

R E V I E W

Radiological diagnosis of coronavirus disease 2019 (COVID-19): a practical guide

Chiara Floridi^{1,2}, Marco Fogante², Andrea Agostini^{1,2}, Alessandra Borgheresi², Michaela Cellina³, Raffaele Natella⁴, Federico Bruno⁵, Diletta Cozzi⁶, Nicola Maggialetti⁷, Pierpaolo Palumbo⁵, Vittorio Miele⁶, Marina Carotti², Andrea Giovagnoni^{1,2}

¹ University Politecnica delle Marche, Department of Clinical, Special and Dental Sciences; ² Division of Special and Pediatric Radiology, Department of Radiology, University Hospital “Umberto I – Lancisi – Salesi” Ancona, AN, Italy; ³ Department of Radiology, ASST Fatebenefratelli Sacco, Milan, Italy; ⁴ Department of Precision Medicine, University of Campania “Luigi Vanvitelli”, Naples, Italy; ⁵ Department of Biotechnology and Applied Clinical Sciences, University of L’Aquila, L’Aquila, Italy; ⁶ Department of Radiology, Azienda Ospedaliero-Universitaria Careggi, Florence, Italy; ⁷ Department of Medicine and Health Sciences “V. Tiberio”, University of Molise, Campobasso, Italy.

Summary. Novel beta-coronavirus (2019-nCoV) is the cause of Coronavirus disease-19 (COVID-19), and on March 12th 2020, the World Health Organization defined COVID-19 as a controllable pandemic. Currently, the 2019 novel coronavirus (SARS-CoV-2) can be identified by virus isolation or viral nucleic acid detection; however, false negatives associated with the nucleic acid detection provide a clinical challenge. Imaging examination has become the indispensable means not only in the early detection and diagnosis but also in monitoring the clinical course, evaluating the disease severity, and may be presented as an important warning signal preceding the negative RT-PCR test results. Different radiological modalities can be used in different disease settings. Radiology Departments must be nimble in implementing operational changes to ensure continued radiology services and protect patients and staff health. (www.actabiomedica.it)

Keywords: SARS-CoV-2, COVID-19, chest CT, chest x-ray, lung US

Introduction

Novel beta-coronavirus (2019-nCoV) is the cause of Coronavirus disease-19 (COVID-19), and on March 12th 2020, the World Health Organization defined COVID-19 as a controllable pandemic.

Person-to-person virus transmission occurs primarily through droplets or via direct contact from an infected individual. Clinical common symptoms are fever, cough, dyspnea, and muscle aches (1). The mortality rate is about 3.0%, and male gender, age ≥ 60 years, delay in diagnosis, and severe pneumonia are associated with increased mortality rates (2).

COVID-19 is highly contagious, and early diagnosis is mandatory to isolate suspected cases and contacts to control the outbreak. Real-time polymerase

chain reaction (RT-PCR) is the standard diagnostic method to detect viral nucleotides from the oropharyngeal or nasopharyngeal swab, but it has a sensitivity of 60-71%; hence, at present, the diagnosis of COVID-19 is mainly based on epidemiological history, clinical symptoms and chest imaging findings (3).

Chest imaging plays an essential role in the detection, evaluation of severity, and follow-up of the disease (4), and healthcare workers in Radiology Departments are exposed to patients with COVID-19 and are at high risk of being infected (5).

The aim of this work is to provide a Practical Guide that summarized the Radiology Department preparedness, the choice of best imaging modalities, the main radiological findings, and differential diagnosis of COVID-19.

Radiology Department Preparedness

The novel coronavirus can be transmitted through respiratory droplets, that may travel up to 183cm from their source, or via direct contact and probably could be transmitted via touching a surface or item that is contaminated with the virus. For all these reasons, the healthworkers exposed to Covid-19 have a high risk of being infected and need strict precautions also in the Radiology Department.

If possible, it is preferable to use the diagnostic imaging portable X-ray equipment to reduce the transportation of the patients. For this purpose, the presence of a portable x-ray equipment in each covid-department is desirable. If the Covid-patients need to be transported to the Radiology department to perform a radiological exam (especially CT and MR examinations) (6-12), they should avoid the conventional routes but use dedicated elevators and designated routes, avoiding to stay in the waiting area. Moreover, if possible, it should be expected a dedicated CT scanner for infected patients. During Covid-patients radiological exams, all the radiologic personal should wear adequate personal protective equipment (PPE), and at the end of radiological exams, they should be able to remove the PPE using a specific room, in order to avoid contamination of themselves or their colleagues. The computed tomography (CT) scanner, the image workstation, mouse, and keyboards need to be disinfected after every contact with suspected and infected patients. Environmental services staff need to have guidelines and to be specifically trained for the professional cleaning of the potentially contaminated surfaces after each high-risk patient contact.

If appropriately prepared, the Radiology Department Personnel can reduce and manage the coronavirus outbreak impact on the facility and the staff (13).

Imaging modalities

Chest X-ray

Chest X-ray (CXR) is the first imaging modality used in clinical suspicion of infective lung disease to detect lung abnormalities, to assess the extension and

complications, and to rule out alternative diagnosis. Pulmonary signs usually compared on the CXR within 12 hours of the onset of symptoms (14).

Suggested Indications in COVID-19

CXR is suggested in the detection of lung abnormalities, with clinical suspicion and waiting for the RT-PCR outcome (30). CXR is suggested in the routine follow-up to obviate the need for computed tomography (CT) and to reduce the burden on CT units (15). The main advantages are the low cost, especially in the settings of limited medical resources, the possibility of bedside examination with a dedicated portable CXR machine, the reduction of the risk of cross-infection related to patients' transport (16). The main disadvantages are the low sensibility in the detection of lung abnormalities in the early stage and the possibility that the radiological findings do not correlate with disease progression (16).

Chest CT

Chest CT, particularly high-resolution CT (HRCT), is the more sensitive imaging modality in the detection of lung infection abnormalities. HRCT is useful in clinical suspicion of pneumonia with normal or nonspecific CXR findings, to assess the extension and complications, to rule out underlying lesions, and to evaluate patients with persistent or recurrent pulmonary opacities (14).

Suggested Indications in COVID-19

Chest CT is suggested for early diagnosis with clinical suspicions, normal or non-definitive lung abnormalities in CXR, and with RT-PCR outcome unavailable or negative (17). Chest CT is suggested in clinical deterioration unaccompanied with CXR worsening and in the follow-up of severe cases to evaluate permanent lung damage (19). The main advantages are the high sensitivity for the detection of lung abnormalities that could be helpful in rectifying RT-PCR false negatives and the high performance in the evaluation of different stages of disease severity (19). The main disadvantages are the risk of transporting critical pa-

tients, the necessity to decontaminate the scan room, the time-consuming of the organization (20) and the higher radiation exposure (21).

Lung ultrasound

Lung ultrasound (LUS) initially seemed to be unsuitable for the study of lung parenchyma and was mainly used to guide puncture of pleural effusion. With advances in ultrasound technology, LUS has been gradually used successfully in the diagnosis and monitoring of infective lung disease (22).

Suggested Indications in COVID-19

LUS is suggested in the serial monitoring of lung aeration in the intensive care unit (ICU) to evaluate lung excursion and compliance to regulate the intensity of respiratory support (23). LUS is suggested to evaluate the re-expansion of the atelectasis areas and to guide invasive diagnostic procedures (23). The main advantages are the possibility of bedside examination, the reduction of radiation exposure, the reduction of the risk of cross-infection related to patients' transport, the real-time images, the opportunity of serial monitoring, and the reduction of healthcare workers exposed during the investigation (24). The main disadvantages are the operator-dependent image interpretation, the necessity of experience to generate high quality and reproducible images, the time-consuming examinations due to the evaluation of many

lung regions and the necessity for the clinician to implement personal safety procedures (24).

PET-CT

Positron emission tomography with 2-deoxy-2-[fluorine-18] fluoro D-glucose integrated with computed tomography (18F-FDG PET-CT) imaging has the ability to delineate infective lung disease quantitatively. In inflammatory conditions, glycolytic metabolism is elevated in the region of leukocyte infiltration associated with inflammatory processes, and consequently, FDG uptake is increased (25).

Suggested Indications in COVID-19

PET-CT is suggested at the early stages of the disease when clinical symptoms are not specific, and differential diagnosis between benign and malignant lesions is challenging (25). The main advantages are the possibility to reflect in changes in uptake patterns and locations during virus exposure and to evaluate all the body when a viral infection causes the damage of other organs and/or it is associated with other diseases (26). The main disadvantages are the limited use in an emergency setting, the complexity of images interpretation, time-consuming of the procedure, the risk of transporting critical patients, and the necessity to decontaminate room (26). Suggested indications for each imaging modalities are summarized in **Table 1**.

Table 1. Suggested Indications of imaging modalities in COVID-19.

Imaging Modalities	Suggested Indications
CXR	<ul style="list-style-type: none"> • detection of lung abnormalities, with clinical suspicion and waiting the RT-PCR outcome. • routinely follow-up to obviate the need for a CT and to reduce the burden on CT units.
Chest CT	<ul style="list-style-type: none"> • early diagnosis with clinical suspicions, normal or non-definitive lung abnormality in CXR and with RT-PCR outcome unavailable or negative. • clinical deterioration unaccompanied with CXR worsening. • follow-up of severe cases to evaluate permanent lung damage.
Lung US	<ul style="list-style-type: none"> • serial monitoring of lung aeration in ICU to evaluate lung excursion and compliance to regulate the intensity of respiratory support. • to evaluate the re-expansion of the atelectasis areas. • to guide invasive diagnostic procedures.
PET-CT	<ul style="list-style-type: none"> • differential diagnosis between benign and malignant lesions

Abbreviations. COVID-19: coronavirus disease-19; CXR: chest X-ray; CT: computed tomography; US: ultrasound, PET: positron emission tomography; RT-PCR: real time-polymerase chain reaction; ICU: intensive care unit.

Imaging Features

Chest X-ray

The main imaging abnormalities are patchy or diffuse asymmetric focal or multifocal unilateral ill-defined areas and airspace opacity with peripheral distribution in the middle and lower peripheral lung zones (**fig. 1**). As the disease progress, compared multifocal consolidation involving one or both lungs with extension into the perihilar and upper lobes. Rarely the opacities are focal and unilateral.

The imaging findings of unfavorable outcomes are the presence of diffuse and confluent airspace opacities that involved four or more lung zones, and the blunting of the costophrenic angles resulting from pleural effusion (27).

Chest CT

The imaging abnormalities increased in number and severity in the first period with a short plateau phase and a gradual decrease. The initial stage (0–4 days after onset of the initial symptoms) is characterized by bilateral, peripheral, and sub-pleural or peribronchovascular areas of patchy or segmental pure ground-glass opacities (GGOs) (**fig. 3**) with the involvement of lower lobes, rare consolidations, reverse halo sign and vascu-



Figure 1. 65-year-old man patient with fever and respiratory failure (RT-PCR test positive): the chest x-ray image shows diffuse multifocal consolidation involving both lungs.

lar dilatation. The progressive stage (5–8 days after the onset of the initial symptom) is characterized by diffuse GGOs, consolidations, interlobular septal thickening, and sometimes crazy-paving pattern. The peak stage (9–13 days after the onset of the initial symptom) is characterized by diffuse consolidations, parenchymal bands, and marked interlobular septal thickening. The

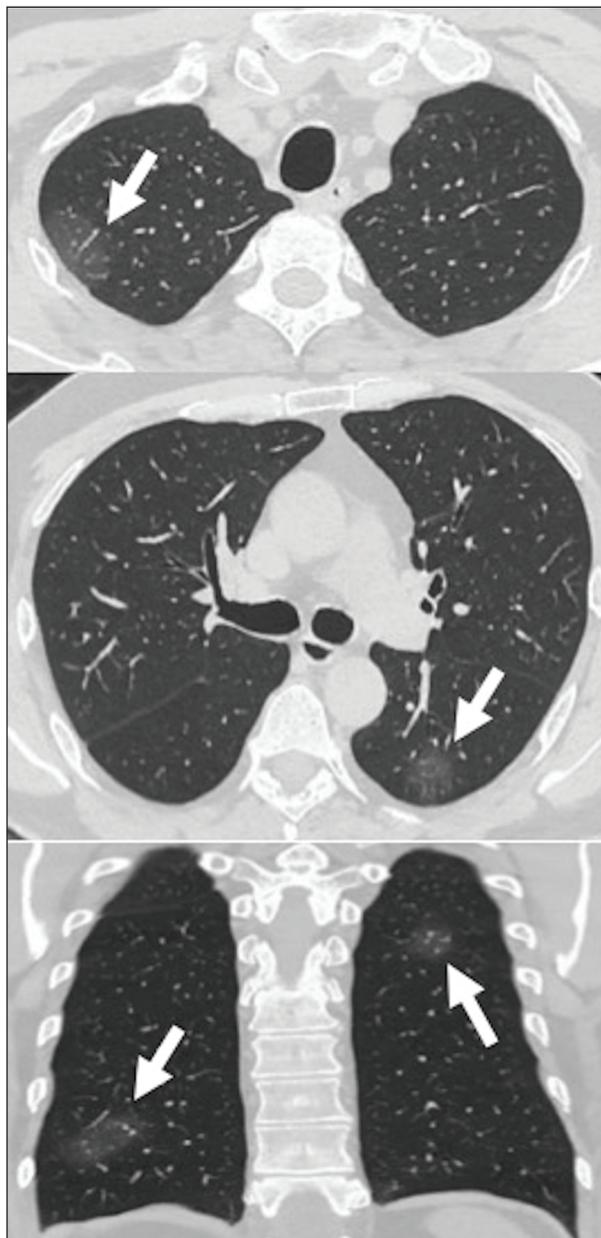


Figure 2. 54-year-old man patient with fever and diffuse thoracic pain (RT-PCR test positive): the multiplanar chest CT images show multifocal and bilateral peripheral areas of patchy pure ground-glass opacities (white arrows).

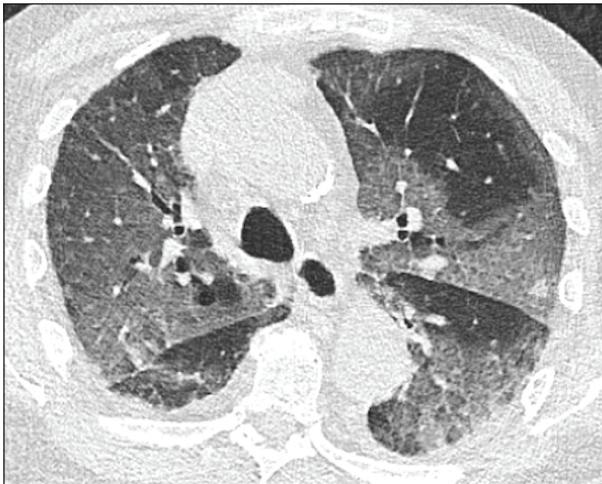


Figure 3. 81-year-old man patient with fever, cough and respiratory failure (RT-PCR test positive): the axial image of chest CT shows multiple bilateral ground-glass areas with marked interlobular septal thickening.

absorption stage (14–30 days after the onset of the initial symptom) is characterized by rare consolidations and diffuse GGOs due to the consolidation absorption. Nodules, tree-in-bud opacities, honeycombing, traction bronchiectasis, cavitation, and lymphadenopathy (defined as lymph node size of ≥ 10 mm in short-axis dimension) are rare. The imaging findings of unfavorable

outcomes are greater involvement of the lungs, pleural effusion, and diffuse fibrosis (28–30). Chest CT findings are summarized in **Table 2**.

Lung Ultrasound

The main imaging abnormalities are vertical hyperechoic artifacts that depart from the pleural line directed in depth, called B lines, and consolidations. If ≤ 3 B lines on a scan are physiological, especially in the middle-basal fields, the presence of a higher number is pathological, and the number of B lines correlates with disease severity. In the early stages, B lines are confined and mainly detected in the subpleural regions of one or both lungs. In the advanced stages, several B lines involve multiple lobes with diffuse consolidations. The imaging findings of unfavorable outcomes are diffuse consolidations in both lungs without a base–apex gradient, irregularity of the pleural line, multiple and diffuse B lines, and the presence of pleural effusion (31).

PET-TC

The main imaging abnormalities are lesions with high ^{18}F -FDG uptake accompanied by an increased

Table 2. Chest CT imaging findings at different stages in COVID-19.

Findings	Stage			
	Initial	Progressive	Peak	Absorption
Days after initial symptoms	0–4	5–8	9–13	14–30
GGO	+++	+++	++	+++
Consolidation	+	++	+++	+
Reverse halo sign	++	+	+	++
Interlobular septal thickening	Rare	++	+++	++
Crazy paving	+	++	+++	Absent
Localization	Bilateral	Bilateral	Bilateral	Bilateral
	Lower lobes	Multiple lobes	Multiple lobes	Lower lobes
	Peripheral and subpleural	Diffuse	Diffuse	Peripheral and subpleural
Bronchiectasis	Rare	Rare	+	Absent
Fibrosis	Rare	Rare	+	++
Honeycombing	Rare	Rare	+	Absent
Vascular dilatation	++	++	++	++
Pleural effusion	Rare	Rare	+	+
Lymphadenopathy	Rare	Rare	Rare	Rare

Abbreviations. COVID-19: coronavirus disease-19; CT: computed tomography; GGO: ground glass opacity.

nodal FDG uptake without evidence of disseminated disease. Although a bilateral involvement of the lung parenchyma can be observed in several benign and malignant lung diseases, tumors presenting as GGOs are unlikely to be FDG-avid (32, 33).

Differential diagnosis

To optimize patient management, medical care, and disease control, it is important to distinguish COVID-19 from other pathologies. Diagnostic imaging (MRI, CT, and US) techniques, gained large application in thoracic and general radiology; they are advised as first-line techniques helping diagnosis, staging, and follow-up (34-43). Compared to non-COVID-19 pneumonia, COVID-19 pneumonia have GGOs, peripheral distribution, reverse halo sign, and vascular dilatation; on the contrary, pleural effusion and lymphadenopathy are rare (44).

The CT appearance of COVID-19 shares some similarities especially with those of the same viral family: Middle East respiratory syndrome (MERS) and severe acute respiratory syndrome (SARS). They manifest similar lung involvement with a peripheral GGOs predominance and crazy-paving pattern. MERS demonstrated a tendency to have subpleural distribution at the lower lobes, and after recovery, airspace disease showed marked improvement but with often residual fibrotic changes. Furthermore, the absence of pulmonary cavitation, pleural effusions, and lymphadenopathy are also characteristic of SARS. Differently with 2019-nCoV, SARS involvement is more common unilateral, and compared to patients with SARS and MERS, COVID-19 progression is relatively slow. Other non-COVID-19 viral pneumonia mainly manifest as peribronchial and perivascular interstitial inflammation; they show multiple interlaced or parallel high-attenuation fibrous streaks and high attenuation reticular patterns caused by infiltration of the interlobular septa. If the pneumonia is secondary to bronchitis and does not involve the alveoli, CT images show bronchioles partially or entirely blocked, tree-in-bud pattern, and localized atelectasis (45).

COVID-19 needs to be differentiated from bacterial pneumonia, mycoplasma pneumonia, and

chlamydia pneumonia. Bacterial pneumonia occurs in the lung parenchyma and mainly manifests as bronchial pneumonia or lobar pneumonia with many inflammatory secretions in the bronchioles and alveoli. Patchy consolidations are frequent, and GGOs are less common. Mycoplasma pneumonia and Chlamydia Pneumonia commonly occur in school-age children and adolescents but rarely occurs in adults. It shows mostly centrilobular nodules and bronchial wall thickening. The proportion of lung consolidation is less in COVID-19 than that in Mycoplasma Pneumonia and Chlamydia Pneumonia.

Also, COVID-19 needs to be differentiated from heart disease. Heart-failure induced pulmonary edema manifests differently with two subtypes: pulmonary alveolar edema and interstitial pulmonary edema. The first one is characterized by local or multiple GGOs, which typically exhibit the high attenuation butterfly sign with both hila as the center, accompanied by signs of interstitial pulmonary edema such as sporadic or local interlobular septal thickening. The second one shows extensive or local interlobular septal thickening in both lungs, peribronchial cuffing, and redistribution of blood flow in both lungs and could be accompanied by GGOs (46). Principal differential diagnoses are summarized in **Table 3**.

Table 3. Differential diagnosis with COVID-19.

MERS
Rapid progression
SARS
Unilateral
Rapid Progression
Viral non COVID
Interstitial peribronchial thickening
Interstitial interlobular thickening
Hilar lesions
Bacterial Pneumonia
Patchy consolidations
Chlamydia and Mycoplasma pneumonia
Centrilobular nodules
Bronchial wall thickening
Lung disease from heart failure
Butterfly sign
Interlobular septal thickening
Abbreviations. COVID-19: coronavirus disease-19; MERS: Middle East respiratory syndrome; SARS: severe acute respiratory syndrome.

Conclusions

Radiologists have a primary role in the COVID-19 early detection of lung abnormality, in the suggestion of disease severity, and potential progression to acute respiratory distress syndrome, and in the detection of possible co-infection in hospitalized patients. Guidelines are necessary to manage patients with known or suspected infection of 2019-nCoV and to minimize the risk of infection in the Radiology Department. The correct management and the rapid and early diagnosis of new cases are a great benefit not only for the patient but also for public health surveillance.

Conflict of interest: Authors declare that they have no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

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Correspondence:

Marco Fogante

University Hospital "Umberto I – Lancisi – Salesi"

Department of Radiology –

Division of Special and Pediatric Radiology

Via Conca 71, 60126 Ancona (AN)

Phone: +39 071 596 4078

E-mail: marco.fogante89@gmail.com

