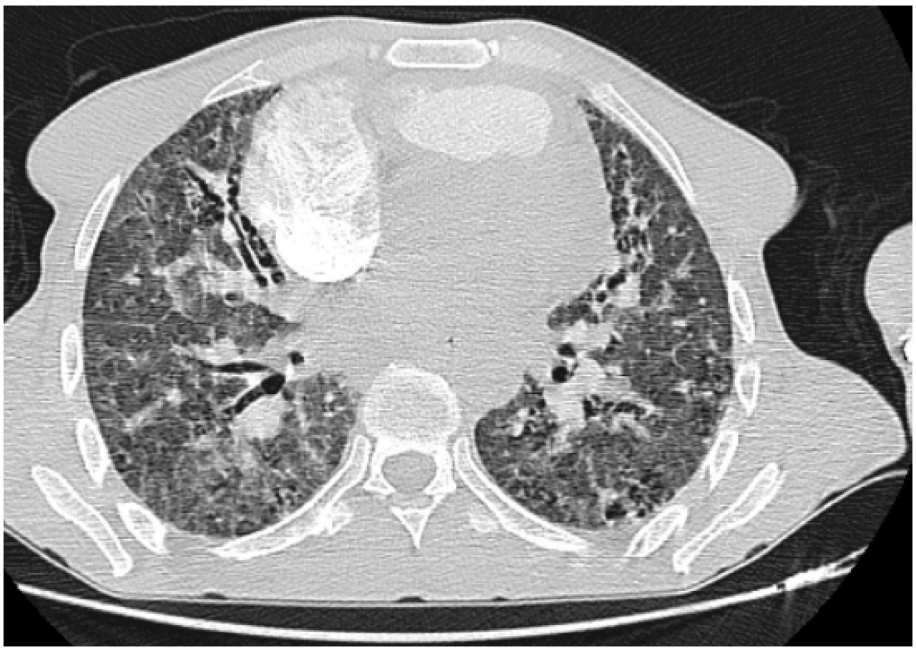

Fig. 1. A 55-year-old man follow-up contrast-enhanced axial chest CT image in lung window, 5 months following initial presentation, showing extensive residual pulmonary ground glass opacities (23 CT severity score), and traction bronchiectasis.

residual respiratory manifestations following recovery, there is emphasis on the post-Covid-19 lung disease [16].

4.1. Etiopathogenesis of post-covid lung disease

There is uncertainty whether anomalies following acute COVID-19 are due to ARDS, mechanical ventilation, viral induced injuries, or the host's immune reaction to it [17]. Aggravation of pre-existing interstitial lung disease [18], a recognized complication following pulmonary infection in patients with fibrosis [19], appears to be another cause of lung disease following COVID-19.

4.2. Histological, radiological, and PFT correlation

In a recent Lancet Infectious disease publication, 8 patients who died from COVID-19 underwent postmortem anatomo-pathologic examination [20]. Substantial fibrotic lung parenchymal remodeling, defined by proliferation of fibroblasts, honeycombing, and airspace obliteration were noted.

Lung biopsies carry an elevated hazard of pneumothorax and are not practical. Nonetheless, a novel publication of a transbronchial biopsy in a Covid-19 61-year-old patient showed organizing pneumonia [21].

Histologic presentations of lung viral infections may be subdivided to 2 models:

1) Bronchiolitis and inflammation contiguous to airways. On imaging: bronchial wall thickening, centrilobular nodules, and tree-in-bud pattern are present. Concentric fibrosis around the bronchioles causing airway reduction, called constrictive (or obliterative) bronchiolitis may occur. It results in remaining dyspnea, and an obstructive physiology on pulmonary function tests. Constrictive bronchiolitis main CT features comprise mosaic attenuation, air trapping, and bronchiectasis.
2) Diffuse alveolar damage, manifesting as GGO and/or consolidation on imaging. Histologically, fibrosis forms 1–2 weeks following acute signs, and is affiliated with reticulations and traction bronchiectasis on CT. Within time, months usually, fibrosis might resolve, nonetheless remaining fibrosis is frequent [21], is usually positioned in the anterior peripheral lung and might be linked to a restrictive defect on PFT.

Organizing pneumonia (OP) is frequent, and usually very steroid-responsive with opacities that rapidly better or clear up under treatment. Remaining fibrosis might persist, and usually mimics nonspecific interstitial pneumonia with basilar dominant interlobular septal thickening, bronchiectasis, and subpleural exemption [22].

Pulmonary fibrosis is not always persistent. Collagen might be absorbed months following the initial injury.

4.3. Prevalence and CT features

The prevalence of radiologic changes following Covid-19 differs based on the cohort studied, the time span following infection, and the initial episode gravity [17].

In our retrospective study addressing COVID-19 pneumonia's mid to long-term follow-up (3–12 months) chest CT findings, and involving 30 patients; 80% had residual lung opacities, among which 30% presented fibrotic changes. The predominant lung opacity was GGO; present in 14 patients (46.7%). Mosaic attenuation was detected in 3 patients (10%).

Han et al. [5]. described the remaining CT features of COVID-19 6 months following the acute illness. In their report, more than 1/3 of patients manifested signs of fibrosis.

Cho and Villacreses et al. [23] discuss these long-term lung abnormalities in a report of 100 cases with lasting (>30 days) respiratory signs following COVID-19 pneumonia. Air trapping was reported in 58% of patients, prevailed in the group of hospitalized patients (73%), and affected 25–35% of the lungs depending on illness severity. Restriction was detected on PFT in the COVID-19 hospitalized patients and ICU sub-groups. GGO, traction bronchiectasis, and other fibrosis signs were much common in ICU patients (94%, 69%, 81% of patients in comparison to 36%, 8%, and 3% of non-hospitalized patients).

114 grave COVID-19 patients' control at six months revealed that thirty-five percent presented fibrosis and a subset of them had DLco diminutions [24]. GGO was described in 21% of cases. GGO and consolidation extent lowered in comparison to the initial scans, while reticular abnormalities increased.

Only 4% of the three-months follow-up CTs of fourty eight grave

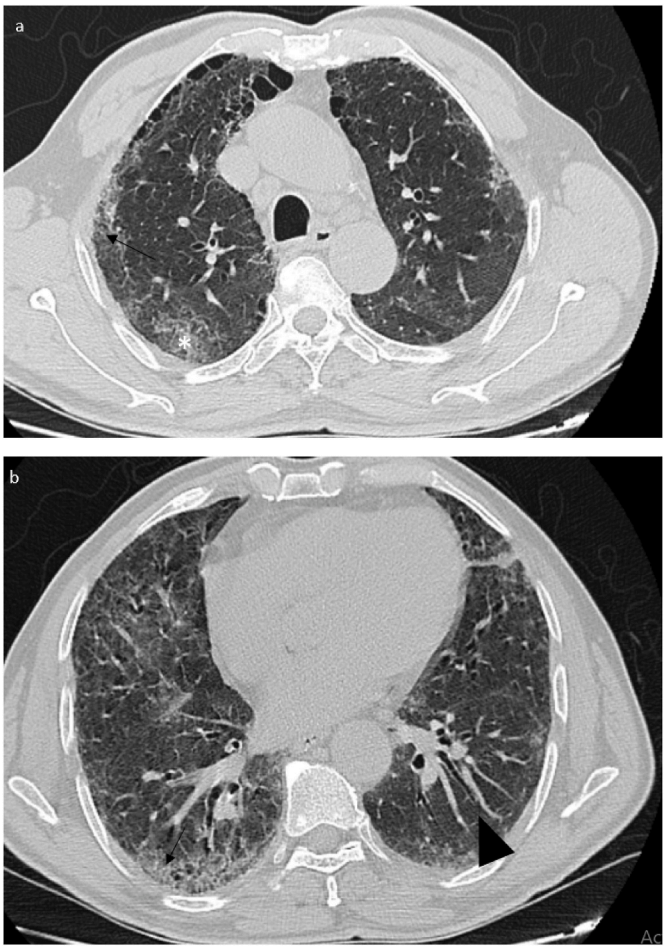

Fig. 2. A 68-year-old male patient with COPD and severe coronavirus disease, 3 months following discharge. Axial non-enhanced chest CT images in lung window (a,b) showing bilateral involvement with residual light GGO (*), sub-pleural interlobular septal thickening (Black arrow), bronchiectasis, and vascular dilatation (Black arrow head).

SARS-Cov-2 survivors, with previous mechanical ventilation, were normal [25]. Eighty-nine percent presented GGO, while fibrotic anomalies (namely parenchymal bands, parenchymal distortion, and bronchiectasis) were observed in sixty-seven percent. Associated lung volumes and DLco reductions were reported. In forty six percent, diminished attenuation due to hypoperfusion or rather bronchioles injury was present. In 25%, novel emphysema and cysts were noticed.

In 12 COVID-19 survivors, follow-up CTs performed at six months noted the occurrence of fibrosis in the same zones affected during the initial infection phase anomalies [26].

40% of patients showed fibrotic changes while 56% of CTs demonstrated ground-glass or consolidative opacities in a meta-analysis of 60 reports [27], analyzing follow-up radiological features of MERS, influenza, and COVID-19 pneumonia.

The changing definitions of CT features and absence of histologic correspondence complicate the COVID-19 follow-up studies' interpretation. It is suggested to classify Post-acute COVID syndrome (PASC) CT appearances like this: mainly GGO, mixed GGO and fibrotic, and mainly fibrotic. GGO or fibrotic bands or their association in the original infection areas, may represent early fibrosis or interstitial lung pathology [28].

A broad definition of fibrosis may inflate its prevalence, thus the designation fibrosis must be kept for particular features: bronchiectasis or bronchiolectasis, honeycombing, or architectural distortion [29]. These anomalies might resolve or progress on follow-up. It is not known

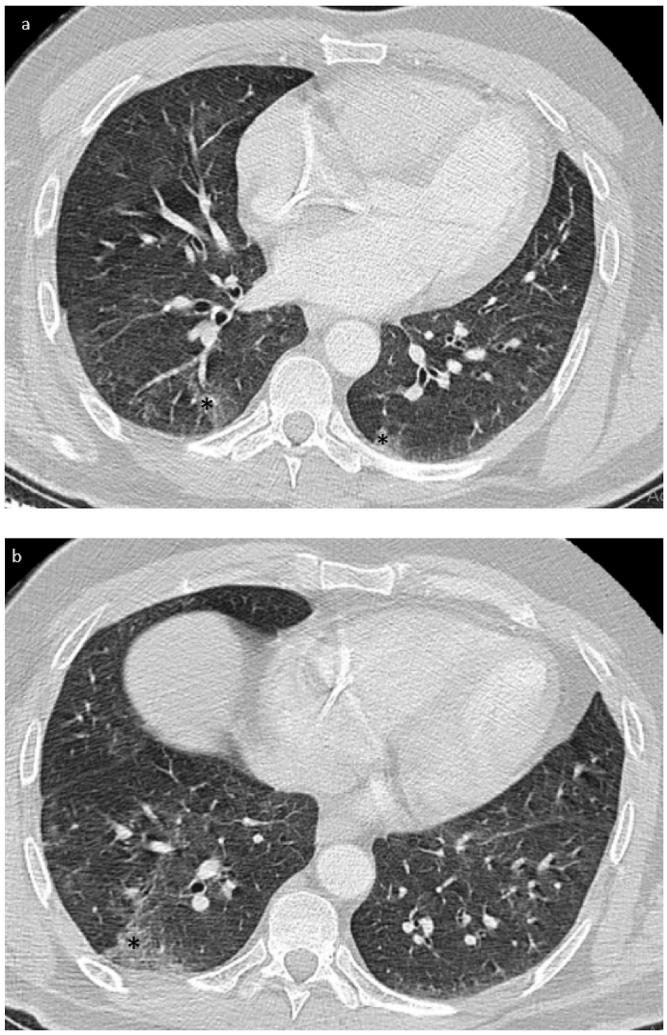

Fig. 3. A 42-year-old-man 9 months follow-up axial non-enhanced chest CT images (a,b) showing residual, multi-focal, bilateral, sub-pleural, patchy ground glass opacities (*).

yet if there is overlap between remaining COVID-19 pulmonary abnormalities and NSIP or UIP.

To appraise COVID-19 infection in the initial phase, different techniques are used, including densitometry and deep learning methods [30,31]. Early phase quantitative CT assessment of severity is an autonomous forecaster of ICU hospitalization and mortality [32–34]. It could as well be used to appraise serial variations in lung volumes and pulmonary opacity [34]. A study of 41 COVID-19 survivors and an identical report of 29 patients demonstrated that quantitative pneumonia CT measures reduced gradually in 6–7 months [35,36].

In order for quantitative CT assessment of severity to be beneficial in evaluating PASC, distinct metrics that differentiate between GGO and fibrotic abnormality are necessary.

4.4. CT evaluation

COVID-19 follow-up Chest CT examination must comprise supine inspiratory and expiratory acquisitions with thin reconstructions (1.5 mm). Novel emphysematous lesions, cysts, and mosaic pattern suggest airflow obstruction. Lung bases prone imaging elucidates if basal anomalies at supine scanning correspond to atelectasis or authentic abnormalities. An acute or chronic pulmonary thromboembolism would also cause PACS symptoms, and computed tomography pulmonary angiograms must be acquired for low suspicion indexes. To understand the

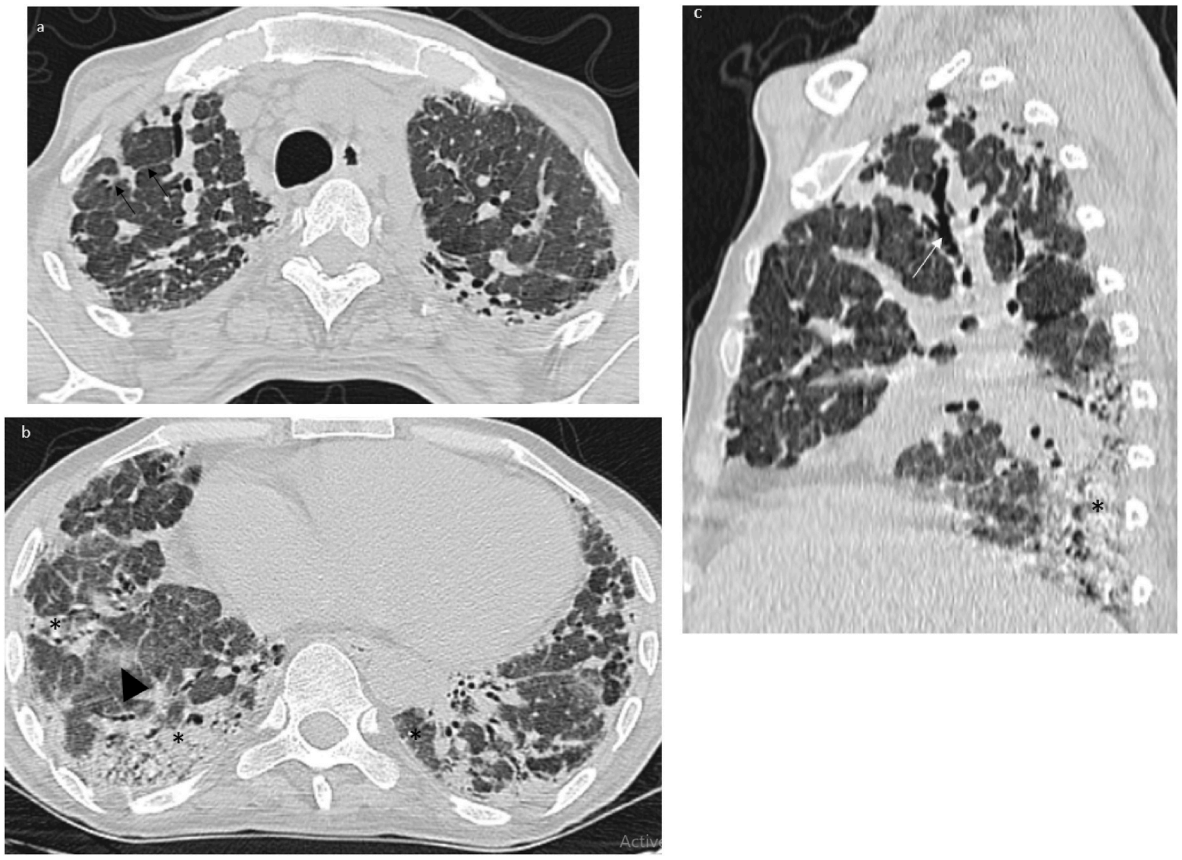

Fig. 4. A 40-year-old-man 7 months follow-up non-enhanced chest CT axial (a,b) and sagittal images (c) showing residual, extensive multi-focal, bilateral, patchy dominant consolidations (*), some ground glass opacities (Black arrow head), alongside bronchiectasis (White arrow), and interlobular septal thickening (Black arrow).

abnormalities temporal course, juxtaposition with initial phase CT is crucial. The majority of studies repeat HRCTs, however considering the irradiation risk, low-dose or ultra-low-dose CTs may have a role in longitudinal follow-ups [37].

The best time for follow-up CT is not known. The British Thoracic Society current guidelines advise a follow-up at 3-months, a convenient interval for lung anomalies to clear that guarantees at the same time that residual findings are handled promptly [38]. High-resolution CT is recommended for remaining substantial lung anomalies on follow-up CXR and lasting respiratory symptoms or physiological dysfunction [38,39].

The international guidelines were respected in our report. The time gap between the acute infection phase and the follow-up was 3 months at least, and all imaged patients presented respiratory symptoms.

4.5. Pulmonary embolism's role

Considering the proof of direct endothelial injury by SARS-CoV-2 [40] and the associated hypercoagulable state [41], there is worry that venous thromboembolism might take a part in Post-acute COVID syndrome. Since the hypercoagulable state's duration is not known, recovering patients might still be at a high hazard for novel or undiagnosed pulmonary embolisms. Seventeen percent and fifteen percent of patients presented PE and DVT, respectively, in a meta-analysis that studied 3342 Covid-19 survivors [42], mainly during the initial stage, and most frequently in the ICU. Pulmonary perfusion scans are suggested as a method of sorting Sars-Cov-2 patients, when pulmonary emboli is suspected, in the presence of pulmonary symptoms and/or DLco reductions that are unexplained by imaging [43].

We performed CT pulmonary angiography in 7 patients who had a pulmonary embolism suspicion (discrepancy between no or minimal parenchymal lung involvement and severe respiratory symptoms, or highly increased D-dimers). No thromboembolism was identified.

Dual-energy CT could play a part in assessing residual signs following COVID-19. Fifty-five D-E computed-tomography angiograms obtained three months post-COVID-19 pneumonia, to explore residual signs, showed disruption of normal opacification correspondent to embolism in 3 cases, and perfusion defects in 32 cases (58%) (4 of which with normal pulmonary parenchyma) implying residual micro-vascular anomalies [44]. Regions of augmented perfusion were noted in 15 cases, and corresponded to tree-in-bud, ground-glass opacities and sub-pleural bands. It was concluded to the frequency of vascular disturbance following Sars-Cov-2 pneumonia.

4.6. Predictors of post-covid lung disease

In a study that analyzed CTs 5 months following discharge, a link was found between the abnormalities magnitude and the illness severity evaluated by the necessity of hospitalization, oxygen, and mechanical ventilation [45]. DLco reduction was correlated to the gravity of disease, and women and older patients had an augmented probability of presenting a diffusion anomaly. Other reports identified high inflammatory indicators (CRP, LDH, and Il-6) [46–49], D-dimers [50], white blood cells [48], albumin [49], older age [50,51], male sex [50,52], comorbidities [50], ICU hospitalization [52], longer hospital stay [48,53], the implementation and duration of mechanical ventilation [49,51], and ARDS [51,53] as factors linked to worsened fibrosis when monitored. Among the risk factors of fibrotic pulmonary illnesses comprising Idiopathic pulmonary fibrosis, a short leukocyte telomere length was linked to fibrosis following COVID-19 [49]. In patients with anterior

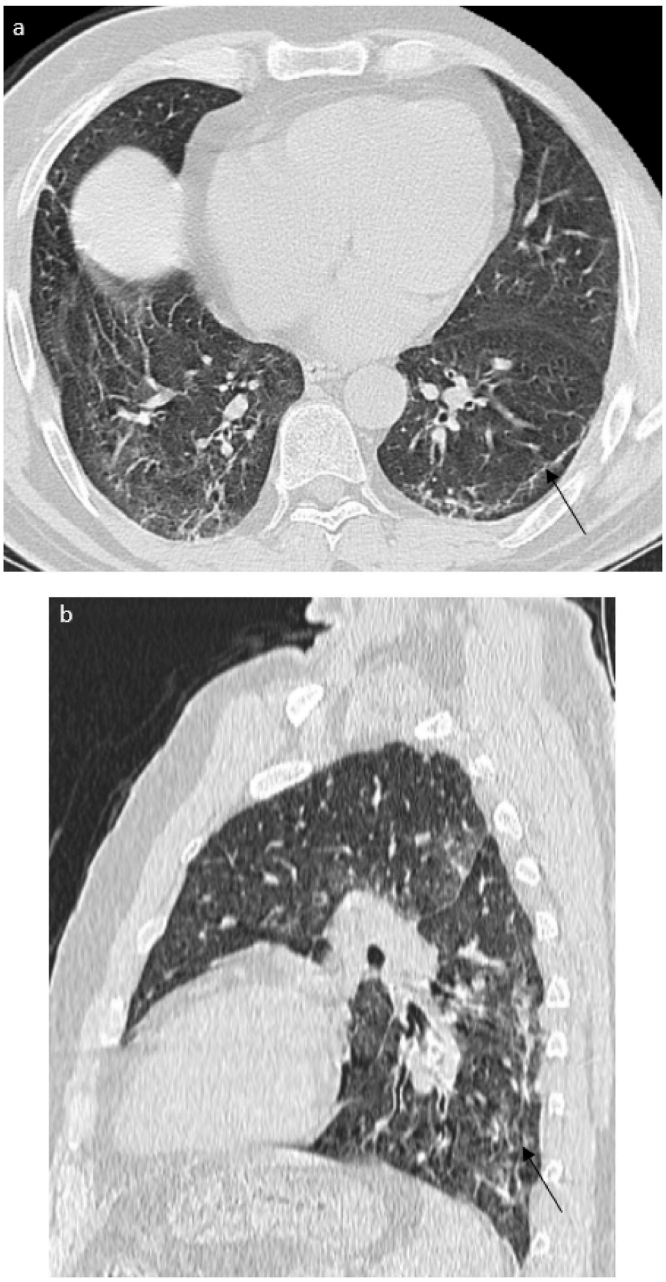

Fig. 5. A 64-year-old man's 12 months follow-up non-enhanced chest CT axial (a) and sagittal (b) images showing residual curvilinear sub-pleural opacities (Black arrow) involving peripheral lung bases.

pulmonary fibrosis, COVID-19 might accelerate it.

Progressive interstitial lung disease development following COVID-19 may be due to autoimmune incitement sparked by SARS-CoV-2 or evolution of previously existing interstitial pulmonary anomalies to clinically considerable ILD [54].

Our cohort comprised one patient with interstitial lung disease indeterminate for UIP pattern and moderate COVID-19 infection. The 3 months follow-up CT showed moderate lung involvement (CT severity score = 14) with signs of fibrosis.

4.7. Treatment

Corticosteroids are considered in the initial phases with CT features of organizing pneumonia. Anti-fibrotic drugs utilized in chronic lung fibrosis are reviewed, specifically nintedanib [55], an inhibitor of tyrosine-kinase that retards advancement in IPF [56]. Genistein is an agonist of estrogen receptor beta, whose stimulation regulates cell cycle, facilitates DNA reparation, reduces inflammation, and has anti-fibrotic properties [57]. A National Institute of Allergy and Infectious Diseases–endorsed COVID-19 clinical trial is currently testing it.

4.8. Limitations

This study has many limitations. First, our monocentric cohort included merely 30 patients. Larger systemic reviews and meta-analysis are advisable to better analyze the COVID-19 sequelae. Second, baseline imaging and pulmonary function tests were not available. Follow-up PFT were not performed. These objective variables offer more accurate informations on the lungs physiological anomalies, and should be included in future studies. Third, the time gap between the positive RT-PCR and Follow-up CT ranged between 3 and 12 months, with an average of 6 months. Prospective longer-term reports are necessary to investigate the durable features of post-COVID fibrosis. Fourth, no children, adolescents nor pregnant women with COVID-19 were included in our study, making future investigations in this population's evolution of symptoms warranted. Fifth, a prone position acquisition was not performed; however, most lung lesions did not meet the criteria of dependent artifactual abnormalities. Sixth, our CT protocol did not include intravenous contrast administration; therefore pulmonary emboli was not searched, nonetheless in 7 patients who benefited from a pulmonary CT angiography, no pulmonary embolus was detected. Seventh, risk factors for CT residual lung anomalies were not identified. Since the long-term effects of COVID-19 remain unclear, preventing infection through vaccination is the best way to reduce their impact [58]. Studies investigating the effects of vaccines on the COVID-19 consequences are also necessary. In addition, improving COVID-19 screening and early diagnosis methods helps precocious detection and precipitates treatment initiation. The succession of COVID-19 infection waves has led to a sizable population of survivors. Long-term post-Covid symptoms impact health, quality of life, and might lead to another public health crisis increasing the global burden of the disease. Elucidating their underlying pathophysiologic mechanisms, and risk factors is crucial for a more scientific basis for the care and rehabilitation of survivors, their surveillance, and setting public health protocols through trials of prevention or treatment interventions. Finally, it is likely that our follow-up study covered the third wave of the pandemic in Morocco; thus, our findings mainly applied to those who experienced infection by the Delta or Omicron variants. Their long-term consequences could help elucidate how the COVID-19 pandemic evolves over time.

Presently, in the third year of the coronavirus pandemic, daily cases have declined to their lowest globally, and restrictions (such as mask use) were lifted across the countries. Currently, the omicron variant of SARS-CoV-2 is the dominant circulating strain [59]. It has the highest transmissibility, and is associated with significantly lessened length of hospital stays and reduced severity and mortality, when compared to the previous COVID-19 hits [60].

5. Conclusion

CT abnormalities following Covid-19's prevalence varies based on the extent of the original lung affection and the time gap since the acute phase. Longitudinal studies indicate that anomalies could remain in patients with established factors of risk. Many areas of incertitude remain and need more studies, namely CT findings clinical and functional impact, the relationship between post-COVID fibrosis and preexisting interstitial lung disease, pathologic correlation of CT abnormalities, long-term outcome, and improvement versus progressive fibrosis predictors. Even if no drug is endorsed for post-COVID lung fibrosis, therapies trials are continuing. The long-lasting effect of CT anomalies on respiratory manifestations, physiology, or life quality is not known. Post-discharge surveillance is crucial to avert a population

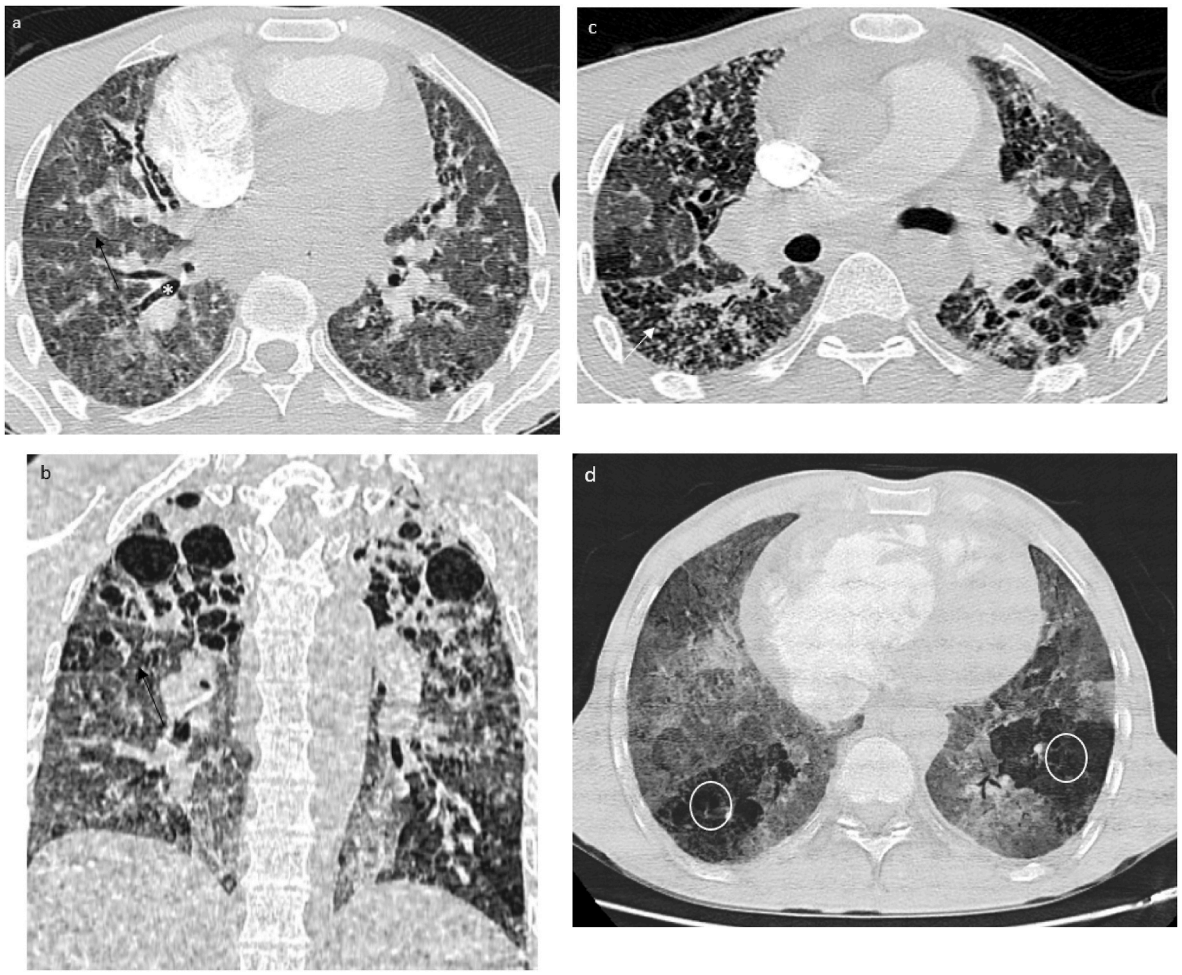

Fig. 6. A 55-year-old man with COPD follow-up contrast-enhanced axial (a,c) and coronal (b) chest CT images in lung window, 5 months after initial presentation, showing extensive residual pulmonary opacities alongside with architectural distortion. Note the disruption of the normal course of the right oblique fissure (Black arrow), associated traction bronchiectasis (*), and extensive honey-combing (White arrow). A mosaic attenuation pattern (White circles) in lower lung lobes best demonstrated on mIP reconstructions using narrow window parameters (d).

with lasting lung injury. Consequently, maintained monitoring of released COVID-19 patients with clinical examination, iterative pulmonary function testing, and HRCT is advised.

Ethical approval

Ethical approval was not required based on our institutional policies for retrospective, de-identified case series.

Sources of funding

No funding was received.

Author contribution

Ramdani, H: Contributed to conception, design, acquisition, analysis and interpretation, drafted manuscript, and gave final approval.

Benelhosni, K: contributed to acquisition, analysis and interpretation, and critically revised the manuscript.

Moatassim Billah, N: Critically revised the manuscript.

Nassar, I: Contributed to conception, design, acquisition, analysis and interpretation, critically revised the manuscript, and gave final approval.

Registration of research studies

Name of the registry: Research Registery

Unique Identifying number or registration ID: researchregistery8178.

Hyperlink to your specific registration (must be publicly accessible and will be checked):

https://www.researchregistry.com/register-now#home/registrationdetails/62eff964156f390023f2da2a/

Guarantor

Hanae Ramdani.

Consent

Informed consent was waived due to the study's retrospective design, based on our institutional policies for de-identified case series.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Declaration of competing interest

The authors declare no conflict of interest.

Acknowledgements

All authors contributed substantially to the design and reporting of this manuscript.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2022.104835.

References

[1] World Health Organization, WHO coronavirus disease (COVID-19) dashboard. https://covid19.who.int/. (Accessed 23 December 2021).
[2] A. Pak, O.A. Adegboye, A.I. Adekunle, K.M. Rahman, E.S. McBryde, D.P. Eisen, Economic consequences of the COVID-19 outbreak: the need for epidemic preparedness, Front. Public Health 8 (2020) 241, https://doi.org/10.3389/fpubh.2020.00241. Published 2020 May 29.
[3] M.P. Revel, A.P. Parkar, H. Prosch, M. Silva, N. Sverzellati, F. Gleeson, A. Brady, COVID-19 patients and the radiology department–advice from the European society of radiology (ESR) and the European society of thoracic imaging (ESTI), Eur. Radiol. 30 (9) (2020) 4903–4909.
[4] https://www.acr.org/Advocacy-and-Economics/ACR-Position-Statements/Recommendations-for-Chest-Radiography-and-CT-for Suspected-COVID19-Infection. (Accessed 30 October 2020).
[5] G.D. Rubin, C.J. Ryerson, L.B. Haramati, N. Sverzellati, J.P. Kanne, S. Raoof, N. W. Schluger, A. Volpi, J.J. Yim, I.B. Martin, D.J. Anderson, The role of chest imaging in patient management during the COVID-19 pandemic: a multinational consensus statement from the Fleischner Society, Chest 158 (1) (2020) 106–116.
[6] Y.M. Zhao, Y.M. Shang, W.B. Song, Q.Q. Li, H. Xie, Q.F. Xu, J.L. Jia, L.M. Li, H. L. Mao, X.M. Zhou, H. Luo, Follow-up study of the pulmonary function and related physiological characteristics of COVID-19 survivors three months after recovery, Eclin. Med. 25 (2020), 100463.
[7] D.S. Hui, G.M. Joynt, K.T. Wong, C.D. Gomersall, T.S. Li, G. Antonio, F.W. Ko, M. C. Chan, D.P. Chan, M.W. Tong, T.H. Rainer, Impact of severe acute respiratory syndrome (SARS) on pulmonary function, functional capacity and quality of life in a cohort of survivors, Thorax 60 (5) (2005) 401–409.
[8] K.M. Das, E.Y. Lee, R. Singh, M.A. Enani, K. Al Dossari, K. Van Gorkom, S. G. Larsson, R.D. Langer, Follow-up chest radiographic findings in patients with MERS-CoV after recovery, Indian J. Radiol. Imag. 27 (3) (2017) 342.
[9] A.H. Parry, A.H. Wani, N.N. Shah, M. Yaseen, M. Jehangir, Chest CT features of coronavirus disease-19 (COVID-19) pneumonia: which findings on initial CT can predict an adverse short-term outcome? BJR| Open 2 (2020), 20200016.
[10] R. Lu, X. Zhao, J. Li, et al., Genomic characterization and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding, Lancet 395 (10224) (2020) 565–574, https://doi.org/10.1016/S0140-6736(20)30251-8.
[11] T.T. Lam, N. Jia, Y.W. Zhang, et al., Identifying SARS-CoV-2-related coronaviruses in Malayan pangolins, Nature 26 (2020), https://doi.org/10.1038/s41586-020-2169-0.
[12] N. Zhu, D. Zhang, W. Wang, et al., China novel coronavirus investigating and Research team. A novel coronavirus from patients with pneumonia in China, 2019, N. Engl. J. Med. 382 (8) (2020) 727–733, https://doi.org/10.1056/NEJMoa2001017.
[13] https://www.researchregistry.com/browse-the- registry#home/?view_2_search=Hanae%20ramdani&view_2_page=1&view_2_sort=field_21|asc.
[14] A.M. Zaki, S. van Boheemen, T.M. Bestebroer, A.D. Osterhaus, R.A. Fouchier, Isolation of a novel coronavirus from a man with pneumonia in Saudi Arabia, N. Engl. J. Med. 367 (19) (2012) 1814–1820, https://doi.org/10.1056/NEJMoa1211721.
[15] R.A. Agha, C. Sohrabi, G. Mathew, et al., The PROCESS 2020 guideline: updating consensus preferred reporting of CasESeries in surgery (PROCESS) guidelines, Int. J. Surg. 84 (2020) 231–235, https://doi.org/10.1016/j.ijsu.2020.11.005.
[16] C.S. Goldsmith, K.M. Tatti, T.G. Ksiazek, et al., Ultrastructural characterization of SARS coronavirus, Emerg. Infect. Dis. 10 (2) (2004) 320–326, https://doi.org/10.3201/eid1002.030913.
[17] M. Hoffmann, H. Kleine-Weber, S. Schroeder, et al., SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor, Cell 181 (2) (2020) 271–280, https://doi.org/10.1016/j.cell.2020.02.052.
[18] M. Fonseca, R. Summer, J. Roman, Acute exacerbation of interstitial lung disease as a sequela of COVID-19 pneumonia, Am. J. Med. Sci. 361 (1) (2021) 126–129.
[19] G. Leuschner, J. Behr, Acute exacerbation in interstitial lung disease, Front. Med. 4 (2017) 176.
[20] F. Grillo, E. Barisione, L. Ball, L. Mastracci, R. Fiocca, Lung fibrosis: an undervalued finding in COVID-19 pathological series [published online ahead of print, 2020 Jul 28], Lancet Infect. Dis. (2020), https://doi.org/10.1016/S1473 3099(20)30582-X.
[21] I.M. Nöbauer-Huhmann, K. Eibenberger, C. Schaefer-Prokop, et al., Changes in lung parenchyma after acute respiratory distress syndrome (ARDS): assessment with high-resolution computed tomography, Eur. Radiol. 11 (12) (2001) 2436–2443, https://doi.org/10.1007/s003300101103.
[22] J.W. Lee, K.S. Lee, H.Y. Lee, et al., Cryptogenic organizing pneumonia: serial high-resolution CT findings in 22 patients, AM. J. Roentgenol. 195 (4) (2010) 916–922, https://doi.org/10.2214/ajr.09.3940.
[23] S.M.H. Tabatabaei, H. Talari, F. Moghaddas, H. Rajebi, Computed tomographic features and short-term prognosis of coronavirus disease 2019 (COVID-19) pneumonia: a single-center study from Kashan, Iran, Radiology: Cardiothoracic Imag. 2 (2) (2020), e200130, https://doi.org/10.1148/ryct.2020200130.
[24] X. Han, Y. Fan, O. Alwalid, et al., Six-month follow-up chest CT findings after severe COVID-19 pneumonia, Radiology 299 (1) (2021) E177–E186.
[25] van Gassel Rjj, J.L.M. Bels, A. Raafs, et al., High prevalence of pulmonary sequelae at 3 Months after hospital discharge in mechanically ventilated survivors of COVID-19, Am. J. Respir. Crit. Care Med. 203 (3) (2021) 371–374.
[26] A. Gulati, P. Lakhani, Interstitial lung abnormalities and pulmonary fibrosis in COVID-19 patients: a short-term follow-up case series, Clin. Imag. 77 (2021) 180–186.
[27] L. Fabbri, S. Moss, F. Khan, et al., Post-viral parenchymal lung disease of COVID-19 and viral pneumonitis: a systematic review and meta-analysis, medRxiv (2021) 2021, 03.15.21253593.
[28] Y. Huang, C. Yan Tan, J. Wu, M. Zhu Chen, Z. Guo Wang, L. Yun Luo, X. Rong Zhou, X. Ran Liu, X. Ling Huang, C. Can Yuan, C. Lin Chen, Impact of coronavirus disease 2019 on pulmonary function in early convalescence phase, Respir. Res. 21 (1) (2020) 163, https://doi.org/10.1186/s12931-020-01429-6.
[29] D.M. Hansell, A.A. Bankier, H. MacMahon, T.C. McLoud, N.L. Müller, J. Remy, Fleischner Society: glossary of terms for thoracic imaging, Radiology 246 (3) (2008) 697–722.
[30] Y. Zhang, Y. Liu, H. Gong, L. Wu, Quantitative lung lesion features and temporal changes on chest CT in patients with common and severe SARS-CoV-2 pneumonia, PLoS One 15 (7) (2020), e0236858.
[31] Y.C. Wang, H. Luo, S. Liu, et al., Dynamic evolution of COVID-19 on chest computed tomography: experience from Jiangsu Province of China, Eur. Radiol. 30 (11) (2020) 6194–6203.
[32] K. Li, X. Liu, R. Yip, et al., Early prediction of severity in coronavirus disease (COVID-19) using quantitative CT imaging, Clin. Imag. 78 (2021) 223–229.
[33] M.L. Chabi, O. Dana, T. Kennel, et al., Automated AI-driven CT quantification of lung disease predicts adverse outcomes in patients hospitalized for COVID-19 pneumonia, Diagnostics 11 (5) (2021) 878.
[34] B. Pang, H. Li, Q. Liu, et al., CT quantification of COVID-19 pneumonia at admission can predict progression to critical illness: a retrospective multicenter cohort study, Front. Med. 8 (810) (2021), 689568.
[35] M. Liu, F. Lv, Y. Huang, K. Xiao, Follow-up study of the chest CT characteristics of COVID-19 survivors seven months after recovery, Front. Med. 8 (2021), 636298.
[36] M.T. Kassin, N. Varble, M. Blain, et al., Generalized chest CT and lab curves throughout the course of COVID-19, Sci. Rep. 11 (1) (2021) 6940.
[37] S. Tofighi, S. Najafi, S.K. Johnston, A. Gholamrezanezhad, Low-dose CT in COVID-19 outbreak: radiation safety, image wisely, and image gently pledge, Emerg. Radiol. 10 (2020) 1–5, https://doi.org/10.1007/s10140-020-01784-3.
[38] P.M. George, S.L. Barratt, R. Condliffe, S.R. Desai, A. Devaraj, I. Forrest, M. A. Gibbons, N. Hart, R.G. Jenkins, D.F. McAuley, B.V. Patel, Respiratory follow-up of patients with COVID-19 pneumonia, Thorax 75 (11) (2020) 1009–1016.
[39] G. Raghu, K.C. Wilson, COVID-19 interstitial pneumonia: monitoring the clinical course in survivors, Lancet Respir. Med. 8 (9) (2020) 839–842.
[40] C.J. Lowenstein, S.D. Solomon, Severe COVID-19 is a microvascular disease, Circulation 142 (17) (2020) 1609–1611.
[41] S. Bilaloglu, Y. Aphinyanaphongs, S. Jones, E. Iturrate, J. Hochman, J.S. Berger, Thrombosis in hospitalized patients with COVID-19 in a New York city health system, JAMA 324 (8) (2020) 799–801.
[42] Y.J. Suh, H. Hong, M. Ohana, et al., Pulmonary embolism and deep vein thrombosis in COVID-19: a systematic review and meta-analysis, Radiology 298 (2) (2021) E70–E80.
[43] R.T. Dhawan, D. Gopalan, L. Howard, et al., Beyond the clot: perfusion imaging of the pulmonary vasculature after COVID-19, Lancet Respir. Med. 9 (1) (2021) 107–116.
[44] M. Remy-Jardin, L. Duthoit, T. Perez, et al., Assessment of pulmonary arterial circulation 3 months after hospitalization for SARS-CoV-2 pneumonia: dual-energy CT (DECT) angiographic study in 55 patients, Eclin. Med. 34 (2021), 100778.
[45] C. Huang, L. Huang, Y. Wang, et al., 6-month consequences of COVID-19 in patients discharged from hospital: a cohort study, Lancet 397 (10270) (2021) 220–232.
[46] S.M.H. Tabatabaei, H. Rajebi, F. Moghaddas, M. Ghasemiadl, H. Talari, Chest CT in COVID-19 pneumonia: what are the findings in mid-term follow-up? Emerg. Radiol. 27 (6) (2020) 711–719.
[47] J.N. Zou, L. Sun, B.R. Wang, et al., The characteristics and evolution of pulmonary fibrosis in COVID-19 patients as assessed by AI-assisted chest HRCT, PLoS One 16 (3) (2021), e0248957.
[48] M. Yu, Y. Liu, D. Xu, R. Zhang, L. Lan, H. Xu, Prediction of the development of pulmonary fibrosis using serial thin-section CT and clinical features in patients discharged after treatment for COVID-19 pneumonia, Korean J. Radiol. 21 (6) (2020) 746–755.
[49] C.F. McGroder, D. Zhang, M.A. Choudhury, et al., Pulmonary fibrosis 4 months after COVID-19 is associated with severity of illness and blood leucocyte telomere length, Thorax (2021), https://doi.org/10.1136/thoraxjnl-2021-217031. Published online April 29, 2021.
[50] W. Huang, Q. Wu, Z. Chen, et al., The potential indicators for pulmonary fibrosis in survivors of severe COVID-19, J. Infect. 82 (2) (2021) e5–e7.

[51] X. Han, Y. Fan, O. Alwalid, et al., Six-month follow-up chest CT findings after severe COVID-19 pneumonia, Radiology 299 (1) (2021) E177–E186.
[52] T.V. Lerum, T.M. Aaløkken, E. Brønstad, et al., Dyspnoea, lung function and CT findings 3 months after hospital admission for COVID-19, Eur. Respir. J. 57 (4) (2021), 2003448.
[53] A. Gulati, P. Lakhani, Interstitial lung abnormalities and pulmonary fibrosis in COVID-19 patients: a short-term follow-up case series, Clin. Imag. 77 (2021) 180–186.
[54] Sabina A. Guler, et al., Pulmonary function and radiological features 4 months after COVID-19: first results from the national prospective observational Swiss COVID-19 lung study, Eur. Respir. J. 57 (2021) 4.
[55] P.M. George, A.U. Wells, R.G. Jenkins, Pulmonary fibrosis and COVID-19: the potential role for antifibrotic therapy, Lancet Respir. Med. 8 (8) (2020) 807–815.
[56] L. Richeldi, R.M. du Bois, G. Raghu, et al., Efficacy and safety of nintedanib in idiopathic pulmonary fibrosis, N. Engl. J. Med. 370 (22) (2014) 2071–2082.
[57] M. Hämäläinen, R. Nieminen, P. Vuorela, M. Heinonen, E. Moilanen, Antiinflammatory effects of flavonoids: genistein, kaempferol, quercetin, and daidzein inhibit STAT-1 and NF-kappaB activations, whereas flavone, isorhamnetin, naringenin, and pelargonidin inhibit only NF-kappaB activation along with their inhibitory effect on iNOS expression and NO production in activated macrophages, Mediat. Inflamm. 2007 (2007), 45673.
[58] C. del Rio, P.N. Malani, COVID-19 in 2022—the beginning of the end or the end of the beginning? JAMA 327 (24) (2022) 2389–2390, https://doi.org/10.1001/jama.2022.9655.
[59] S. Collie, J. Champion, H. Moultrie, L.G. Bekker, G. Gray, Effectiveness of Bnt162b2 vaccine against omicron variant in South Africa, N. Engl. J. Med. 386 (5) (2022) 494–496, https://doi.org/10.1056/NEJMc2119270.
[60] A. Lind, R. Barlinn, E.T. Landaas, L.L. Andresen, K. Jakobsen, C. Fladeby, et al., Rapid sars-Cov-2 variant monitoring using pcr confirmed by whole genome sequencing in a high-volume diagnostic laboratory, J. Clin. Virol. 141 (2021), 104906, https://doi.org/10.1016/j.jcv.2021.104906.