Comprehensive literature review on the radiographic findings, imaging modalities, and the role of radiology in the COVID-19 pandemic

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Abstract
Since the outbreak of the coronavirus disease 2019 (COVID-19) pandemic, over 103214008 cases have been reported, with more than 2231158 deaths as of January 31, 2021. Although the gold standard for diagnosis of this disease remains the reverse-transcription polymerase chain reaction of nasopharyngeal and oropharyngeal swabs, its false-negative rates have ignited the use of medical imaging as an important adjunct or alternative. Medical imaging assists in identifying the pathogenesis, the degree of pulmonary damage, and the characteristic features in each imaging modality. This literature review collates the characteristic radiographic findings of COVID-19 in various imaging modalities while keeping the preliminary focus on chest radiography, computed tomography (CT), and ultrasound scans. Given the higher sensitivity and greater proficiency in detecting characteristic findings during the early stages, CT scans are more reliable in diagnosis and serve as a practical method in following up the disease time course. As research rapidly expands, we have emphasized the CO-RADS classification system as a tool to aid in communicating the likelihood of COVID-19 suspicion among healthcare workers. Additionally, the utilization of other scoring...
The current standard for the definitive diagnosis of coronavirus disease 2019 (COVID-19) is reverse-transcription polymerase chain reaction (RT-PCR) from the upper respiratory tract via nasopharyngeal and oropharyngeal swabs[1]. The diagnostic accuracy of real-time RT-PCR is as high as 95%-97%. However, the limitations of RT-PCR lies in its much lower diagnostic accuracy; it has high specificity but variable sensitivity ranging from 60%-70% to 95%-97%, respectively[3-5].

Medical imaging plays a key role in assisting the clinical decisions made towards the diagnosis, management, and follow-up of COVID-19 patients. This review presents the current literature related to the characteristics and key findings of COVID-19 in common radiological imaging modalities such as chest x-rays (CXRs), computed tomography (CT), and lung ultrasonography (LUS). To objectively stratify the severity of COVID-19, CXRs and CT scans are used in conjunction with various classifications systems such as CO-RADS, MuLBSTA, and the Radiological Assessment of Lung Edema (RALE) to facilitate the appropriate evaluation and treatment for infected cases. These are also explored within this review. Other imaging modalities such as magnetic resonance imaging (MRI), positron emission tomography (PET), and echocardiography are less commonly used but can be ordered to assess certain complications and treatment responses. Prior to reviewing these topics, the fundamental basics of COVID-19 pathophysiology are highlighted in the following section.

Pathophysiology of COVID-19
Aerosolization of respiratory droplets containing the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is the primary mode of transmission of COVID-19. The SARS-CoV-2 virion can further inoculate the mucous membranes via the facial T-zone (eyes, nose, and mouth). The current suggested model of pathogenesis for SARS-CoV-2 infection is composed of three phases: Viral replication, hyperactive immune system, and pulmonary destruction[6]. These phases are discussed in the following subsections.
Viral replication
Viral particles manifest their infectivity through replication within the host cell in the following five steps: Attachment, penetration, biosynthesis, maturation, and release [7]. SARS-CoV-2 binds with high affinity to angiotensin-converting enzyme 2 (ACE2) receptors and transmembrane protease serine 2 (TMPRSS2) receptors. Interestingly the ACE2 receptors are predominantly expressed with high density within the type II pneumocytes of the lung[8]. These receptors are also found in the heart (pericytes), ileum (enterocytes), kidney (podocytes), and bladder (urothelial cells)[8]. Once SARS-CoV-2 attaches to host receptors (ACE2 and TMPRSS2), the virion fuses with the membrane and enters the cell via endocytosis. Subsequently, inside the cell, the viral RNA enters the nucleus and alters the replication machinery to biosynthesize viral proteins. Upon maturation of the new viral particles, they are released to infect and continue their vicious cycle in other nearby cells[7].

Hyperactive immune system
Immune hyperactivity is a result of the stress-induced apoptosis of the affected cells and the viral RNA being recognized as a foreign genome by Toll-like receptors[9]. This leads to a cytokine storm (release of tumor necrosis factor, interleukin 6 [IL-6], IL-1β, C-C motif chemokine ligand 2), which is stimulated by macrophages and dendritic cells and causes the infiltration of several inflammatory mediators in the alveolar-capillary interface[9]. Since there is a high density of ACE2 receptors along the peripheries of the lung parenchyma, the majority of damage early on is seen at these sites as a characteristic pulmonary ground-glass opacity (GGO) detected by a CT scan.

Pulmonary destruction
Although the purpose of inflammatory mediators is to fight against the virus until development of the adaptive immune system, their excessive infiltration damages this membrane, causing a build-up of fluid within the alveolar sacs and lung injury that further reduces ventilation[10]. The migration of fluid into the alveolar sacs is governed by the imbalance in Starling forces; \( F = k \left( (P_w - P_l) - s \left( \pi_t - \pi_l \right) \right) \)[11]. The diffuse alveolar damage caused by the viral particles results in an increased capillary wall permeability (high k value), thereby increasing the force at which fluid migrates from the capillaries to the alveolar space. Figure 1 summarizes the findings of Gralinski et al [12] as an illustration of the progressive development within an infected alveolus, both pathologically and radiologically[12]. The normal alveolar wall is comprised of type I and II pneumocytes, while the alveolar macrophages and surfactant reside in the alveolar space. In an acute setting of infection, the pneumocytes secrete inflammatory cytokines and exhibit cytopathic effects, while surfactant levels decrease. As the disease progresses, ventilation is impeded as pulmonary edema and airway debris coincide within the alveolar spaces, alongside the formation of hyaline membrane. Radiologically, the initial features of localized pulmonary edema is seen as GGOs (highly attenuated patches on CXR/CT) and as the severity of tissue damage increases, the pulmonary edema becomes more diffuse and is seen as wide areas of consolidation on the chest imaging modalities[13].

The radiodensities vary between each material and can be quantified using the Hounsfield scale, measured as Hounsfield units. Air, lung, ground glass, water, consolidation, and metal have radiodensities of -1000, -900, -800 to -100, 0, 30, and > 100, respectively[14]. The varying radiodensity of ground glass is associated with the severity of tissue damage and pulmonary edema as a more severe alveolar damage would elicit a higher radiodensity due to a greater fluid accumulation. Extreme tissue damage with complete alveolar consolidation presents as increased attenuation with anomalous opacities on chest imaging.

CHEST RADIOGRAPHY AND CT IMAGING
The role of imaging during the COVID-19 pandemic has yet to be fully explored. CXR and chest CT scans are not an official primary component of diagnosis but rather a supporting feature for diagnosis specifically to determine severity and the appropriate treatment response required. The high rate of false-negative results and fear of viral spread during sample transfers in RT-PCRs show the need for a systematic approach in the diagnosis of COVID-19 through a combination of clinical signs and radiological findings on CXR and CT, which are important in determining the severity of disease and guiding treatment responses[15]. It is important to note that chest CTs have the additional advantage of detecting changes of COVID-19 pneumonia in asymptomatic
CLASSICAL FINDINGS IN CHEST RADIOGRAPHY

Admitted in-patients presenting with COVID-19 provide a large repository of radiological images due to the ease of evaluations via solitary portable CXR. Findings of COVID-19 on CXR include hazy opacification, which is the radiographic equivalent to GGO found on a chest CT scan. These hazy opacifications have a predilection for the basal lung and its peripheries. These opacifications may be unilateral or bilateral. In severe cases, the middle to upper fields of the lung may become affected. In the penultimate disease stage (days 10-12), the areas of opacity coalesce and become denser. This presents as patchy consolidates similar to the pattern of acute respiratory distress syndrome (ARDS)[13]. The compilation of diagnostic factors such as signs, symptoms, oxygen saturation, and CXR appearance can offer a faster and inexpensive method for severity assessment. Most notable CXR findings included bilateral chest involvement 76.8% (95% confidence interval [CI]: 62.5%-87%), consolidation 75.5% (95% CI: 50.5%-91%), GGO 71% (95% CI: 40%-90%), and unilateral chest involvement in 16.5% (95% CI: 8.5%-29.5%)[17]. Some less common CXR findings include reticular interstitial thickening in 39.9% (n = 107/268), nodules 9.3% (n = 25/268), and pneumothorax, or pleural effusion (1%-3%)[18]. These findings could be a consequence of COVID-19 or pre-existing comorbidities, or just coincidental. Figure 2 shows a collection of chest radiographs with abnormal findings with a background of a positive SARS-CoV-2 PCR test. Examples of bilateral patchiness (Figure 2A), unilateral GGO (Figure 2B), pneumothorax (Figure 2C), and linear patchiness (Figure 2D) are modified from Singh et al[15], Martini et al[19], Rampa et al[20], and Kaufman et al[21]. Examples of nodular (Figure 2E) and reticular consolidations (Figure 2F) are modified from Yasin et al[22].

One large study (n = 1198) showed that the sensitivity and specificity of CXR for detecting features of COVID-19 pneumonia were 56% (95% CI: 51%-60%) and 60% (95% CI: 54%-65%), respectively[23]. In comparison, the chest CT provides an increase in sensitivity by 29% (95% CI: 19%-38%) in comparison to CXR[23]. This variable explains the limited usage of CXR in the screening, diagnosis, or follow-up of COVID-19 patients.
CLASICAL CT FINDINGS OF COVID-19 PNEUMONIA

While CXR is a practical method of screening, a recent meta-analysis showed that chest CTs are superior in the screening and assessment of COVID-19 pneumonia due to its increased sensitivity of 91.9% (95% CI: 89.8%-93.7%) [2]. CT is proficient in detecting early signs of COVID-19 pneumonia in comparison to CXR. This is evident by the detection of early-stage GGOs and consolidative opacities, which are often not visible on CXR or may appear normal with minimal interstitial markings [24]. In similar patients where CXR detects minimal interstitial markings, subtle opacities, or occult signs, CT would display identifiable GGO. Figure 3 shows a summary of the meta-analysis of classical and ancillary CT imaging findings by Bao et al [25].

Ancillary late-stage CT finding of COVID-19 pneumonia includes crazy-paving, which is defined by the Fleischner Society as diffuse GGO with superimposed...
Pal A et al. Review of COVID-19 radiographic findings

Figure 3 Summary of the frequency distribution of classical and ancillary computed tomography imaging findings in coronavirus disease 2019 pneumonia. The whiskers indicate the 95% confidence interval. GGO: Ground-glass opacity.

thickened intralobular lines and interlobular septa. The discovery of crazy-paving on a CT image is radiographic evidence of progressive COVID-19[26]. Additionally, diffuse patchy consolidation with reticular configuration becomes more predominant later in the disease course. Other classical chest CT findings that rule-in COVID-19 are lateralization of GGO early in the disease course, with multifocal, bilateral, and basilar lobe predominance, peripheral GGO with a rounded or oval morphology[18]. Figure 4 shows a collection of some notable classical chest CT findings in the axial plane of COVID-19 patients. Examples of classical findings such as GGOs (Figure 4A), air bronchograms (Figure 4B), bronchial thickening (Figure 4E), and pleural adhesions (Figure 4F) are all modified from Fu et al[27]. Additionally, examples of GGO superimposed with consolidation (Figure 4D) and crazy paving sign (Figure 4C) are modified from Gillespie et al[26] and Ali et al[28].

Additionally, Figure 5 shows the common lobes wherein classical CT findings of COVID-19 are distributed based on the findings of a meta-analysis by Bao et al[25]. Although the exact mechanism is unidentified, the increased incidence of findings in the lower lobes may be related to the anatomical structure of the trachea and bronchi, alongside the gravitational force that allows the virion particles to settle at the base more readily. Furthermore, since the right main bronchus bifurcates at a smaller angle and is wider than the left main bronchus, the virion particles can travel more easily towards the right lower lobe.

**NON-CLASSICAL CT FINDINGS OF COVID-19 PNEUMONIA**

Less commonly reported imaging findings that may help to rule-in COVID-19 is subsegmental vascular engorgement[29]. Furthermore, another uncommon but positive feature that rules in COVID-19 is the atoll sign on CT, also referred to as the reverse halo sign[18]. This is defined as a focal rounded area of GGO which is surrounded by a complete or nearly complete ring of denser consolidation which is observed on CT[30]. Other causes of the reverse-halo sign may be chronic lung injury, and notably, may raise the concern of pulmonary infarction. Interestingly, one meta-analysis indicates that these non-classical CT findings might be more common than previously predicted. Figure 6 shows the summary of results from a meta-analysis conducted by Ojha et al[31] to tabulate the incidence of non-classical CT findings in COVID-19 patients.

Figure 7 displays a collection of chest CTs in the axial plane that are examples of the ancillary findings in COVID-19. Examples of vascular enlargement (Figure 7A) are modified from Kwee et al[32]. Examples of subpleural curvilinear opacities (Figure 7B) and reverse halo sign (Figure 7F) are modified from Kong et al[33]. Additionally, examples of reticular pattern (Figure 7C), pulmonary nodules (Figure 7D), and
A collection of chest computed tomography that displays some of the classical findings of coronavirus disease 2019 pneumonia[26-28]. A: Ground-glass opacity (GGO); B: Consolidation and air bronchogram; C: Crazy paving; D: GGO superimposed with consolidation; E: Bronchiectasis, reticular thickening, with vascular enlargement; F: Pleural adhesion. A, B, E and F: Citation: Fu Z, Tang N, Chen Y, Ma L, Wei Y, Lu Y, Ye K, Liu H, Tang F, Huang G, Yang Y, Xu F. CT features of COVID-19 patients with two consecutive negative RT-PCR tests after treatment. Science Report 2020; 10: 11548. Copyright ©The Author(s) 2020. Published by Springer Nature; C: Citation: Gillespie M, Flannery P, Schumann JA, Dincher N, Mills R, Can A. Crazy-Paving: A Computed Tomographic Finding of Coronavirus Disease 2019. Clinical Practice and Cases in Emergency Medicine 2020; 4: 461-463. Copyright ©The Author(s) 2020. Published by UC Irvine; D: Citation: Ali TF, Tawab MA, ElHariri MA. CT chest of COVID-19 patients: what should a radiologist know? Egyptian Journal of Radiology and Nuclear Medicine 2020; 51: 120. Copyright ©The Author(s) 2020. Published by Springer Nature.

Bilateral hilar lymphadenopathy (Figure 7E) are modified from Meirelles et al[34], Zhang et al[35], Mughal et al[36], respectively.

Negative features that rule-out COVID-19 include lobar consolidation, which is more commonly seen in bacterial pneumonia rather than COVID-19 pneumonia, along with lack of GGO. Moreover, in early disease, there is a notable absence of features such as pleural effusion, mediastinal lymphadenopathy, lung cavitation and discrete pulmonary nodules such as the tree-in-bud sign in centrilobular nodules[24]. Ultimately, CT has an extremely high sensitivity of 94% in the detection of COVID-19; however, due to multiple pathologies which may be causative for the features seen in CT; CT has a particularly poor, and varying specificity of 25%-80%[37].

NON-COVID-19 CAUSES OF GGO

There are many causative pathologies unrelated to COVID-19, which may present as GGO on imaging, and this is the reason for the low specificity of CT imaging (25.1%, [95% CI: 21.0%-29.5%]) in diagnosing COVID-19 pneumonia[2]. Acute causes have
Figure 5 Summary of the frequency distribution of lesions in the lung lobes on computed tomography imaging of coronavirus disease 2019 patients. CI: Confidence interval; LLL: Left lower lobe; LUL: Left upper lobe (LUL); RLL: Right lower lobe; RML: Right middle lobe; RUL: Right upper lobe.

Figure 6 Summary of the frequency distribution of classical and ancillary computed tomography imaging findings in coronavirus disease 2019 pneumonia. The whiskers indicate the 95% confidence interval. The data are adapted from the meta-analysis conducted by Ojha et al[31].

abrupt signs on imaging arising in less than 4 wk. This may be pneumonia caused by a myriad of viruses such as influenza A or B, herpes simplex virus type 1, and cytomegalovirus[10]. In addition, acute eosinophilic pneumonia (AEP) may present as bilateral patchy GGO areas with interlobular septal thickening[38]. Drug toxicity due to cytotoxic drugs such as cyclophosphamide or bleomycin may manifest as scattered or diffuse areas of GGO[39]. Additional presentations may be due to chronic diseases lasting greater than 4 wk. Chronic eosinophilic pneumonia may also give rise to similar signs as AEP. Moreover, early lung cancer such as lung adenocarcinoma may be detected early by the appearance of GGO, improving surgical outcomes[40].

Ultimately, the varying causes of GGO on imaging demonstrates why CT alone is not
Figure 7 A collection of chest computed tomography that displays some of the atypical findings of coronavirus disease 2019 pneumonia [32-36]. A: Comb sign in the right lobe characterized by vascular enlargement; B: Curvilinear opacities in the subpleural area; C: Reticular pattern bilaterally; D: Multiple nodules and cavitation; E: Bilateral hilar lymphadenopathy; F: Atoll sign also known as reverse halo. A: Citation: Kwee TC, Kwee RM. Chest CT in COVID-19: What the radiologist needs to know. Radiographics 2020; 40: 1848-1865. Copyright ©The Author(s) 2021. Published by Radiographics; B and F: Citation: Kong W, Agarwal PP. Chest imaging appearance of COVID-19 infection. Radiology: Cardiothoracic Imaging 2020; 2: e200028. Copyright ©The Author(s) 2020. Published by the Radiological Society of North America, Inc; C: Citation: Meirelles GSP. COVID-19: A brief update for radiologists. Radiologia Brasileira 2020; 53: 320-328. Copyright ©The Author(s) 2020. Published by Radiology brasil; D: Citation: Zhang Q, Douglas A, Abideen ZU, Khanal S, Tzarnas S. Novel coronavirus (2019-nCoV) in disguise. Cureus 2020; 12: e7521. Copyright ©The Author(s) 2020. Published by Cureus; E: Citation: Mughal MS, Rehman R,Osman R, Kan N, Mirza H, Eng MH. Hilar lymphadenopathy, a novel finding in the setting of coronavirus disease (COVID-19): A case report. Journal of Medical Case Reports 2020; 14: 124. Copyright ©The Author(s) 2020. Published by BMC.

enough to accurately diagnose a patient with COVID-19 without clinical context, medication history, and RT-PCR/serology COVID-19 testing.

**TIME COURSE: LAGGING OF COVID-19 FEATURES ON RADIOLOGICAL IMAGING**

Although the preliminary imaging modality for patients presenting with COVID-19 is a solitary portable anteroposterior chest radiograph, many patients will have an early negative CXR/CT result. This can be due to a lack of macroscopic lung involvement at the time of presentation or minute findings on CXR/CT. During the early stages of disease (0-3 d), the viral particles take over host cell machinery, replicating and inducing a cytokine storm in the form of an acute infection. Gu et al.[41] reported that nearly 13% of CT scans depict a normal finding in this early phase, while 63.2% of the cases exhibit a classical GGO appearance. A proposed hypothesis suggests that the
SARS-CoV-2 virion has not accumulated at an adequate density to induce pulmonary parenchymal damage. Therefore, the chest CT appears as a minimally hazy opacification with normal-appearing underlying vessels and bronchial structures. As the disease course progresses to the intermediate stage (4-7 d), there will be diffuse alveolar damage and GGO evolves into consolidation. The majority of the structures on chest CT will appear obscured in comparison to the primary GGO feature seen in the early stages. In the final stage (8-14 d), fibrotic lesions are significantly increased due to scarring of the lung tissue secondary to the resolution of organizing pneumonia [42]. Consolidation is also markedly enhanced in over 78% of the cases; however, the fibrotic lesions help distinguish the case presentation of late-stage from intermediate-stage disease in the majority of patients. Figure 8 summarizes the frequencies of typical CT findings (GGO, consolidation, fibrosis) based on the temporal stages of disease according to data from Gu et al[41].

ULTRASONOGRAPHIC PATTERNS IN COVID-19

Clear ultrasonographic patterns can be found in patients with COVID-19. Large numbers of B-lines, irregularity of the pleural line, and small clusters of subpleural pulmonary consolidations also frequently occur in the posterior and inferior areas[54, 58]. Poggiali et al[44] concluded a strong correlation between LUS findings and concurrent CT scans in patients ($n = 12$) with COVID-19. These results also revealed diffuse B patterns and bilateral lung involvement with GGO in all of these patients [58]. Additionally, both imaging modalities also detected organizing pneumonia in four patients[59]. A summary of results from Norbedo et al[59] and McDermott et al [60] showed typical LUS findings in pediatric and adult patients with COVID-19. The literature review conducted by Norbedo et al[59] in pediatric patients ($n = 18$) with COVID-19 revealed LUS findings of B-line vertical artifacts, pleural irregularities, and small subpleural consolidations, as well as white patchy lung areas. A similar review conducted by Norbedo et al[59] on adult patients ($n = 43$) with COVID-19 revealed consistent LUS findings; irregular B-lines (focal), multifocal and confluent; thickening of pleural line with pleural line subpleural consolidations; and a variety of patterns...
Figure 8 Summarizes the frequencies of chest classical and ancillary computed tomography findings at different stages of disease progression (early \( n = 155 \), intermediate \( n = 155 \), and late \( n = 155 \)). Data acquired from Gu et al\(^41\).

including multifocal small, non-translobar, and translobar with occasional mobile air bronchograms. The authors also concluded that pleural effusion in COVID-19 patients is uncommon\(^59\).

LUS is able to detect dynamic changes associated with COVID-19. The main early-stage ultrasound finding was focal B-lines, which becomes multifocal and confluent as the disease progresses with further development of consolidations. During convalescence, B-lines and consolidations gradually disappear and are replaced by A-lines\(^57,61,62\).

Interestingly, one study showed that LUS findings in patients with COVID-19 pneumonia exhibited typical patterns consistent with COVID-19 in 38.5% of cases \( (n = 52) \) and atypical patterns in 61.5% of cases \( (n = 83) \)\(^63\). The ability of LUS to diagnose COVID-19 can be inferred from its sensitivity of 76.9%, specificity of 77.1%, positive predictive value of 57.7%, and negative predictive value of 89.2%\(^63\). Additionally, when comparing LUS to chest CT, the results suggest a sensitivity and specificity of 65% and 72.7%, respectively\(^63\). Figure 9 shows a simplified flowchart for triaging patients presenting with respiratory symptoms during the COVID-19 pandemic in the emergency department as suggested by Schmid et al\(^63\).

12-ZONE SCORING SYSTEM

In clinical practice, there are various scoring systems to quantify the extent of lung involvement, and in the context of COVID-19, we observed the most prominent one to be the 12-zone scoring system, used as a tool to assess regional and global lung aeration in ARDS as well as COVID-19 pneumonitis\(^61,64-66\). A total of 12 areas in the right and left lung are examined, namely the anterosuperior, anteroinferior, laterosuperior, lateroinferior, posterosuperior, and posteroinferior lung regions on each side of the lung. Scoring of each area is performed in accordance with the most severe lung ultrasound finding detected in the corresponding intercostal spaces and is given a score from 0-3, tallying up to a maximum of 36. Figure 10 outlines the assessed zone and the criteria for each of the values. The Australasian College of Emergency Medicine proposed a severity classification of patients based on this score as normal (0), mild (1-5), moderate (> 5-15), and severe (> 15)\(^65\).

One study by Speidel et al\(^67\) showed that the lung ultrasound scoring system (LUSS) had promising diagnostic efficacy with an odds ratio (OR) of 1.30, a 95% CI between 1.09 to 1.54 \( (P = 0.003) \), and an area under the curve (AUC) of 0.85 (95% CI: 0.71 to 0.99)\(^67\). Utilization of a cutoff of 8 of 36 points in participants \( (n = 10/11) \) with a primary diagnosis of COVID-19 were correctly predicted with a sensitivity of 91% (95% CI: 59% to 100%)\(^67\). In the cohort without a primary diagnosis of COVID-19
Figure 9 Shows a simplified flowchart guiding the triage in patients presenting with respiratory symptoms during the coronavirus disease 2019 pandemic using lung ultrasonography in the emergency department. 1Unilateral appearance of more than 1 of any 4 criteria means coronavirus disease 2019 suspected. COVID-19: Coronavirus disease 2019; LUS: Lung ultrasonography.

(others, n = 38). COVID-19 was correctly ruled out in 29 of these 38 patients (specificity = 76%, 95% CI: 60% to 89%) [67]. LUS, therefore, is a promising screening tool in hospitalized patients suspected of COVID-19. A summary of the results by Speidel et al [67] are shown in Figure 11 of typical LUS findings (B-line, and subpleural consolidations) and LUS scores at varying lung zones in patients with and without a primary diagnosis of COVID-19.

LUS appears to have a promising role in screening clinically suspected or diagnosed COVID-19, only when it is implemented as an adjunct with other diagnostic modalities. An amalgamation of LUS findings with clinical history, physical examination, and knowledge of pretest probability will supplement increasing efficacy. POCUS may facilitate the physician in undertaking the appropriate management pathway or rule out an alternative diagnosis. The practicality of utilization of LUS will remain dependent on resource availability, personnel expertise, and flexibility of LUS configuration for each situation.

DISADVANTAGES OF LUS

LUS has been criticized for its low specificity in the diagnosis of COVID-19. This is because described features including confluent B-lines, consolidations, and irregular pleural lines simply refer to the lung surface density state and are not pathognomonic for COVID-19 [68]. Additionally, LUS cannot detect deep lesions as the aerated parenchyma blocks the transmission of ultrasonography. In order for the lesion to
detected, it must extend to the pleural surface. Furthermore, LUS does not exclude COVID-19 in subjects with no pulmonary complications, and therefore cannot be used as a diagnostic tool by itself to stratify patients who may or may not be infected with COVID-19[47].

ROLE OF MRI, PET, AND ECHO IMAGING

There is no documented role of pulmonary MRI in the diagnosis of COVID-19 pneumonia. Cardiac MRIs may be helpful in the future to detect complications such as myocarditis and cardiomyopathy. Fluorodeoxyglucose PET (FDG-PET) scans are not used in emergencies, but some studies explain its utilization in describing the subtleties of typical pulmonary findings in COVID-19 pneumonia. The FDG-PET avidity corresponds to the GGOs in CTs, and this is because of the increased glucose requirement by the neutrophils at the site to fight the infection. There is a theoretical possibility of utilizing FDG-PET in the future to monitor treatment response, predict recovery and survey the long-term consequences of COVID-19.

Deep vein thrombosis and peripheral thrombosis are common in areas with high COVID-19 prevalence due to an increased risk of hypercoagulability; therefore, the use of compression ultrasonography is expected to increase. CT pulmonary angiography is mainly used to confirm the prognosis of pulmonary embolism (PE) and stratify patients with acute PE. Point of care echocardiography might be useful as the sensitivity of right ventricular dilation in detecting PE using POC echocardiography can be as high as 90%. Echocardiography can also be used to evaluate COVID-19-related acute cardiac injuries as abnormalities in echocardiography are linked to a worse prognosis and more severe disease[13].
CLASSIFICATION SYSTEMS

CO-RADS classification system

In March 2020, a classification system by the Dutch Association for Radiology was implemented to aid with making the diagnosis of COVID-19. This system was called CO-RADS which stands for COVID-19 reporting and data system and was developed to report CT findings with ease and replicability among other physicians, as prior to this, no system had been developed directly for COVID-19. The system assigns the CT scan a CO-RAD score between 1 to 5 depending on the radiological findings of the chest, and in some cases, a score of 0 and 6 can be used. Level 1 classification indicates a very low level of suspicion for COVID-19 as these cases do not have any nodules bilaterally and only have normal/benign findings[69]. Infections that can be considered level 1 for COVID-19 include mild or severe emphysema, perifissural nodules, lung tumor indications, and fibrosis[69]. This category is also known as negative for pneumonia. Level 2 is as having a low likelihood of COVID-19, but encompasses infectious diseases such as bronchitis, infectious bronchiolitis, bronchopneumonia, lobar pneumonia, and pulmonary abscesses[69]. CT features include those similar to an atypical pulmonary appearance like tree-in-bud sign, a centrilobular nodular pattern, lobar or segmental consolidation, and lung cavitation. Level 3 is the “middle ground” where the viewer can be unsure of the diagnosis as the features seen are those consistent with COVID-19 but also with viral pneumonia or non-infectious causes[69]. Findings in this level consist of perihilar GGO, homogenous extensive GGO with or without sparing of some secondary...
pulmonary lobules, or GGO together with smooth interlobular septal thickening with
or without pleural. GGO can also be seen on CT, which is characteristic of COVID-19,
but the opacities seen are also compatible with organizing pneumonia. Although
levels 4 and 5 have similar findings, the presence of GGO with or without consolid-
ations in lung areas close to the visceral pleura indicates a CO-RADS score of level 5
[69]. A summary of the CO-RADS categories and its criteria outlined by Prokop et al
are outlined in Table 1.

A study by Bellini et al[70] analyzed the diagnostic yield of CO-RADS in identifying
lung involvement in patients suspected of COVID-19 (n = 572, COVID-19 (n = 142), not
COVID-19 (n = 430)) by multiple radiologist and physicians at different levels of
expertise. Overall, CO-RADS showed promising accuracy for lung involvement with a
mean AUC of 72% (95% CI: 67% to 75%)[70]. The receiver operating characteristic
(ROC) curve revealed that application of a threshold ≥ 4 resulted in a moderate
specificity of 81% (95% CI: 76% to 84%) and a low sensitivity of 61% (95% CI: 52% to
69%). The CO-RADS rating among all readers was moderate as shown by Fleiss’
Kappa statistic of 0.43 (95% CI: 0.42 to 0.44) and with a substantial agreement for
categories; CO-RADS 1 (Fleiss’ K = 0.61 (95% CI: 0.60 to 0.62) and for CO-RADS 5
(Fleiss’ K = 0.60 (95% CI: 0.58 to 0.61))[70].

MULBSTA SCORING SYSTEM

Another scoring system used for COVID-19 is known as the MuLBSTA score, which
looks at key components such as multi-lobar infiltration, hypo-lymphocytosis, bacterial
coinfection, smoking history, hypertension, and age. Five points are assigned
for multi-lobar infiltration, 4 points if the lymphocyte count is less than or equal to 0.8
× 10^9/L, 4 points for bacterial infiltration that is confirmed by lab results or on CT, 3
points for those who are currently smoking (2 for those who have previously been
smokers), 2 points for hypertension, and 1 point for age above 60-years-old. A total
score of 12 was used as the cut-off; those with scores between 0 and 11 were
considered low risk while those with a score of ≥ 12 are considered high-risk patients.
Those who are in the high-risk category are more likely to require intensive care unit
treatment or were more likely to die due to the infection. This scoring system became
useful as it helps to predict the prognosis of patients based on other clinical features
and co-morbidities[66]. A retrospective study by Ma et al[71] (n = 530), showed that the
ROC curve analysis on the MuLBSTA early warning scoring system for severe COVID-
19 patients has an accuracy of 92.7% (95% CI: 89.2% to 96.3%), sensitivity of 65.1%, and
specificity of 95.4%. These outcomes indicate that MuLBSTA is a good early warning
system for severe COVID-19 patients.

RALE CLASSIFICATION

This system aims to associate the course and severity of CXR in COVID-19 with the
diagnostic RT-PCR result. The RALE score involves individually assessing each lung
and depending on how much of the lung is involved, a score is assigned to it. With no
involvement, the score is 0; less than 25% lung involvement is 1, 25% lung
involvement is 2, 50% of the lung is 3, and a level 4 classification is given when the
lung is involved more than 75%. The overall score is calculated by adding the two
scores, indicating the involvement of each lung[66]. The RALE score can be used to
predict the outcomes of patients with COVID-19 pneumonia and their need for
mechanical ventilation (MV). Interestingly, this scoring system is practical and only
one of the few ones that incorporate a prognostic value. This makes it a valuable proxy
system to compare against an artificial intelligence (AI) model.

One study by Ebrahimian et al[72] evaluated the implementation of AI such as the
commercially available AI algorithm (qXR v2.1 c2; Qure.ai Technologies, Mumbai,
Maharashtra) has been on the rise. This model was trained on patient data with a
positive SARS-CoV-2 RT-PCR assay. The AI score had a strong positive correlation
with RALE score for each site of the patient CXR (r² = 0.79 to 0.86; P < 0.0001)[72]. It
also revealed that patients that received MV or deceased had a significantly higher AI
or RALE score when compared to those not requiring MV or attained convalescence
[72]. This study concluded that instead of comparing the RALE and AI score to the
baseline CXRs, combining the RALE and AI score over progressive serial CXRs with
clinical and lab data would drastically improve the predictability of both the AI score
and the subjective RALE score.
Table 1 Association between CO-RADS categories and level of suspicion for pulmonary involvement of coronavirus disease 2019

| CO-RADS category | Suspicion level for pulmonary involvement of COVID-19 | Summary |
|------------------|------------------------------------------------------|---------|
| 0                | Not interpretable                                   | Scan insufficient for assigning score |
| 1                | Very low                                            | Normal or non-infectious scan |
| 2                | Low                                                 | Typical for other infection but not COVID-19 |
| 3                | Ambiguous                                           | Non-specific features of COVID-19 |
| 4                | High                                                | Increased suspicion of COVID-19 |
| 5                | Very high                                           | Typical features of COVID-19 |
| 6                | Proven                                              | Positive RT-PCR test for COVID-19 |

Table modified from Prokop et al[69]. COVID-19: Coronavirus disease 2019.

**BRIXIA SCORE**

This score was designed and implemented for serial monitoring by the ‘Radiology Unit 2 of ASST Spedali Civili di Brescia’ and was later validated for risk stratification on a greater population by Borghesi et al[73]. According to this scoring system, the lung is divided into six different zones, three on each of the lungs, in either anteroposterior or posteroanterior views. With regards to the scoring of the zones, the score given can be between and including 0-3 based on the involvement of the lung. A score of 0 is given if there are no abnormalities seen on X-ray, a score of 1 is given when there are interstitial infiltrates. Two is given if there are interstitial and alveolar infiltrates, with the interstitial markings being more prominent. A score of 3 is assigned when there are both interstitial and alveolar infiltrates present, with the latter being more prominent. These scores are given to each of the 6 zones and are then aggregated to get a final score. This type of semiquantitative scoring makes CXR interpreting faster and more streamlined for evaluation[73]. The Brixia score becomes more useful when serial CXRs are performed as this enables documentation of additional sub-scores. The H-score is the highest Brixia score documented during the serial CXRs. Contrastingly, the L-score is the lowest Brixia score documented during the serial CXRs. Additionally, the Brixia score is documented at admission (A-score) and discharge/death (E-score).

One study by Maroldi et al[74] retrospectively assessed the clinical value of the Brixia score in 953 COVID-19 patients. In this study, the H-score was significantly higher with a median of 12 and interquartile range (IQR) between 9 to 14 in the deceased cohort compared to the discharged cohort (median: 8; IQR 5 to 11). Similarly, the L-score (7 vs 5; P < 0.0003), A-score (9 vs 8; P < 0.039), and E-score (12 vs 7; P < 0.0001) were all higher in the deceased cohort compared to the discharged cohort[74]. Overall, logistic regression showed a significant predictive value for H-score of OR 1.25. The ROC curve revealed an AUC of 0.863[74]. Additional Cox proportional hazards regression revealed age has a hazard ratio (HR) of 4.17 (P = 0.0001), H-score of < 9 has a HR 0.36 (P = 0.0012) and worsening of H-score compared to a score below 3, which has a HR of 1.57 (P = 0.0227) and is associated with a worse outcome[74]. These outcomes demonstrate the importance of the Brixia score in the monitoring and assessment of COVID-19 pneumonia and its strong correlation with a patient’s prognosis.

**PERMANENT LUNG SCARRING POST COVID-19**

Research into the evolution of COVID-19 pneumonia imaging during the follow-up in the later stages of the disease is an interesting area. Zhao et al[75] demonstrated that at 3 mo, typical lung features (GGO, interstitial thickening, and crazy paving) were almost resolved, with some fibrosis. High-resolution CT scans of patients (n = 55) revealed that 67.27% had GGO (n = 37), 27.27% had interstitial thickening (n = 15), and 5.45% had crazy-paving patterns (n = 3)[75]. However, the study only included 55 patients who had non-critical COVID-19 pneumonia. Long-term follow-up studies with a larger sample size are crucial to better understand the trends in recovery. The available literature reports consistent findings of partial healing of GGO and consol-
idation from approximately day 14. In some patients, CT findings also demonstrated signs of fibrosis. In February to March 2020, a case series provided the earliest reports of follow-up CT findings. Partial healing of a mixed pattern of GGO and consolidation occurred from the day 14 onwards according to Duan and Qin[76], and Shi et al[77]. Wei et al[79], reported lung fibrosis in COVID-19 patients on day 12 which was corroborated by a case presented by Li et al[78] which described similar findings on day 14. Pan et al[80] presented a retrospective study (n = 63) following up COVID-19 patients. These patients were re-examined in intervals of 3-14 d wherein enlarged fibrous stripes and solid white nodules were documented. Pan et al[42] reported that after 14 d, 65% had GGO (n = 13/20) and 75% had consolidation (n = 15/20), but crazing-paving pattern was absent in all 20 patients. Bernheim et al[51] found that in 25 patients, after 6-12 d, 88% had GGO (n = 22/25) and 60% had consolidation (n = 15/25). Crazy-paving pattern was present in 20% of patients (n = 5), and 24% had bronchial wall thickening (n = 6) but no patients had underlying pulmonary fibrosis [81]. Wang et al[82] reported that during days 12-17 there was a notable increase in the mixed pattern, although GGO were still predominant. Xiong et al[83] observed that after an average of 11.6 d the follow-up CT showed progressive GGO, consolidation, interstitial thickening, fibrous stripes, and air bronchograms. These findings aid our understanding of the recovery patterns in infected patients. Furthermore, follow-up and management plans will need high-quality evidence to guide clinical decision-making and monitor treatment efficacy with supplemental oxygen and antifibrotic agents.

AI INTERVENTIONAL SYSTEMS

AI is a broad concept that refers to a set of advanced computational algorithms that utilizes heuristic pattern recognition for a given training dataset and therefore makes predictions on unseen testing datasets. Radiomics utilizes data-characterization algorithms for extracting and evaluating features from radiological medical images and further uses them to creating statistical models with the intent to provide support for diagnosis and management[84]. Radiologic parameters considered for analysis include size, shape and textural features that have useful spatial information on pixel or voxel distribution and patterns[85]. Integration of AI into radiomic datasets has the potential to streamline COVID-19 diagnosis. In early February 2020, Beijing-based AI company Intervision launched the “Coronavirus artificial intelligence solution,” an algorithm that utilizes CT imaging data to diagnose COVID-19 on CT[86]. The reports revealed an increased ability to read images in 10 s, drastically improving clinical workflow efficiency, and reducing variable human error, while continuously improving diagnostic accuracy[87].

Another study developed a deep-learning COVID-19 diagnosis system from a dataset including 11356 CT volumes from COVID-19, influenza-A/B, non-viral community-acquired pneumonia and non-pneumonia subjects from China[88]. The basic workflow of the deep-learning-based diagnosis model contains utilization of CT data as the input, the lung is then segmented, COVID-19 diagnosis is made based on the location of infectious slices (Figure 12). This study found that the AI system outperformed very experienced radiologists based on speed. Another study by Harmon et al[89] showed that the use of the AI system that can detect COVID-19 pneumonia with 90.8% accuracy, 84% sensitivity, and 93% specificity. A total of 1280 patients from China, Italy, and Japan were used to train the deep-learning algorithms, and the system was tested independently on 1337 patients, with normal controls from oncology, emergency, and pneumonia-related indications. There was a 10% false-positive rate of incorrectly diagnosed COVID-19 related patients. This indicates potential for overlapped diagnosis with other pneumonia etiologies. Another limiting factor in using AI is the need for thousands of high-quality CT studies to train the AI. Overall, AI systems could be trained to be extremely accurate, sensitive, and specific for COVID-19 diagnosis. However, it may be more useful in specific assessment of imaging findings of COVID-19[88,89].

A subsequent study conducted by Yu et al[90] investigated various pre-trained deep learning AI models against 246 severe cases and 483 non-severe COVID-19 cases and found that DenseNet-201 with cubic SVM model achieved a high severity classification accuracy of 95.20% and 95.34% for ten-fold cross-validation and leave-one-out validation, respectively. These effective results show that the utility of the proposed pipeline model was able to achieve a rapid and accurate identification of the severity of COVID-19, indicating its potential for use by clinicians in not just diagnosis but also
In May 2020, radiologist Laghi [91] wrote a correspondence letter in The Lancet detailing her concern that the diagnostic value of AI algorithms in CT scans was not supported by scientific evidence. In fact, since the high-resolution CT findings are not pathognomonic of COVID-19 infection and have poor accuracy in screening asymptomatic individuals according to the American College of Radiology, there have been growing concerns over the integration of AI radiology into the screening of this disease [92].

RADIOLOGY PANEL: FIRST AND SECOND WAVE

First wave experience
The overwhelming nature of COVID-19 has strained global healthcare services and greatly impacted radiology departments. To cope with increasing admissions during peaks, radiologists and radiology trainees have experienced redeployment to areas of clinical need. One hospital saw 21% of their total radiology employees reassigned to other duties [93]. Following official guidelines [94], medical facilities also rescheduled non-urgent elective procedures, and this had a major effect on total imaging volume. While the exact drop varies within institutions, a large New York metropolitan health system reported an 87%, 4%, and 45% reduction in outpatient, inpatient, and emergency imaging respectively, during the pandemic [95].

Moreover, it has become increasingly evident that COVID-19 is not limited to the lungs, rather it can affect other organs too. An early published clinical cohort of COVID-19 displayed acute cardiac injury, shock, and arrhythmia in 7.2%, 8.7%, and 16.7% of patients respectively, with a higher prevalence in patients requiring intensive care [96]. Neurological manifestations have also been recorded; another observational study demonstrated neurological symptoms in 36.4% of hospitalized COVID patients [97]. Alongside observations of kidney involvement and hypercoagulability in patients, this leaves a potentially important role for radiologists when considering

Figure 12: Basic workflow of the artificial intelligence system. AI: Artificial Intelligence; COVID-19: Coronavirus disease 2019.
COVID-19 as a multisystem disease\cite{98,99}.

Regarding the role of imaging, our understanding has changed with the course of the pandemic. Chest CT was temporarily part of the official diagnostic criteria for COVID-19 due to the nature of the early emergency in China; however, since then, chest CT findings are no longer considered diagnostic. Current guidelines establish that RT-PCR assays are the standard for definitive COVID-19 diagnosis\cite{100,101}. Instead, CXR and chest CT have been the most common imaging modalities specified for presumptive diagnosis, triage and management of patients with suspected or known COVID-19 infection\cite{102}. After the diagnosis is confirmed, the role of imaging may be limited but while waiting for PCR positive it can be very useful for clinicians. Portable CXR is often used as the primary imaging study in suspected patients, chest CT is far more sensitive in detecting lung lesions but has been reserved for more specific cases\cite{4,15}.

### FORWARD PREPARATION FOR THE SECOND WAVE

As radiologists get ready for the second wave of COVID-19, it is important to continue developing on lessons learned from the 1st wave. With that in mind, a general framework that can be applied to radiology departments when preparing for the second wave and beyond is the concepts of building, sustaining, and adapting\cite{103}.

The main idea of the first strategy is to create capacity before it is needed. This can be done by increasing hours of staff, getting more manpower, or by expanding operations into other sites as seen in Singapore General Hospital’s (SGH) Emergency Department\cite{103}. When faced with increased local transmission of COVID-19, management of an adjacent Ambulatory Surgery Centre was transferred to the ED, allowing for operations to be ramped up and for portable radiology services to grow \cite{104}. Additional capacity can also be created by increasing portable imaging capability through renting extra units so they can be deployed into operations when needed\cite{105}.

Moving on to the second strategy of sustaining, the central idea here is to operate at a pace that is maintainable in the long-term. This would involve preserving supplies such as Personal Protective Equipment, preventing staff burnout, simplifying hastily designed processes, and alternating work times or work sites\cite{103}. In the University of Alabama at Birmingham, home picture archiving and communication system workstations were rapidly deployed in anticipation of a potential COVID-19 crisis \cite{106}. With this measure, the number of people coming on-site could be limited in the long-term while also contributing to social distancing amongst radiologists.

Lastly, the third strategy, adapting, highlights the importance of being flexible. Some ways this can be achieved include rapidly scaling up responses, reconfiguring spaces, improvising, and embracing new roles when faced with increased demands \cite{103}. This is demonstrated at SGH, where in order to monitor changes in the pandemic, a smaller radiology disease outbreak task force was assembled to assess overnight incidents and anticipate changes during the day\cite{4}.

### CONCLUSION

The burden of this disease is evident through the rampant rise in fatality, morbidity, and mortality rates across the world. Despite the integration of stringent public health measures, this spread continues and is leaving an everlasting impact on both humanity and the economy. Radiologists have significantly adjusted their practices in accordance with the pandemic and as frontline workers, it is essential for them to identify the classical findings associated with COVID-19 and use their expertise towards engaging in optimal strategies to slow disease progression. Advances in the role of radiology in COVID-19 research have piled up within a short-period, hence it is prudent to remain acquainted with important findings. Some notable findings consist of the early stage of disease producing a classical GGO appearance on majority of the CT scans, and the late stage of disease showing highly specific fibrotic lesions due to scarring of the lung parenchyma. The purpose of identifying these characteristic features and associating them with a time course can be crucial towards the management plan for each patient. Additionally, the role of radiology can further be integrated into the scoring systems discussed in this review for risk stratification and appropriate assessment and treatment strategies for infected cases. Nevertheless, medical imaging has been suggested to have promising value as a rapid adjunctive
tool in patients with COVID-19 through assisting with the diagnosis, evaluating patients with clinical deterioration, and providing the multidisciplinary team with vital examinations that could support the management strategies.

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