Imaging Profile of the COVID-19 Infection: Radiologic Findings and Literature Review

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Five keywords:
2019 novel coronavirus; Wuhan; CT chest; chest radiograph; review

Abbreviations (no more than 10):
CT = Computed Tomography
CXR = Chest radiograph
RT-PCR = Reverse Transcription Polymerase Chain Reaction
SARS = Severe acute respiratory syndrome

Key Results:
1. Chest radiograph and CT findings of 21 patients with confirmed 2019 novel coronavirus infection in Shenzhen and Hong Kong are described and compared

2. A literature review and tabulation of the radiographic features in original publications are presented

3. One asymptomatic patient had evidence of consolidation on chest CT

Summary Statement:
Chest radiograph and CT findings of 21 confirmed COVID-19 patients are described along with a literature review of other publications describing the radiological findings of this novel coronavirus.

Abstract:

Background: COVID-19 (formerly known as the 2019 novel coronavirus [2019-nCoV]) has rapidly spread in mainland China and into multiple countries worldwide. The radiographic profile of this infection continues to evolve as more cases present beyond the epicenter of Wuhan, China.

Purpose: We present 21 COVID-19 cases from two Chinese centers with CT and chest radiograph (CXR) findings, as well as follow-up imaging in 5 cases.

Materials and Methods: Retrospective study in Shenzhen and Hong Kong. Patients with COVID-19 infection were included. A systematic review of the published literature on COVID-19 infection's radiological features.

Results: The predominant imaging pattern is of ground-glass opacification with occasional consolidation in the peripheries. Pleural effusions and lymphadenopathy were absent in all cases. Patients demonstrate evolution of the ground-glass opacities into consolidation, and subsequent resolution of the airspaces changes. Ground-glass and consolidative opacities visible on CT are sometimes undetectable on chest radiographs, suggesting that CT is a more sensitive imaging modality for investigation. The systematic review identified 4 other studies confirming the findings of bilateral and peripheral ground glass with or without consolidation as the predominant finding on CT chest examinations.

Conclusion: The COVID-19 infection pulmonary manifestation is predominantly characterized by ground-glass opacification with occasional consolidation on CT. Radiographic findings in patients presenting in Shenzhen and Hong Kong are in keeping with 4 previous publications from other sites.

Unstructured Abstract:

The 2019 novel coronavirus (2019-nCoV), initially reported in Wuhan, China, has been declared a global health emergency. CT has been used on a massive scale to help identify and investigate suspected or confirmed cases of COVID-19. We present the findings of 21 confirmed COVID-19 infection in Shenzhen and Hong Kong, China. We found that the most common findings on chest CT were bilateral ground-glass opacities with or without consolidation in the lung periphery. Pleural effusions and lymphadenopathy were absent in all patients. A systematic review was undertaken to summarize the 4 previous publications on the imaging findings of this emerging infection in a total of 233 patients. Ground glass with or without consolidation were the most common findings in all publications, in alignment with our own findings.

Introduction:

On 30th January 2020, COVID-19, formerly known as 2019 novel coronavirus (2019-nCoV), was declared to be a global health emergency by the World Health Organization[1]. Dramatic measures have been put in place to halt the progression of the virus, and as of 6th February, COVID-19 has infected over 28,000 patients with 564 confirmed deaths [2]. Knowledge of COVID-19 is still evolving, but anecdotal evidence is available suggesting that patients can be asymptomatic and infective for up to 14 days [3]. It is clear that our understanding of the radiological features of COVID-19 is incomplete, and as it continues to rapidly spread, there is an urgent need to consolidate the emerging knowledge on its radiologic profile.

In China, the disease epicenter, imaging has been at the forefront of investigation for patients with suspected or confirmed COVID-19 infection. As a result, computed tomography (CT) of the chest has been utilized on an unprecedented scale. Whilst the previous outbreak of severe acute respiratory syndrome (SARS) predominantly induced a spike in chest radiograph utilization, the literature on COVID-19, so far, has mainly focused on the role of CT for identifying patients and assessing disease progression.

Since the first initial published cases in Wuhan, COVID-19 has spread beyond to involve all provinces in China and into 19 countries overseas[2].

In this study, we add to the evolving radiologic profile of COVID-19 with the presentation of the CT chest and CXR findings of 21 cases in Shenzhen and Hong Kong, China, supplemented with further insight about the timing of symptom onset versus imaging findings, clinical symptoms, hematological and biochemical markers, as well as CT and radiographic follow-up imaging. Furthermore, we performed a literature review to provide an up-to-date synthesis of the radiographic portrait of the COVID-19 infection.

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Methods:

Study approval was obtained from the Institutional Review Boards of the University of Hong Kong-Shenzhen Hospital, Hong Kong West, and Eastern Cluster. Patients with confirmed COVID-19 infection were identified and enrolled in the study. Reverse transcription polymerase chain reaction (RT-PCR) methods for identifying COVID-19 have been previously described [3]. Two additional patients with travel to Wuhan, contact history, clinical symptoms, blood results, and negative swabs for other diseases were diagnosed as infected by COVID-19. Written consent was obtained for patients in Shenzhen, whilst consent requirements were waived for the cases recruited in Hong Kong according to local institutional review board requirements. Eighteen patients were recruited from Shenzhen and three were recruited from Hong Kong. Six patients recruited from Shenzhen have been previously reported, but the radiological appearances were only briefly mentioned [3]. All patients had at least one chest CT performed, while four patients also had follow-up CT. Five patients had chest radiographs (CXR), three of which had follow-up CXR on a daily basis. Two patients had six follow-up CXR and one patient had ten follow-up CXR.

Clinical Parameters and Blood Tests:

Clinical data, such as symptoms and past medical history, were obtained directly from the patient or through the electronic patient database. Onset of symptoms to time of CT examinations, as well as time interval between CT examinations and CXR examinations were obtained. Hematological and biochemical blood test results were gathered via the electronic patient record system.

Image Acquisition:

Volumetric CT thorax images were acquired at 1-mm slice thickness and reformatted with lung and soft tissue windows. No intravenous contrast was administered. Conventional CXR were acquired in the posteroanterior projection at initial presentation. Follow-up films were

acquired in the anteroposterior projection. All of the radiologic studies followed usual clinical acquisition parameters according to local protocols.

Image Interpretation:

All available CT and CXR images of the relevant patients were obtained and reviewed by two thoracic radiologists jointly (MYN, 8 years of experience with cardiothoracic fellowship training & EYPL, 12 years of experience).

CT images were classified as having ground glass opacities, consolidation, cavitation or nodular opacities. The distribution of these lung changes were also classified based on (i) upper zone predominance, lower zone predominance or no zonal predominance, (ii) peripheral or central predominance or neither, (iii) lobes involved (iv) presence of pleural or pericardial effusions (v) presence of enlarged mediastinal or hilar lymph nodes (defined as a lymph node with short axis measurement ≥10mm, only on CT). CXR images were assessed in a similar manner, allowing for technical differences between methods.

Patients with follow-up CT or CXR images were compared to determine if there was either progression, stability, or improvement of the lung changes.

Radiological lesions were diagnosed based on the Fleischner Society glossary of terms[4]. Ground-glass opacities were defined as an increase in opacification of the lung which does not obscure the blood vessels and airways. Consolidation was defined as a homogenous opacification that obscures blood vessels and airway walls. Reversed CT halo sign was defined as a rounded area of ground glass surrounded by a complete or almost complete ring of consolidation.

Comparison and Synthesis of Radiographic Findings with Published Literature:

Previous publications were searched in order to obtain a larger consensus of radiographic appearances on CT chest and CXR examinations. The search terms “Wuhan” and “coronavirus” were used in PubMed for original research publications written in the English

language since 1st December 2019 to 7th February 2020. Only publications with >10 patients were included in the final sample. Fifty-six publications were found. Twenty-eight publications were removed on inspection of the title. Twenty-five publications were removed based on review of the abstract and full paper, leaving four eligible publications for detailed review.

Statistical Analysis:

Findings are presented as medians and interquartile ranges due to the small sample size. Categorial variables are described as whole numbers, with percentages in brackets.

Results:

Of the 18 patients, 13 were male and 8 were female. The patients' ages ranged from 10 to 74 years. All patients were symptomatic, except for one patient who was the child of a family cluster confirmed to have COVID-19. Clinical symptoms, past medial history, history of travel to Wuhan and hematological and biochemical results are summarized in Table 1.

Chest CT Findings:

CT thorax examinations were performed at a median of 3 days from onset of symptoms (interquartile range 1-7 days). Of the 21 cases, 2 patients had normal chest CTs. The CT lesions and distribution across the 21 reported cases are listed in Table 2. Briefly, the predominant feature was ground-glass opacification (n=18, 86%) followed by consolidation (n=13, 62%) (see figure 1). Eleven cases had predominantly ground-glass opacities, four had mixed appearances and four had predominantly consolidative changes. The ground-glass and consolidative opacities were peripheral in all patients with lung findings (n=18), apart from one patient who had perihilar ground glass changes. Eight patients showed lower zone predominance, eight patients showed equal distribution between the upper and lower zones and three patients showed upper zone predominant changes. Subpleural sparing, pleural effusions, pericardial effusion, cavitation, mediastinal and hilar lymph node enlargement were not seen in any of the patients.

Ground-glass and consolidative opacities were most frequently seen in the left lower lobe (n=17, 81%), right lower lobe and left upper lobe (both n=16, 76%), whilst the right middle lobe had the lowest involvement (n=10, 48%) (see Table 2). The reversed CT halo sign was seen infrequently (n=2).

Chest Radiograph Findings:

Five patients had CXR along with CT thorax examinations (Table 3). Of these, two patients showed normal CXR findings, despite also having CT examinations performed on the same day showing ground glass opacities (Figure 2). The other three CXR examinations showed

consolidation. One CXR showed lower zone predominance, whilst the other two CXR examinations did not show any zonal predominance. In these three patients, their CXR examinations did not demonstrate the peripheral predominance that was visible on their respective CT examinations.

CT and CXR Follow-Up:

Four of twenty-one patients had a follow-up CT. Three patients had follow-up CT performed four days after the initial CT, while one patient had follow-up CT three days after the initial CT. In one patient, there was a reduction in the consolidation (Figure 3). The second patient had a normal CT thorax examination at presentation. On subsequent CT, the CT remained normal with no new lung changes. The third patient's CT showed progression of the lung changes with new ground-glass nodules in other lobes. The preceding ground-glass opacities increased in size, with some peripheral consolidation (Figure 4). The fourth patient showed the previously observed ground glass opacities becoming smaller areas of consolidation.

Three different patients had daily CXR. In two patients, there was progression in the lung consolidation over a period of 3-4 days (Figure 5A). Subsequent CXR show improvement over the subsequent two days (Figure 5B). The third patient showed no significant changes over an 8-day period.

Literature Review of Radiographic Appearances of COVID-19:

We identified four articles[5-8] with more than 10 patients describing the CXR or CT findings of COVID-19 infected patients (Table 4). The studies had 99 patients, 41 patients, 21 patients, and 51 patients, in chronological order of publication date (from January 30th, 2019 through February 6th, 2020), with the mean or median age of patients around 50 years old. Two studies briefly described the CT appearances of the lung findings, in which they described a predominantly bilateral pneumonia or consolidation. In the study by Huang et al. [6] of 41 patients, they described predominantly consolidation in patients in the intensive

care unit, whilst the patients outside the intensive care setting had a mixture of ground-glass opacities and consolidation. In Chen et al.'s study [5] with 99 patients, in addition to the CT findings, they found that bilateral pneumonias were the most common finding on chest radiograph. In Chung et al.'s paper [7], the CT findings were typically ground glass (57%) and peripheral distribution in 33% of patients. Lung cavitation, discrete pulmonary nodules, pleural effusions, and enlarged lymph nodes were absent. They also found normal chest CTs in 14% of patients. Song et al. [8], described predominantly ground-glass opacities (77%), but a larger amount of peripheral distribution (86%) and lower lobe involvement (90%). They further showed that there was improvement in follow-up chest CTs in 54% of the patients, contrasting with imaging progression seen in 31% of patients.

Discussion:

Our study confirms that ground-glass opacities and consolidation in the lung periphery has been the imaging hallmark in patients with COVID-19 infection. Furthermore, solid pulmonary nodules, cavitation, pleural effusions and mediastinal/ hilar lymph node enlargement were not typically observed. We performed a review of the recent literature to synthesize the findings in 233 patients infected with COVID-19 (including 21 reported herein). All studies have shown consistent findings, with bilateral ground glass and consolidation being the most frequent findings on CT and CXR. Peripheral predominance of the lung opacities has been also found across studies. Furthermore, we identified one asymptomatic patient chest CT abnormalities. Despite many potential biases related to patient selection and retrospective nature of the study, our findings suggest that CXR may lack sensitivity to identify some of the manifestations of the COVID-19 infection in the lungs, which are otherwise evident on CT.

While the disease profile of COVID-19 is dynamic and continues to rapidly evolve, there are still many open questions. As is evident in our synthesis, there are cases where patients confirmed with COVID-19 infection have no chest CT abnormalities, contrasting with subclinical infection presenting with positive imaging findings on CT [7]. It is crucial that the clinical impacts of screening asymptomatic patients with chest CT be determined. A more thorough analysis about the existence of any potential benefit on clinical outcomes needs to be addressed against the known financial costs and exposure to ionizing radiation associated with CT scanning.

As more and more suspected cases arise, there are issues with having enough available RT-PCR kits to confirm COVID-19 infection. This has led to chest CT being utilized to aid diagnosis in the absence of RT-PCR, as demonstrated in a recent case report from China [9]. Our experience in the Guangdong province has seen an unprecedented use of CT in an infectious disease outbreak. The power of this tool in helping to raise suspicion as well as to

follow the course of the disease is becoming increasingly apparent. Here in the Guangdong province, chest CTs are being requested on every patient suspected of having COVID-19. Thus, in addition to aiding in disease screening and follow-up evaluation, further investigation is also necessary to determine the role of CT in helping guiding therapy.

Of note, our cases bear striking similarities compared to SARS (Figure 6). Both pathogens demonstrate predominantly ground-glass opacities, with consolidation occasionally seen[10, 11]. The progression of the lung changes of COVID-19 on CT imaging is also similar to SARS, with the ground-glass and consolidation getting worse or better over several days [12]. This would be expected, as the two infectious agents are part of the coronavirus family. SARS had a mortality rate of 9.5%[13], whilst the current novel coronavirus appears to have a mortality rate around 2%, based on the number of confirmed cases and deaths [2].

Our study has several limitations, but mainly, our sample size is small and our follow-up interval short. Such limitations preclude the possibility of any deep analysis about potential prognostic imaging variables that could aid in the prediction of worse outcomes. Moreover, it does not address the role of imaging in guiding or monitoring medical therapy in the infected individuals. Notwithstanding, our study continues to add knowledge about the disease in a growing number of centers apart from the epicenter of the outbreak in Wuhan. Last, it also presents CXR findings in a small number of patients, information that has been lacking in most of the recent imaging reports of the disease.

In conclusion, we present the CT and CXR findings of 21 patients infected with COVID-19 in Shenzhen and Hong Kong, providing a composite radiologic profile with a systematic review of the current literature.

Table 1: Patient Characteristics including Travel History, Symptoms, Past Medical History and Hematological and Biochemical Findings.

Sex	13 Male (62%) 8 Female (38%)
Age (years)	56 (IQR 37-65years old)
Travel to Wuhan	17 (81%)
Contact with Confirmed COVID-19 infected Patient	3
Symptoms:	
Fever	19 (90%)
Temperature (Celsius)	38 (IQR 37.4-38.4)
Heart Rate (beats per minute)	90.5 (IQR 82.5 - 103)
Systolic Blood Pressure (mmHg)	126 (IQR 119.5-150)
Diastolic Blood Pressure (mmHg)	78 (IQR 74 - 87.5)
Respiratory Rate (breaths per minute)	19 (IQR 18-20)
Saturations (%)	97% (IQR 96-98%)
Cough	10 (48%)
Sputum	3 (15%)
Hemoptysis	0 (0%)
Sore Throat	2 (10%)
Diarrhea	2 (10%)
Chest Pain/ Pleuritic Chest Pain	1 (5%)
Dyspnea	0 (0%)
Past Medical History:	
Diabetes	3 (14%)
Hypertension	3 (14%)

Chronic Obstructive Pulmonary Disease	0 (0%)
Malignancy	0 (0%)
Chronic Liver Disease	1 (5%)
Human Immunodeficiency Virus	0 (0%)
Hematological Results:	
Hemoglobin (g/dL) (male normal range 13·3–17·1; female normal range 11·5–14·8)	13.8 (IQR 13.2-15.3)
White Cell Count (x10^9 cells/Liter) (normal range 3·9–9·9)	5.3 (IQR 4.3 – 6.2)
Neutrophil Count (x10^9 cells/Liter) (normal range 2·0–7·4)	3.33 (IQR 3 – 3.91)
Lymphocyte Count (x10^9 cells/Liter) (normal range 1.1–3.6	1.29 (IQR 0.7 – 1.65)
Platelet Count (x10^9 cells/Liter) (normal range 162–341)	169 (IQR 148 – 196)
Prothrombin Time (s) (normal range 11.0–14.5)	12.7 (IQR 12.2 – 13)
Activated Partial Thromboplastin Time (s) (normal range 26·0–40·0)	36 (IQR 34 – 41)
Biochemistry Results:	
D-Dimer (µg/ml) (normal range 0·0–0·5)	0.4 (IQR 0.26 – 0.6)
Sodium (mmol/L); (normal range 136-145)	139 (IQR 136 – 141)
Potassium (normal range 3·5–5·1)	3.86 (IQR 3.7 – 4)
Urea (mmol/L) (normal range 2·8–8·1)	4.45 (IQR 3.4 – 5.5)
Creatinine (µmol/L) (normal range 44–80)	72 (IQR 55-84)
Albumin (normal range 35·0–52·0)	42.2 (IQR 39.4 – 45.8)
Total Bilirubin (normal range 0·0–21·0)	7.0 (IQR 5.9 – 8.8)
Alanine Aminotransferase (normal range 0·0–33·0)	22.5 (IQR 15.6 – 34.4)
Aspartate Aminotransferase (normal range 0·0–32·0)	25.5 (IQR 20.1 – 35.2)
Lactate Dehydrogenase (normal range 135–214)	218 (IQR 183 – 252)

Creatine Kinase (normal range 0–170)	78 (IQR 69-137)

IQR = Interquartile range

Table 2. Computed Tomography (CT) Chest Findings.

Symptom Onset to 1st CT Scan	3 days (IQR 1-7)
Lobar Involvement	
RUL	14 (67%)
RML	10 (48%)
RLL	16 (76%)
LUL	16 (76%)
LLL	17 (81%)
CT Lung Lesion Appearances	
Ground-Glass Opacities	18 (86%) 4 had ground-glass nodules (19%)
Consolidation	13 (62%)
>50% findings were ground-glass opacities	11
>50% findings were consolidations	4
Equal mix of ground-glass and consolidation	4
Cavitation	0
Solid Nodules	1*
Pleural Effusion	0
Pericardial Effusion	0
Enlarged Mediastinal or Hilar Lymph Nodes (≥10mm in short axis measurement)	0
No abnormal findings	2
Predominant Distribution	
Peripheral	18 (86%)
Perihilar	1 (5%)
Neither peripheral or perihilar	2**
Upper zone	3 (14%)
Lower zone	8 (38%)
Similar upper and lower zone involvement	8 (38%)

RUL = Right upper lobe; RML = Right Middle Lobe; RLL = Right Lower Lobe; LUL = Left Upper Lobe; LLL = Left Lower Lobe

*Appearance consistent with a solitary intrapulmonary lymph node

** CT showed no abnormalities

Table 3. Chest Radiograph Findings in 5 Patients.

Lung Changes	
Normal Chest Radiograph Findings	2
Consolidation	3
Predominantly Consolidation	2
Bilateral Lung Involvement	2
Pleural Effusion	0
Predominance	
Upper zone	0
Lower zone	1
Similar upper and lower zone involvement	2

Table 4. Comparison of Papers Published by 7th February, 2020.

	Current Study	Chen et al[5]	Huang et al[6]	M Chung et al.[7]	Song et al. [8]
No. of Patients	21 patients	99 patients	41 patients	21 patients	51 patients
Age	56 years (IQR 37-65years old)	Mean 55.5 years (SD:13.1)	Median 49 years (IQR: 41-58)	Mean 51 years (range: 29-77years)	Mean 49 (range 16-76 years)
Imaging Modality	CT & CXR	CT & CXR	CT only	CT only	CT only
CXR Findings					
Consolidation	60%	100%			
Pleural Effusion	0	N/A			
Progression Visible	Yes	N/A			
Improvement Visible	Yes	N/A			
Normal CXR	2	0			
CT Findings					
Time Between Onset & 1st CT	Median 3 days (IQR 1-7 days)	N/A	8 days	N/A	Classified as (i) ≤4 days or (ii) >4days
Consolidation	62%	100%	Typically present	29%	59%
Ground Glass	86%	14%	Typically present	86%	77%
Predominant Distribution	Peripheral (86%) Lower Zone (38%) Similar Upper & Lower Zone (38%)	Bilateral (75%)	Bilateral (98%)	Peripheral (33%) Bilateral (76%)	Peripheral (86%) Bilateral (86%) Lower lobes (90%)

Lymphadenopathy	0%	N/A	N/A	0%	6%
Pleural Effusion	0%	N/A	N/A	0%	6%
CT Follow-up					
Number of CT Follow-up Cases	4 patients	1 patient	1 patient	8 patients	13 patients
Time Interval Between Symptom Onset and 1st CT	5-10 days (1 patient was asymptomatic)	N/A	8 days	N/A	Classified as (i) ≤4 days or (ii) >4days
Time Difference Between CTs	3-4 days	14 days	4 days	1-4 days (Mean 2.5 days)	N/A
Improvement	2 (50%)	1 (100%)	1 (100%)	0 (0%)	7 (54%)
Progression	1 (25%)	0 (0%)	0 (0%)	7 (88%)	4 (31%)
Stable	1 (25%) [Patient had normal CT at presentation]	0 (0%)	0 (0%)	1 (13%) [Patient with normal CT]	2 (15%)

CT = Computed Tomography; CXR = Chest radiograph; IQR= Interquartile range; SD= standard deviation

Figure 1. A 65-year-old female patient who had travelled to Wuhan, China, subsequently developing fever and cough 5 days after arrival. She subsequently returned to Shenzhen, China, and had this chest CT 7 days after symptom onset. Coronal and axial CT images (A & B) showing a mixture of ground glass and consolidation in the periphery of the lungs (red arrows), with absence of pleural effusions, which was the typical appearance of patients with confirmed COVID-19 infection.

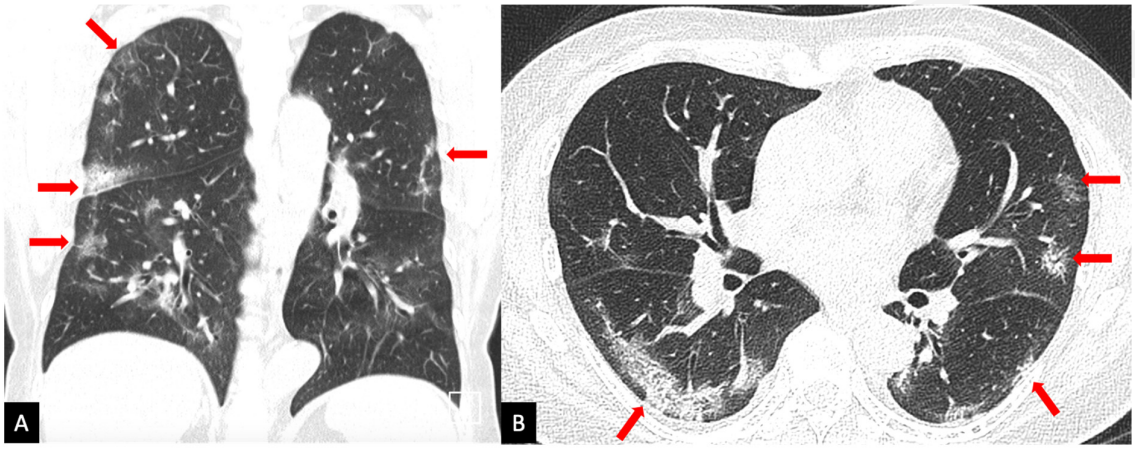


Figure 2. Comparison of chest radiograph (image A) and CT thorax coronal image (image B). The ground glass opacities in the right lower lobe periphery on the CT (red arrows) are not visible on the chest radiograph, which was taken 1 hour apart from the first study.

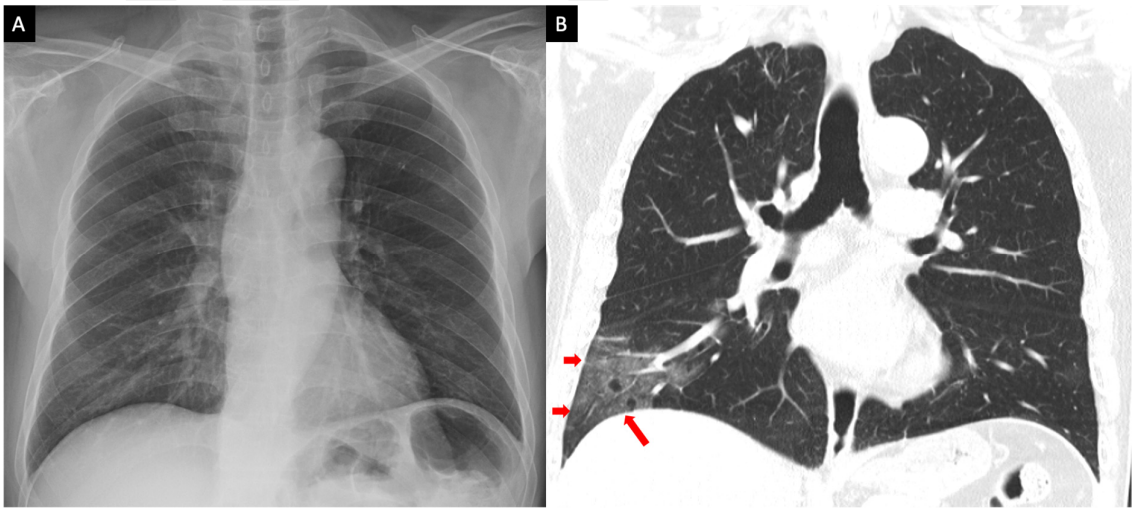


Figure 3. A 10-year-old asymptomatic child with confirmed COVID-19 infection, who had travelled to Wuhan, China with his family. Image A shows the initial CT scan at time of presentation, with consolidation in the left lower lobe apical segment. Image B shows mild improvement in the lung consolidation 4 days later.

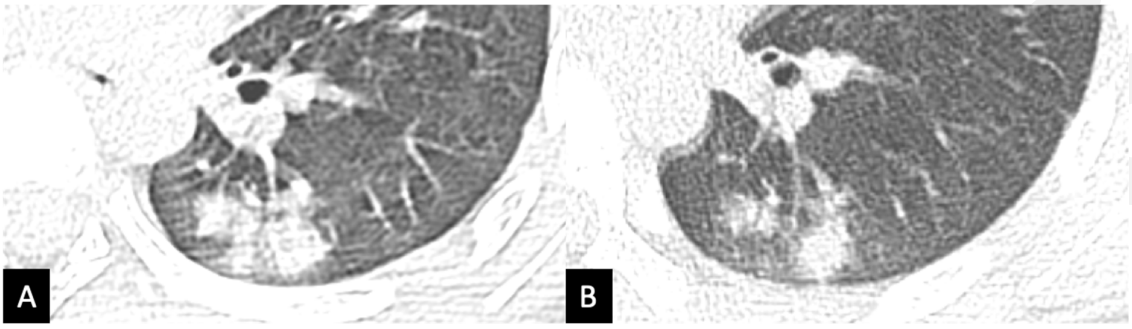


Figure 4. CT Chest follow-up in a patient who had no previous travel to Wuhan, China, but had contact with a patient with confirmed COVID-19 infection. Axial slices from day 0 of presentation to the hospital shows ground-glass opacities in the left lower lobe (image A, arrow), but not in the right upper lobe (image C). Subsequently, 3 days later, the follow-up CT showed increase in the ground glass changes with some peripheral consolidation (reversed halo, image B, arrow) and new ground-glass opacities in the right upper lobe periphery (image D, arrow).

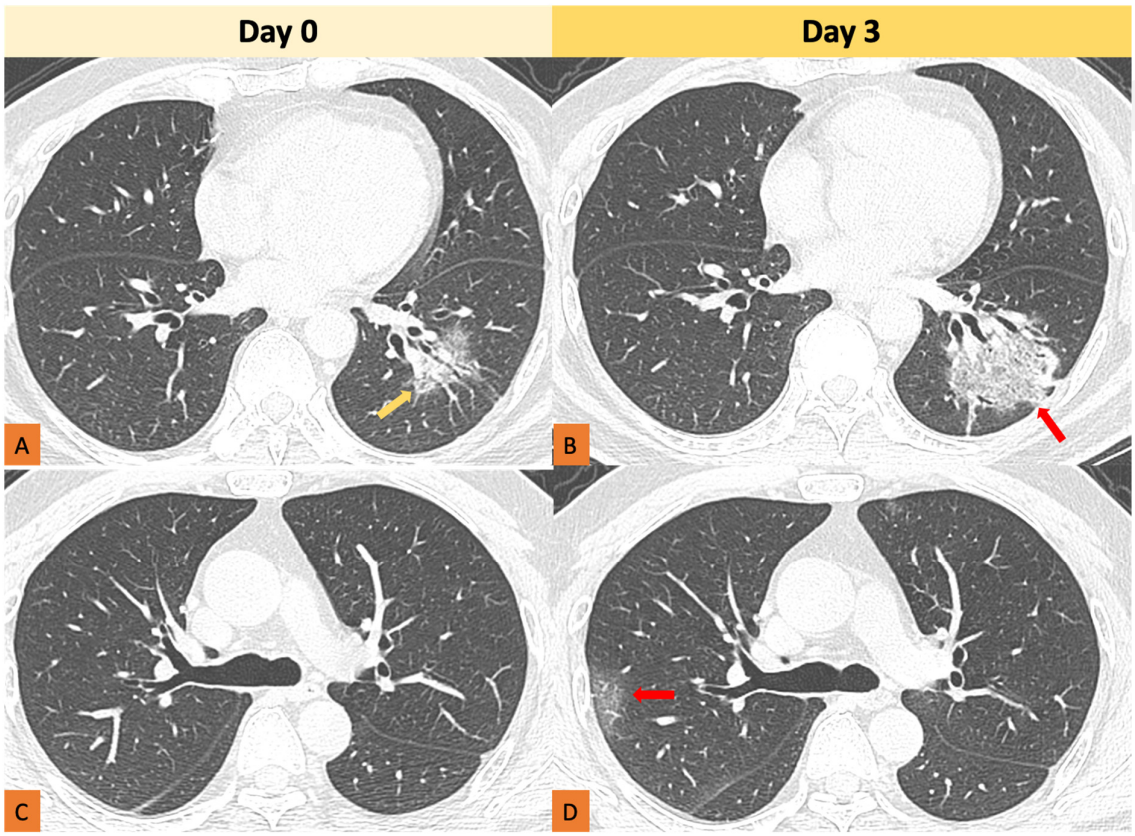


Figure 5. Chest radiographs of an elderly male patient from Wuhan, China, who travelled to Hong Kong, China. These are 3 chest radiographs selected out of the daily chest radiographs acquired in this patient. The consolidation in the right lower zone on day 0 persist into day 4 with new consolidative changes in the right midzone periphery and perihilar region. This midzone change improves on the day 7 film.

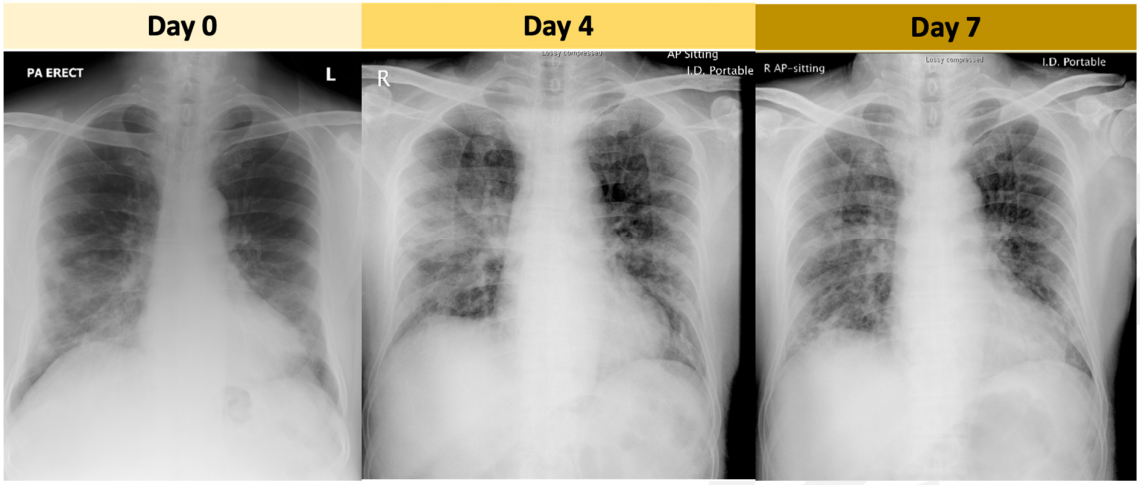
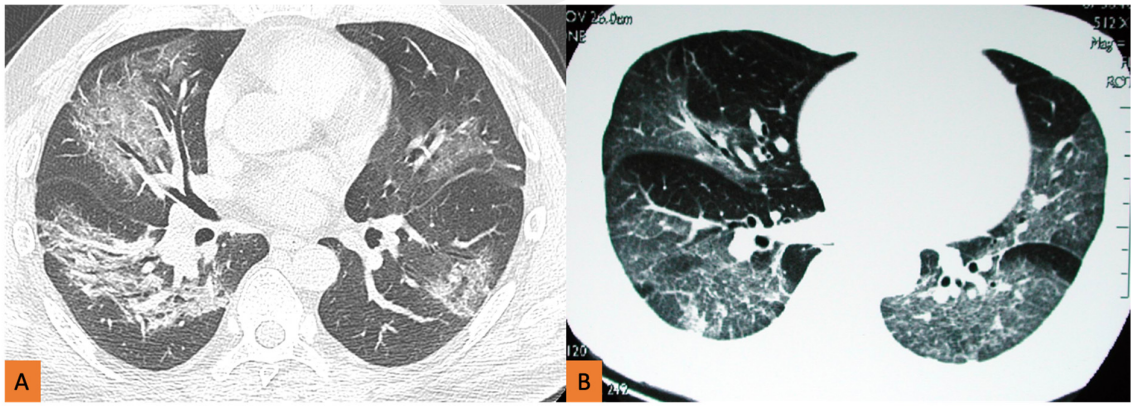


Figure 6. Axial CT images showing a case of COVID-19 (image A) and a case of severe acute respiratory syndrome (SARS) from 2003 (image B). Both cases demonstrate similar predominantly ground-glass opacities affecting both lungs.



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