(CC BY 4.0) | ISSN 2525-3409 | DOI: http://dx.doi.org/10.33448/rsd-v9i8.6831 Abordagem dos principais achados de imagem decorrentes da Síndrome Respiratória causada pelo COVID-19 Approach to the main imaging findings resulting from Respiratory Syndrome caused by COVID-19 Aproximación a los principales hallazgos de imagen resultantes del Síndrome **Respiratorio causado por COVID-19** Recebido: 17/07/2020 | Revisado: 20/07/2020 | Aceito: 22/07/2020 | Publicado: 02/08/2020 Rosana Brambilla Ederli ORCID: https://orcid.org/0000-0003-2630-2464 Paulista State University, Brazil E-mail: roederli@hotmail.com **Maikiane Aparecida Nascimento** ORCID: https://orcid.org/0000-0002-6843-2809 Dr. Anuar Auad State Hospital for Tropical Diseases, Dr. Giovanni Cysneiros State Public Health Laboratory, Brazil E-mail: maikiane.nascimento@hotmail.com **Elorraine Coutinho Mathias Santos** ORCID: https://orcid.org/0000-0003-4491-5635 University of Oeste Paulista, Brazil E-mail: lohcoutinho_02@hotmail.com João Pedro Brambilla Ederli ORCID: https://orcid.org/0000-0001-6254-9873 University of Oeste Paulista, Brazil E-mail: jpbrambilla@outlook.com.br **Ildeny Alves dos Santos** ORCID: https://orcid.org/0000-0003-4884-036X Dr. Anuar Auad State Hospital for Tropical Diseases, Dr. Giovanni Cysneiros State PublicHealth Laboratory, Brazil E-mail: ildenysantos6@gmail.com

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Resumo

O SARS-CoV-2 pertence à família dos coronavírus, e é caracterizado como uma doenca infecciosa que ameaça à saúde pública mundial. O diagnóstico definitivo é feito por testes moleculares específicos em amostras respiratórias, como, por exemplo, o esfregaço da garganta. Entretanto, na maioria das vezes, as doenças infecciosas são diagnosticadas através da sintomatologia, exames laboratoriais e exames de imagem, tendo destaque principal para o raio-x, tomografia computadorizada e ressonância magnética. O presente estudo se propôs a analisar os principais exames de imagens encontrados na síndrome respiratória causada pelo novo coronavírus. Essa pesquisa trata-se de uma revisão narrativa da literatura científica publicada até o momento, possuindo natureza qualitativa e descritiva. A pesquisa ocorreu nas bases de dados das bibliotecas virtuais de saúde e foram refinadas por Latin American and Caribbean Literature in Health Sciences (LILACS), Scientific Electronic Library (SCIELO), BIREME (Biblioteca Regional de Medicina), e MEDLINE. Dentre os autores consultados foram observadas recorrências de opacidades em vidro fosco, isoladas ou multifocais, consolidações, como a cardiomegalia, diminuição do espaço aéreo, aerobocogramas e derrame pleural. Além do mais, alguns achados possuíram características atípicas. Nós concluirmos, em suma, que há diversos padrões encontrados para caracterizar a doença pulmonar, com características principais de opacificações bilaterais, periféricas e basais, com morfologias arredondadas, presença de linfonodomegalia, derrame pleural, escavação e

nódulos nos casos mais graves. Por este modo, sugere-se que os exames de imagem sejam utilizados de maneira complementar ao diagnóstico laboratorial.

Palavras-chave: COVID-19; Exames de imagem; Síndrome respiratória.

Abstract

SARS-CoV-2 belongs to the family of coronaviruses and is an infectious disease that threatens public health worldwide. The definitive diagnosis of the new coronavirus is made by molecular tests used in breathing tests, such as, for example, or rubbing the throat. However, most of the time, infectious diseases are diagnosed employing symptoms, laboratory, and image exams, like x-ray, computed tomography, and nuclear magnetic resonance imaging. The present study aimed to analyze the main imaging tests found in the respiratory syndrome caused by the new coronavirus. This research deals with a narrative review of the literature published so far, having a descriptive and qualitative nature. A search took place in the databases of virtual health libraries. It was refined by Latin American and Caribbean Literature in Health Sciences (LILACS), Electronic Scientific Library (SCIELO), BIREME (Regional Library of Medicine), and MEDLINE. Among the authors published, the occurrence of ground-glass opacities, isolation, or multifocal, consolidations such as cardiomegaly, decreased air space, aerobocograms, and pleural effusion were observed. Also, some findings had atypical characteristics. We conclude that in several formed patterns found to characterize a lung disease, with main optional bilateral, peripheral, and essential features, with rounded morphologies, presence of lymph node enlargement, pleural effusion, excavation, and nodules in the most severe cases. In this way, it is suggested that the imaging exams be complementary to the laboratory diagnosis.

Keywords: COVID-19; Imaging exams; Respiratory syndrome.

Resumen

SARS-CoV-2 pertenece a la familia de los coronavirus y es una enfermedad infecciosa que amenaza la salud pública en todo el mundo. El diagnóstico definitivo del nuevo coronavirus se realiza mediante pruebas moleculares utilizadas en pruebas de respiración, como, por ejemplo, o frotar la garganta. Sin embargo, la mayoría de las veces, dado que las enfermedades infecciosas se diagnostican mediante síntomas, exámenes de laboratorio y de imágenes, la principal característica es la radiografía, la tomografía computarizada (TC) y la resonancia magnética (RMN). El presente estudio tiene como objetivo analizar las principales pruebas de imagen encontradas en el síndrome respiratorio causado por el nuevo coronavirus.

Esta investigación se ocupa de una revisión narrativa de la literatura publicada hasta ahora, que tiene una naturaleza descriptiva cualitativa. Se realizó una búsqueda en las bases de datos de bibliotecas virtuales de salud y fueron refinados por Literatura Latinoamericana y del Caribe en Ciencias de la Salud (LILACS), Biblioteca Científica Electrónica (SCIELO), BIREME (Biblioteca Regional de Medicina) y MEDLINE. Entre los autores consultados, se observó la aparición de opacidades en vidrio esmerilado, aislamiento o multifocal, consolidaciones como cardiomegalia, disminución del espacio aéreo, aerobocogramas y derrame pleural. Además, algunos hallazgos tenían características atípicas. En Conclusión, varios patrones caracterizan una enfermedad pulmonar, con características opcionales bilaterales, periféricas y básicas principales, con morfologías redondeadas, presencia de agrandamiento de ganglios linfáticos, derrame pleural, excavación y nódulos en los casos más graves. De esta manera, se sugiere que los exámenes de imagen sean complementarios al diagnóstico de laboratorio.

Palabras clave: COVID-19; Exámenes de imagen; Síndrome respiratório.

1. Introduction

In December 2019, in China, a group of patients was admitted to local hospitals, presenting with severe pneumonia with unknown cause (Singhal, 2020). The new virus, belonging to the Coronavirus family, was named SARS-CoV-2, more popularly known as COVID-19 (Zhu et al., 2020). It is responsible for the lower respiratory infection that can cause acute respiratory distress syndrome (Huang, et al., 2020a). Modeling studies reported a doubling time of the epidemic to 1.8 days (Singhal, 2020). The virus has spread throughout the world, infecting approximately 10 million people and a further 500,000 deaths (World O. Meters, 2020).

Viral transmission occurs from one infected individual to another, which can be done through objects, mucous membranes, secretions, coughing, among others, and the capacity of contagion (R0) are 2.74 people. The risk group includes people over 60 years of age, mainly hypertensive, diabetics, cardiopathy and individuals with chronic respiratory disease (Lima, 2020). Patients who contract the pathogen may frequently have a fever, fatigue, cough, headache, hemoptysis, and sputum (Guan, et al., 2020). Besides, they may suffer from loss of taste and smell (Triglle, et al., 2020).

So far, specific therapeutic agents and preventive vaccines are unavailable for COVID-19. Nevertheless, many drugs are tested to discover their efficacy for SARS-CoV-2.

The drugs include baricitinib, chloroquine, remdesivir, hydroxychloroquine, the interleukin-6 receptor monoclonal antibody (IL-6) tocilizumab, the anti-influenza drugs favipiravir, and umifenovir (Triggle, et al., 2020).

In order to prevent the new coronavirus, social isolation is recommended in principle in order to prevent contagion with other people (Singhal, 2020). Also, health organizations recommend habits related to personal hygiene, such as cleaning personal objects - cell phones, washing hands, using alcohol gel 70%, avoiding physical contact, among other recommendations (Lima, 2020).

The definitive diagnosis of the new coronavirus is made from specific molecular tests on respiratory samples, by throat smear, nasopharyngeal smear, sputum, endotracheal aspirates, and bronchoalveolar lavage. Also, the virus can be detected in feces and, in more severe cases, in the blood (Singha, 2020). Although definitive laboratory diagnosis is made with methodologies such as reverse transcription-polymerase chain reaction (RT - PCR) and serological methods (such as enzyme immunoassay (ELISA), imaging tests can provide valuable information regarding the disease (Huang, et al., 2020a).

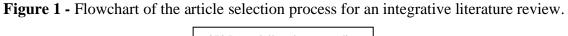
X-ray, utilizing ionizing radiation, is capable of producing images of structures of the human body. Structures with high density appear lighter - bones, while structures with low density appear dark - lung, heart. This technique is quite indicated for evaluations of lung diseases. Computed Tomography (CT), in turn, is based on the operation of an X-ray device that rotates around the patient and creates sliced images, which are later gathered in the computer and automatically there is a reconstruction of the image, allowing its visualization (Araújo-Filho, et al., 2020).

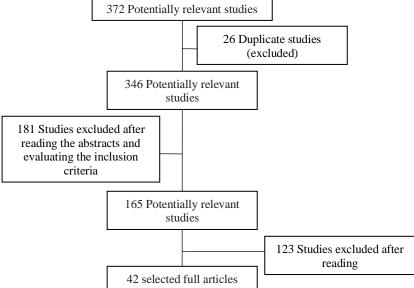
Nuclear Magnetic Resonance (NMR), on the other hand, uses radio waves and a powerful magnetic field for imaging. It has great prominence in the diagnosis of infectious processes because it allows its location, characterization, evaluation of responses, and monitoring. However, this technique presents a very high cost and limitations of use for patients with some metal fragments in the body (Castarelli, et al., 2020).

Most of the time, the diagnosis of infectious diseases is based on symptoms, laboratory tests, and imaging, especially X-ray, CT, and MRI. However, for COVID-19 these exams are only indicated for evaluation of possible complications and alternative diagnostic research, and should not be used in the initial screening of suspect patients (Chate, et al., 2020, Farias, et al., 2020, Moreira, et al., 2020a, Muniz, et al., 2020). Given the above, this study aimed to analyze the main imaging examinations of the respiratory syndrome caused by the new coronavirus through a narrative review of the literature.

2. Methodology

This research deals with a review of the scientific literature published so far, of a qualitative and descriptive nature, carried out from July 2020. The search occurred in the virtual health library databases, refined by the sources of Latin American and Caribbean Literature in Health Sciences (LILACS), Scientific Electronic Library (SCIELO), BIREME (Regional Library of Medicine), and MEDLINE. Data were collected by simple random sampling according to the scientific research elaboration manual proposed by Pereira et al. (2018). The inclusion criteria adopted were: an experimental study with images published, article integrality available, in Portuguese, Spanish, or English, published in 2020, in the databases mentioned above, and which addressed imaging findings of the new COVID-19. The exclusion criteria recommended were published articles that did not address the proposed theme. Below is the flowchart of the article selection process for an integrative literature review (Figure 1).





Source: Authors.

3. Literature review and discussion

Among the authors studied, the recurrence of isolated or multifocal frosted glass opacities was observed, as frequent findings we notice the presence of consolidations, such as cardiomegaly, reduction of airway space, aerobronchograms and pleural effusion. Moreover,

there were atypical findings, which included: pneumothorax, encephalomyelitis, myocarditis, gangrene, lymphadenopathy, cavitation, hemorrhagic colitis, and myasthenia gravis. These data are described in Frame 1.

Pneumonia caused by COVID-19 presents some common radiological findings. Extensive bilateral opacification in frosted glass is found at CTs - which in most cases involve the lobes and inferior consolidations, vascular thickening, reduction of air spaces, and pleural effusion. Chest radiological examination shows that about 72.9% of patients who acquired pneumonia through the new coronavirus showed bilateral lung injury, and among these, 68.5% were characterized by frost-glass opacities (Rodriguez-Morales, et al., 2020).

Author	Magazine	Place	Туре	Ν	Image Findings
Araujo-Filho et al.	J Bras. Pneumol	Brazil	Case report	1	Frosted glass opacities, focal consolidations and mixed opacities, inverted halo, generally with bilateral and multifocal involvement, peripheral distribution and predominance in lung fields
Bai et al.	Radiology	China	Transversal	424	Peripheral distribution, frosted glass opacity, and vascular thickening
Beitzke et al.	J Cardiovasc Imaging	USA and Europe*	Review	-	MRI: Myocarditis, stress-induced cardiomyopathy
Bernheim et al.	Radiology	China	Transversal	121	Bilateral and peripheral frosted glass, lung opacities, consolidations, crazy paving, and reverse halo signal
Carvalho et al.	The American Journal of Gastroenterology	USA	Case report	1	Small right pleural effusion. Inflammation of the transverse, ascending, and descending colon
Chate et al.	J Bras Pneumol.	Brazil	Transversal	12	Occasionally, pulmonary opacities in frosted glass, consolidations, with predominantly peripheral distribution, sometimes associated with thin reticulation (configuring the pattern of mosaic paving), vascular thickening and the inverted halo signal
Chung et al.	Radiology	China	Transversal	21	Opacities in frosted glass, opacities with morphology, peripheral distribution, consolidation, crazy paving
Craver et al.	Fetal and Pediatric Pathology.	USA	Case report	1	Eosinophilic Myocarditis
Farias et al.	Clinics.	Brazil	Review	-	Frosted glass opacities, consolidations, and crazy paving pattern, bilateral and multifocal distribution

Frame 1 - Typical and atypical findings described in the literature for new COVID-19.

Moreira et al. 2020a	Journal of the Brazilian Society of Tropical Medicine	Brazil	Case report	1	Few opacities of frosted glass scattered in both lungs, with predominant peripheral distribution
Moreira et al. 2020b	Journal of the Brazilian Society of Tropical Medicine	Brazil	Case report	1	Frosted glass opacity, small foci of consolidation
Muniz et al.	Journal of the Brazilian Society of Tropical Medicine	Brazil	Case report	1	Multifocal opacities in frosted glass, some areas of consolidation
Novara et al.	European Review for Medical and Pharmacological Sciences	Italy	Transversal	-	Coagulopathy and DIC
Novi et al.	Neurol Neuroimmunol Neuroinflamm	Italy	Case report	1	Acute disseminated encephalomyelitis after SARS-CoV-2 infection
Ramaswamya et al.	Journal of Neuromuscular Diseases	USA	Case report	1	Refractory Myasthenia Gravis
Rosa et al.	Einstein	Brazil	Transversal	14	It has frosted glass opacity. Mosaic paving. Pleural spill. Inverted Halo sign. Consolidation. Lymphadenomegaly.
Ucpinar &Yanc	Journal of Infection and Public Health	Turkey	Case report	1	Bilateral frosted glass opacities, pneumo- mediastinum, pneumothorax
Vetrugno et al.	Echocardiography	Italy	Review	-	Repetition of the pleural line at the same distance from the skin to the pleural line in the LU. Presence of B2 lines
Yang et al.	Eur Radiology	China	Review	-	Chest radiography: Progressive opacities and consolidations in patients with a severe state. The lung looks whitish
Zhang et al.	Clinical Perspectives	China, USA, Canada	Case report	1	Frosted glass attenuation, left ventricle dilated

Legend: CBR - Brazilian College of Radiology and Imaging Diagnosis; ICD - Disseminated Intravascular Coagulation; LU - Pulmonary Ultrasound. * Italy, Germany, France, and the United Kingdom. Source: Elaborated by the authors.

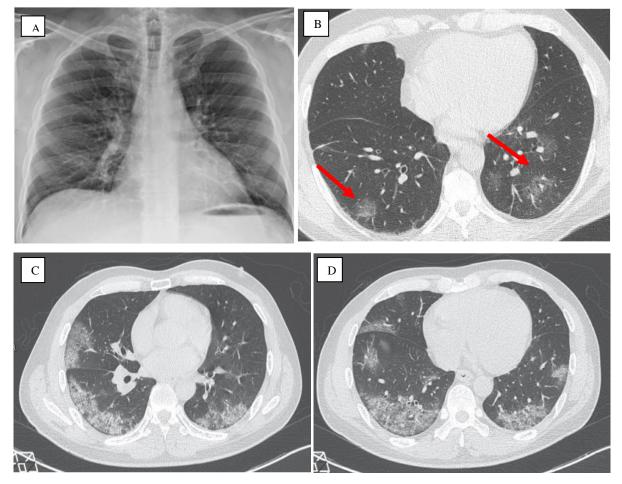
In the frame above, it is possible to notice that the works are concordant in the typical presentations of VOCID, besides several authors reported the presence of atypical findings as gangrene, pneumothorax, myocarditis, colitis, and others.

In X-ray, radiographic findings are usually absent in the early stages, when computed tomography already shows typical findings. (Figure 2). However, about 50% of patients may have standard CT soon after the onset of symptoms (0-2 days).

When altered, the x-ray usually shows opacity in parenchymatous and compromising the lower lobes. In the most severe cases of late diagnosis, thick stripes towards the hilum can be noted, which represents lymphatic dissemination of the disease, presence of the disseminated form.

Bilateral consolidations and pulmonary edema are also observed. The presence of opacity in a "butterfly wing" pattern has not been widely reported in the literature.

Figure 2 - Above, in A radiography of a patient seen with respiratory symptoms (positive PCR for SARS-CoV2) without pulmonary changes, and in B CT of the same day with some foci of frosted glass opacities (arrows) demonstrating higher sensitivity of tomography at the first signs of the disease. Source: Brazilian College of Diagnostic Imaging, 2020. Below are images of chest CT (axial sections), lung window, showing opacities in frosted glass, multifocal and bilateral, with peripheral and posterior predominance. Find in a patient with COVID-19 infection (laboratory-confirmed by RT-PCR). Source: Araújo-Filho, 2020.

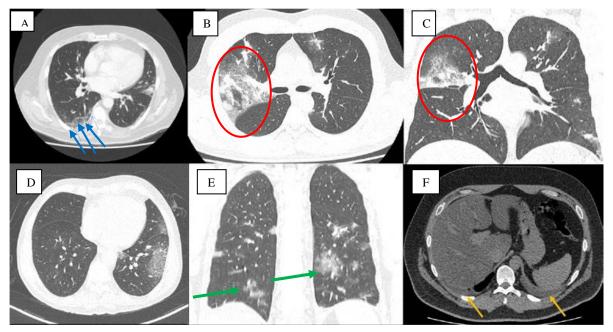


Source: Authors.

The image above in "A" shows a radiograph of a patient positive for coronavirus, in which no complications are presented in the lung. In image "B" we observe the tomography of a patient with foci of opacities in frosted glass, the attenuation changes. In "C" we see the image of another patient with a more advanced stage of pulmonary involvement, presenting important opacification of the lobes.

Among the causes of diffuse pulmonary opacification is pulmonary edema, which can occur by increased capillary permeability (non-hydrostatic) or by increased pulmonary venous pressure. Pulmonary consolidation is defined as the replacement of air from the alveoli by fluid, cells, or by a combination of these two. In radiological exams, these alterations are characterized by opaque images, causing erasure of the pulmonary vessels (Figure 3).

Figure 3 - Tomographic sections of different patients exemplifying the spectrum of COVID-19 findings in our casuistry. In A, a 61-year-old male patient presenting peripheral and posterior frosted glass opacities in the lower lobes (blue arrows in the right lower lobe), besides another opacification focus of the parenchyma in the lingula. In B and C, a 41-yearold male patient with extensive frosted glass opacities (red circles) with interlobular septum thickening and reticulated permeation (mosaic paving) in the upper right lobe, besides other small, sparse foci in the upper and lower lobes of the left lung. In D, an 85-year-old male patient with opacities in frosted glass, associated with thin reticulation and thickening of some interlobular septa, with more significant extension in the periphery of the left lower lobe, but also present in the lingula and, more discretely, in the right lower lobe. In E and F, a 42-yearold male patient presented with frosted glass opacities and discrete foci of bilateral consolidation (green arrows), predominating in the more posterior regions of the lower lobes. This patient also presented with minimal bilateral pleural effusion (arrows), a relatively uncommon finding in patients with COVID-19. Additionally, signs suggestive of hepatic steatosis were identified. Source: Chate, et al., 2020.



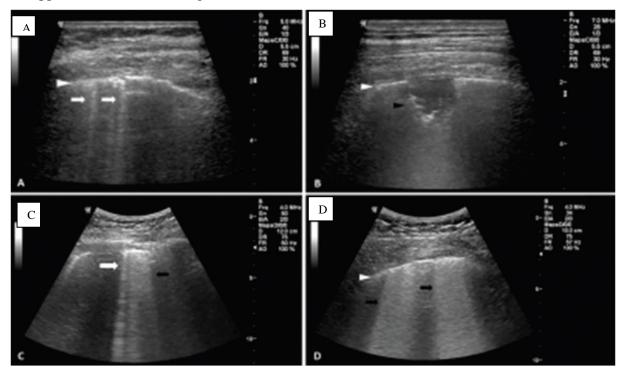
Source: Authors.

As shown in the figure above, from sections performed at the tomography of patients with positive for coronavirus, it can be observed in "A" foci with alteration in the peripheral lung coloration, referring to opacities in frosted glass. In "B" and "C" the patient has an excellent opacity in frosted glass, which leaves more noticeable, with thickening of interlobular septa in the lung. In "D" the patient also has opacity in frosted glass, with the

thickening of some interlobular septa. In "E" and "F" the patient presented opacity in frosted glass, and some foci of bilateral consolidations - slightly whitish structures, besides presenting pleural effusion, which is characterized by the accumulation of fluid in the lung, which gives white coloration.

Other works also highlight the use of less conventional tools in imaging diagnosis, such as the use of ultrasonography (US) (Figure 4). Preliminary studies of case series (China), in February 2020, bring evidence that patients hospitalized due to pulmonary involvement, by COVID-19, present to the ultrasonographic examination: pattern of sparse B lines, in different regions of both lungs, and less frequently, areas of pulmonary consolidation. (Huang, et al., 2020b, Peng, et al., 2020). On the other hand, there is no scientific evidence, so far, that the US of the chest plays a useful role in the diagnosis or initial evaluation of patients with COVID-19. It is important to emphasize that chest US does not replace techniques such as high resolution computed tomography in these patients. (Chung, et al., 2020, Feng, et al., 2020)

Figure 4 - Lung ultrasound. Linear (A and B) and convex (C and D) transducers in intercostal spaces show irregular and thickened pleural line (white arrowhead); hypoechogenic image with irregular contours, compatible with subpleural consolidation (black arrowhead); multifocal B-lines (white arrow), some of which are coalescent (black arrow), characterizing the appearance of a white lung on ultrasound (A). Source: Farias et al., 2020.



Source: Authors.

In the image above, it is possible to observe that the thoracic US provides essential information about the disease in the patient in question. This technique identified the occurrence of subpleural consolidations, once unidentified in ultrasonography.

Extracardiac thoracic ultrasonography is a proven method for the identification of pulmonary edema and consolidation, pleural effusion, and pneumothorax. It is particularly useful in the evaluation of patients in intensive and semi-intensive care, trauma, and emergencies (Oliveira, et al., 2020).

Although more studies are needed to confirm the role of US, it may prove useful in the follow-up of severe bedside COVID-19 patients, as already used in other causes of an acute respiratory syndrome (Poggiali, et al., 2020)

When indicated, the protocol is a high-resolution CT scan (HRCT), if possible, with a low dose protocol. The use of intravenous contrast media, in general, is not indicated, being reserved for specific situations to be determined by the radiologist (Brazilian College of Diagnostic Imaging, 2020).

They can be performed according to the following parameters: (1) Patients with clinical and laboratory suspicion of the disease, especially those with a more severe clinical condition. (2) Chest CT should not be performed for screening the disease, but in symptomatic hospitalized patients with normal radiographs or with undetermined findings. (3) Imaging tests are indicated in the evaluation of complications and alternative diagnostic research. The tomographic findings found that according to the time of evolution of the disease are described in Frame 2.

Initial Phase	- They can be healthy (around 50%);
(0-2 days from	- Focal opacities with frosted glass attenuation or consolidations (about 17%);
onset of	- Bilateral multifocal opacities (about 28%);
symptoms)	- Lung lesions have peripheral distribution in approximately 22% of cases.
	Sequential CTs have shown the progression of lung lesions
Intermediate	- CT can be normal in less than 10% of cases;
Phase	- Consolidation at about 55%
(3 to 5 days)	- Most of the involvement is bilateral (about 76%), with peripheral distribution (64%)
	- Reticular opacities in approximately 9% of cases.
	- CT can be normal in less than 5% of cases
	- Consolidation in 60% of cases;
Late Phase	-Involvement is bilateral in about 88%, with peripheral distribution (72%)
(6 to 12 days)	-Reticular opacities around 20 %.
	-There are different degrees of resolution of pulmonary changes, but complete resolution
	may not occur until around the 26th day.

Frame 2 - Radiological evolution of COVID-19 at C

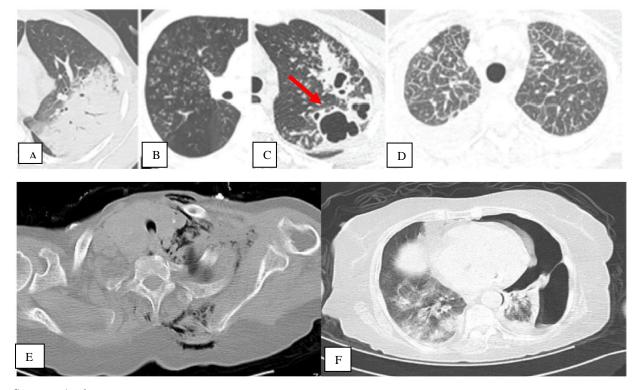
Source: Elaborated by the author.

Frame 2 summarizes the main findings of the disease according to clinical evolution. In the first days, CT may be unaltered or with minor focal changes, opaque, with or without consolidation. As the disease evolves, the size and frequency of consolidations increase, becoming evident in up to 90% of patients. Finally, in the later phases, abnormalities are observed in the vast majority of patients, consolidations, and the involvement becomes bilateral.

Unusual characteristics were also found, such as pleural and pericardial effusion, lymphadenopathy, cavitation, pneumothorax, emphysema, encephalomyelitis, gangrene, hemorrhagic colitis, myocarditis, and myasthenia gravis (Figure 5). During the acute phase of infection with COVID-19, about 36% of the cases evaluated in one study developed

neurological symptoms, 25% of which can be attributed to the direct involvement of the central nervous system (Figure 6). Additionally, hemorrhagic lesions of the white matter associated with axonal lesions and surrounding macrophages were found in the cerebral hemispheres. The subcortical white matter, on the other hand, was arranged in scattered groups of macrophages, associated with an appearance similar to acute perivascular disseminated encephalomyelitis (Needham, et al., 2020).

Figure 5 - Atypical findings of COVID-19. Axial CT images show (A) isolated segmental consolidation; (B) discrete small centrilobular nodules, some of them with the "tree-in-bud" pattern; (C) lung cavitations; and (D) bilateral smooth interlobular septal thickening with pleural effusion. Fonte: Farias, et al., 2020. Em (E) e (F), axial CT scan of the level of superior thoracic aperture in the mediastinal window: (E) subcutaneous emphysema between the deep structures of the neck and posterior thoracic wall. Axial CT scan of the thorax in lung window; (F) massive left-sided pneumothorax. Bilateral ground-glass patchy opacities are also seen representing COVID-19 lung involvement. Source: Ucpinar, et al., 2020.

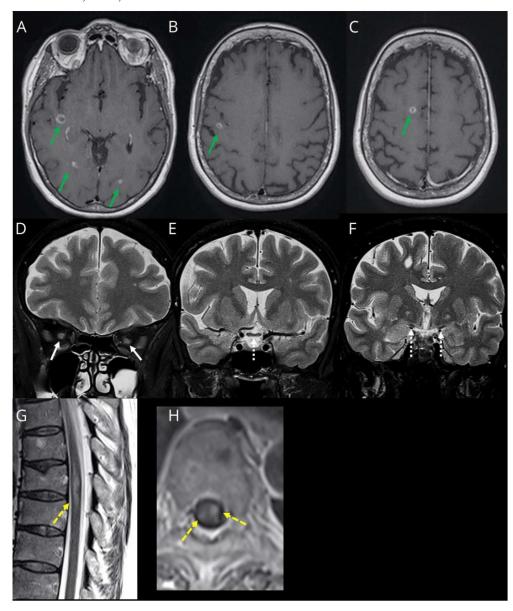


Source: Authors.

In the image above, it is possible to observe some atypical findings of patients with COVID-19. The presence of consolidation was found, which is defined as the replacement of air from the alveoli by fluid, cells, or a combination of these two. In radiological

examinations, these alterations are characterized by opaque images, causing erasure of the pulmonary vessels, without significant loss of volume of the affected segment (Araujo-Filho, et al., 2020). Also, nodules and cavitations were observed. These cavitations are defined as a lung area filled by air in the center of a nodule or consolidated area. Pneumothorax denotes the presence of air in the pleural space. Subcutaneous emphysema is the accumulation of gases or air (emphysema) in the subcutaneous tissues below the skin. Since air usually comes from the thoracic cavity, most subcutaneous emphysema occurs in the chest, neck, and face.

Figure 6 - (A–C) Postgadolinium (Gd) T1-weighted (T1w) sequence of the brain in the axial plane showing six enhancing lesions (green arrows), most of which with ring enhancement and some of which with nodular enhancement. Incomplete ring enhancement is shown about the right temporal lesion (dashed green arrow). (D–F) T2-weighted (T2w) fat-saturated sequence in the coronal plane with evidence of (D) hyperintense signal of the optic nerves bilaterally (white arrows), which is best seen when compared with the average signal within (E) the optic chiasm and (F) the optic tracts (dashed white arrows). (G) T2w sequence of the thoracic spine in the sagittal plane showing a hyperintense spindle-like T8 lesion, involving less than two metameric levels (dashed yellow arrow). (H) Post-Gd T1w sequence of the spine in the axial plane at the level of T8 showing eccentric areas of enhancement respectively located posteriorly to the right and anteriorly to the left (dashed yellow arrow). Source: Novi, et al., 2020.



Source: Authors.

Although the neurological manifestations of COVID-19 have not been adequately studied, there is growing evidence that reports infection caused by Sars-CoV-2 and its ability to generate neurological deficits in a substantial proportion to affected patients. Although these symptoms appear in the acute phase of infection, little is known about the long-term consequences for the brain. In the literature at the moment, it is known that patients in severe cases of COVID-19 had high levels of pro-inflammatory cytokines and respiratory dysfunction, factors of which suggest a cognitive decline. Pathogenically, this can generate direct adverse effects of immune reaction, worsening of pre-existing cognitive deficits, or induction of a new neurodegenerative disease (Heneka, et al., 2020).

There are at least four possible pathogenic mechanisms that can explain the detrimental effect of COVID-19 on the CNS: (1) direct viral encephalitis, (2) systemic inflammation, (3) organ dysfunction, and (4) cerebrovascular changes. In which neurological manifestations of COVID-19 may arise from a combination of the above (Needham, et al., 2020).

Any combination of these mechanisms, or an isolated factor, puts COVID-19 survivors at risk of developing long-term neurological consequences and may aggravate a preexisting neurological disorder or initiate a new disorder. This concern is supported by findings that show that one-third of patients have cognitive impairment and motor deficit at the time of discharge (Heneka, et al., 2020).

According to scientific literature, there were neuropathological findings in the autopsy of a patient who died due to complications caused by COVID-19, which revealed a series of neuropathological lesions, with characteristics similar to vascular and demyelinating etiologies. Hemorrhagic lesions of the white matter were present in the cerebral hemispheres with surrounding axonal lesions and macrophages. The subcortical white matter had scattered groups of macrophages, a variety of associated axonal lesions, and an appearance similar to perivascular acute disseminated encephalomyelitis (Needham, et al., 2020). When the study is done related to the peripheral nervous system (PNS), few reports are showing a direct involvement, but in general, the literature points out that there are complications in taste/palate, nerve pain, and skeletal muscle injuries. (Asadi-Pooya & Simani, 2020).

Therefore, it is worth emphasizing that there is a known risk of Guillain-Barre syndrome (GBS) attributable to viral infections (Needham, et al., 2020). The logic is that there is a molecular imitation between specific viral proteins and proteins in peripheral nerves (e.g., gangliosides), which lead to an attack by innocent bystanders against myelin or axon of peripheral nerves, among the existing symptoms the patient may present lower limb weakness

and facial diplegia. However, causality is still uncertain (Toscano, et al., 2020). Because the predominant manifestations of COVID-19 are related to respiratory dysfunctions, neurological manifestations can be neglected in the cases caused by COVID-19.

With the above, we believe that imaging is a valuable tool to complement the clinical suspicion; serving to locate the foci of infection and to guide biopsies and surgeries, as well as complement the diagnosis of the new coronavirus. It is also essential to be aware of the atypical findings of the disease and not to neglect possible neurological alterations that may be associated with the disease.

4. Conclusion and Suggestions

COVID-19 infection is associated with significant morbidity, especially in patients with chronic medical conditions that cause detectable imaging changes. In short, diversified patterns of lung disease are found, with main characteristics of bilateral, peripheral, and basal opacifications, with rounded morphologies, presence of lymph nodes, pleural effusion, excavation, and nodules in the most severe cases. About 50% of patients may have a normal examination soon after the onset of symptoms (0-2 days). In the scenario of severe lung disease, organization and fibrosis may occur. These findings are not indicated for the initial screening of suspect patients, but they help satisfactorily in the evaluation of severe complications.

As suggestions, we recommend that the imaging exams be used in a complementary way to the laboratory diagnosis. We also emphasize the rational use of techniques that involve risk to the patient, such as excessive exposure to ionizing radiation, for example. In order to guide the performance of professionals, we also suggest the use of the *Clinical Management Protocol for New Coronavirus 2019-nCoV established by the Brazilian* Ministry of Health (MS) as a tool for better decision making.

This study indicates that the characteristics of COVID-19 are similar in the multiple studies published; however, new work must be done to expand scientific knowledge on the subject.

References

Araújo-Filho, J. A. B., Sawamura, M. V. Y., Costa, A. N., Cerri, G. G., & Nomura, C. H. (2020). COVID-19 pneumonia: what is the role of imaging in diagnosis? *Brazilian Journal of Pneumology*, *46* (2), 1-2. doi:10.36416/1806-3756/e20200114

Asadi-Pooya, A. A., & Simani, L. (2020). Central nervous system manifestations of COVID-19: A systematic review. *Journal of the Neurological Sciences*, *413*, 1-5. doi:10.1016/j.jns.2020.116832

Bai, H. X., Hsieh, B., Xiong, Z., Halsey, K., Choi, J. W., & Tran, T. M. L. (2020) Performance of radiologists in differentiating COVID-19 from viral pneumonia on chest CT. *Radiology*, 295 (3), 686-691. doi:10.1148/radiol.2020200823

Beitzke, D., Salgado, R., Francone, M., Kreitner, K. F., Natale, L., Bremerich, J., Gutberlet, M., & Executive Committee of the European Society of Cardiovascular Radiology (ESCR). (2020). Cardiac imaging procedures and the COVID-19 pandemic: recommendations of the European Society of Cardiovascular Radiology (ESCR). *The international journal of cardiovascular imaging*, 1–10. doi:10.1007/s10554-020-01892-8

Bernheim, A., Mei, X., Mingqian, H., Yang, Y., Zahi A. F., Ning, Z., Diao, B. L. K., & Zhu, X. (2020). Chest CT Findings in Coronavirus Disease-19 (COVID-19): Relationship to duration of infection. *Radiology*. 295, 685–691. doi:10.36416/1806-3756/e20200114

Brazilian College of Radiology and Diagnostic Imaging. (2020). *Results of the image in COVID-19. CBR identification and interpretation guide*. Retrieved from https://cbr.org.br/wp-content/uploads/2020/03/Interpretac%CC%A7a%CC%83o-dos-achados-de-imagem_21_03_20.pdf

Cantarelli, B. C. F., Oliveira, R. S., Alves, A. M. A., Ribeiro, B. J., Velloni, F., & D'Ippolito, G.. (2020). *Evaluation of the inflammatory activity of Crohn's disease by sectional imaging methods. Brazilian Radiology*, 53 (1), 38-46. doi:10.1590/0100-3984.2018.0096

Carvalho, A., Alqusairi, R., Adams, A., Paul, M., Kothari, N., & Peters, S. (2020). SARS-CoV-2 Gastrointestinal Infection Causing Hemorrhagic Colitis: Implications for Detection and Transmission of COVID-19 Disease. *Am J Gastroenterol, 115*, 942–946. doi:10.14309/ajg.00000000000667

Chate, R. C., Fonseca, E. K., Steps, R. D., Teles, G. B. Shoji, H., & Szarf, G. (2020). Tomographic presentation of a lung infection at COVID-19: the initial Brazilian experience. *J Bras Pneumol*, 46 (2), 1-4. doi:10.36416/1806-3756/e20200121

Chung, M., Bernheim, A., Mei, X., Zhang, N., Huang, M., Zeng, X., Cui, J., Xu, W., Yang, Y., A., & Fayad, Z. (2020). CT Imaging Features of 2019 Novel Coronavirus (2019-nCoV). *Radiology*, 295 (1), 202-207. doi:10.1148/radiol.2020200230.

Craver, R., Huber, S., Sandomirsky, M., McKenna, D., Schieffelin, J., & Finger, L. (2020). Fatal Eosinophilic Myocarditis in a Healthy 17-Year-Old Male with Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2c). *Fetal and Pediatric Pathology, 39* (3), 263–268. doi:10.1080/15513815.2020.1761491

Farias, L.P. G., Fonseca, E. K. N., Strabelli, D. G., Loureiro, B. M., Neves, I. S., & Rodrigues, T. P. (2020). Imaging findings in COVID-19 pneumonia. *Clinics*, 27, 1-8. doi:10.6061/clinics/2020/e2027

Feng, P., Tianhe, Y., Peng, S., Gui, S., Liang, B., Li, L., Zheng, D., Wang, J., Hesketh, R. L., & Yang, L. (2020). The course of lung changes on chest CT during recovery from 2019 novel coronavirus (COVID-19) Pneumonia. *Radiology*, 295, 715–721. doi:10.1148/radiol.2020200370

Guan, W. J., Ni, Z., Hu, Y., Liang, W. H, Ou, C. Q., & He, J. X. (2020). Clinical Characteristics of Coronavirus Disease 2019 in China. *The New England journal of medicine*, 382 (18), 1708-1720. doi:10.105/NEJMoa2002032

Heneka, M. T, Golenbock, D., Latz, E., Morgan, D., & Brown, R. (2020). Immediate and long-term consequences of COVID-19 infections for the development of neurological disease. *Alzheimer's Research & Therapy, 12* (69), 1-3. doi:10.1186/s13195-020-00640-3

Huang, Y., Wang, S., Liu, Y., Zhang, Y., Zheng, C., Zheng, Y., & Zhang, C. (2020a). A Preliminary Study on the Ultrasonic Manifestations of Peripulmonary Lesions of Non-Critical Pneumonia (COVID-19). *Research Square*, 1-37. doi:10.2139/ssrn.3544750

Huang, Y., Wang, S. Li, X., Ren, L., Zao, J., & Hu, J., (2020b). Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*, *395*, 497–506. doi:10.1016/S0140-6736(20)30183-5

Lima, C. M. A. O. (2020). Information about the new coronavirus disease (COVID-19). *Brazilian Radiology*, *53* (2), 5-6. doi:10.1590/0100-3984.2020.53.2e1

Moreira, B. L., Brotto, M. A., & Marchiori, E. (2020a). Chest radiography and computed tomography findings from a Brazilian patient with COVID-19 pneumonia. *Journal of the Brazilian Society of Tropical Medicine*, *53*, 1-2. doi:10.1590/0037-8682-0134-2020

Moreira, B. L., Santana, P. R., Zanetti, G., & Marchiori, E. (2020b). COVID-19 and acute pulmonary embolism: what should be considered to indicate a computed tomography pulmonary angiography scan? *Journal of the Brazilian Society of Tropical Medicine*, *53*,1-2. doi:10.1590/0037-8682-0267-2020

Muniz, B. C., Milito, M. A., & Marchiori, E. (2020). COVID-19 - Computed tomography findings in two patients in Petrópolis, Rio de Janeiro, Brazil. *Journal of the Brazilian Society of Tropical Medicine*, *53*, 1. doi:10.1590/0037-8682-0147-2020

Needham, E. J., Chou, S. H., Coles, A. J., & Menon, D. K. (2020). Neurological Implications of COVID-19 Infections. *Neurocritical care society*, *1*, 1-5. doi:10.1007/s12028-020-00978-4

Novara, E., Molinaro, E., BenedettI, I., Bonometti, R., Lauritano, E. C., &. Boverio, R. (2020). Severe acute dried gangrene in COVID-19 infection: a case report. European *Review for Medical and Pharmacological Sciences*, *24*, 1-3. doi:10.26355/eurrev_202005_21369

Novi, G. Rossi, T., Pedemonte, E., Saitta, L., Rolla, C., Roccatagliata, L., et al. (2020). Acute disseminated encephalomyelitis after SARS-CoV-2 infection. *Neurol Neuroimmunol Neuroinflamm*, 7, 1-4. doi:10.1212/NXI.000000000000797

Oliveira, R. R., Rodrigues, T. P., Savoia, P., Gomes, A. C., & Chammas, M. C. (2020). Lung ultrasound: an additional tool in COVID-19. *Radiol Bras, 1*, 1-11. doi:10.1590/0100-3984.2020.0051

Peng, Q., Wang, X., & Zhang, L. (2020). Findings of lung ultrasonography of novel coronavirus pneumonia during the 2019–2020 epidemic. *Intensive Care Med*, 46, 849–850. doi:10.1007/s00134-020-05996-6

Pereira, A. S., Shitsuka, D. M., Parreira, F. J., & Shitsuka, R. (2018). *Methodology of scientific research*. Retrieved from https://repositorio.ufsm.br/bitstream/ handle/1/15824/Lic_Computacao_Metodologia-Pesquisa-Cientifica.pdf?sequence=1

Poggiali, E., Dacrema, A., & Bastoni, D. (2020). Can Lung US Help Critical Care Clinicians in the Early Diagnosis of Novel Coronavirus (COVID-19) Pneumonia? *Radiology*, 295 (3) 13:200847. doi:10.1148/radiol.2020200847

Ramaswamy, S. R., & Govindarajan, R. (2020). COVID-19 in Refractory Myasthenia Gravis-A Case Report of Successful Outcome. *Journal of Neuromuscular Diseases*, 7, 1-4. doi:10.3233/jnd-200520

Rodriguez-Morales, A., Cardona-Ospinaa, J. A., Gutiérrez-Ocampo, E., Villamizar- Peña, R., Holguin-Rivera, Y., & Escalera-Antezana, J. P. (2020). Clinical, laboratory and imaging features of COVID-19: a systematic review and meta-analysis. *Travel Med. Infect Dis, 34*, 1-14. doi:10.1016/j.tmaid.2020.101623

Rosa, M. E., Matos, M. J., Furtado, R. S., Brito, V. M., Amaral, L. T., & Beraldo, G. L.. (2020). COVID-19 findings identified in chest computed tomography: pictorial assay. *Einstein*, *18*, 1-6. doi:10.31744/einstein_journal/2020RW5741

Singhal, T. (2020). A Review of Coronavirus Disease-2019 (COVID-19). *Indian journal of pediatrics*, 87 (4), 281-286. doi:10.1007/s12098-020-03263-6

Toscano, G., Palmerini, F., Ravaglia, S., et al. (2020). Guillain–Barré Syndrome Associated with SARS-CoV-2. *The New England journal of medicine*, *382* (26), 1-3. doi:10.1056/NEJMc2009191

Triggle, C. R., Bansal, D., Farag, E., Ding, H., & Sultan, A. A. (2020). COVID-19: Learning from Lessons to Guide Treatment and Prevention Interventions. *mSphere*, *5* (3), e00317-20. doi:10.1128/mSphere.00317-20

Ucpinar, B. A., Sahin, C., & Yanc, Y. (2020). Spontaneous pneumothorax and subcutaneous emphysema in COVID-19 patient: Case report. *Journal of Infection and Public Health, 13* (6), 887-889. doi:10.1016/j.jiph.2020.05.012

Vetrugno, L., Bove, T., Orso, D., Barbariol, F., Bassi, & F., Boera, E. (2020). Our Italian experience using lung ultrasound for identification, grading and serial follow-up of severity of lung involvement for management of patients with COVID-19. *Echocardiography*, *37* (4), 625-627. doi:10.1111/echo.14664

Yang, W., Sirajuddin, A., Zhang, X., Liu, G., Teng, Z., Zhao, S., & Lu, M. (2020). The role of imaging in 2019 novel coronavirus pneumonia (COVID-19). *European radiology*, 1–9. doi:10.1007/s00330-020-06827-4

World O Meters. (2020). *COVID-19 coronavirus pandemic*. (2020). Retrieved from https://www.worldometers.info/coronavirus/

Zhang, L., Wang, B., Zhou, J., Kirkpatrick, J., Xie, M., & Johri, A. M. (2020). Bedside Focused Cardiac Ultrasound in COVID-19 from the Wuhan Epicenter: The Role of Cardiac Point-of-Care Ultrasound, Limited Transthoracic Echocardiography, and Critical Care Echocardiography. *Journal of the American Society of Echocardiography*, *33* (6), 667-82. doi:10.1016%2Fj.echo.2020.04.004

Zhu, N., Zhang, N., Wang, W., Li, X., Yang, B., Song, J., et al. (2020). A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med.*, 382 (8), 727-33. doi:10.1056/NEJMoa2001017

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