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Review on radiological evolution of COVID-19 pneumonia using computed tomography

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Abstract

BACKGROUND

Pneumonia is the main manifestation of coronavirus disease 2019 (COVID-19) infection. Chest computed tomography is recommended for the initial evaluation of the disease; this technique can also be helpful to monitor the disease progression and evaluate the therapeutic efficacy.

AIM

To review the currently available literature regarding the radiological follow-up of COVID-19-related lung alterations using the computed tomography scan, to describe the evidence about the dynamic evolution of COVID-19 pneumonia and verify the potential usefulness of the radiological follow-up.

METHODS

We used pertinent keywords on PubMed to select relevant studies; the articles we considered were published until October 30, 2020. Through this selection, 69 studies were identified, and 16 were finally included in the review.

RESULTS

Summarizing the included works' findings, we identified well-defined stages in the short follow-up time frame. A radiographic deterioration reaching a peak roughly within the first 2 wk; after the peak, an absorption process and repairing signs are observed. At later radiological follow-up, with the limitation of little

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evidence available, the lesions usually did not recover completely.

CONCLUSION

Following computed tomography scan evolution over time could help physicians better understand the clinical impact of COVID-19 pneumonia and manage the possible sequelae; a longer follow-up is advisable to verify the complete resolution or the presence of long-term damage.

Key Words: COVID-19; Computed tomography; Pneumonia; Radiological evolution; Follow-up; Long-term consequences; Lung damage; SARS-CoV-2

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Core Tip: Given the recent discovery and study of severe acute respiratory syndrome coronavirus 2 infection, the evolution of coronavirus disease 2019 pneumonia has not been entirely defined yet. Chest computed tomography is an effective method to identify and follow coronavirus disease 2019 pneumonia over time. In this review, we considered the radiological changes on computed tomography scan and described the possible clinical pulmonary sequelae in order to understand the long-term outcome of coronavirus disease 2019 pneumonia better.

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INTRODUCTION

SARS-CoV-2, which stands for severe acute respiratory syndrome coronavirus 2, was first identified in December 2019 in Wuhan, China. The coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2 has rapidly spread from China to all around the world within a few months, leading the World Health Organization to declare it a pandemic on March 11, 2020[1].

The transmission of SARS-CoV-2 happens through direct, indirect or close contact with infected people through infected secretions, such as saliva and respiratory secretions or their respiratory droplets. The main organ affected is the lung, with pneumonia being the major manifestation of the infection[2].

The gold standard for SARS-CoV-2 diagnosis is real-time reverse transcription-polymerase chain reaction. However, computed tomography (CT) is recommended for initial evaluation and diagnosis, and it is also useful in monitoring the disease progression and evaluating the therapeutic efficacy[3,4].

Until now, many reports have focused on CT scan features at diagnosis[5-7]. On the other hand, there are relatively few studies evaluating serial temporal changes in patients who underwent repeated CT examinations and, particularly, in the late follow-up.

Our aim is to review the literature currently available on the radiological follow-up of COVID-19-related lung alterations using the CT scan to describe the evidence about the dynamic evolution of COVID-19 pneumonia.

MATERIALS AND METHODS

We conducted this systematic review according to the Preferred Reporting Items guidelines for Systematic Reviews and Meta-Analysis (PRISMA) Statement[8]. The primary aim was to collect, describe and discuss the dynamic radiological evolution of COVID-19 pneumonia.

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Search strategy

Two authors (Casartelli C and Perrone F) carried out a comprehensive systematic search for published articles on the MEDLINE/PubMed library until October 31, 2020. Given the absence of articles on this topic before December 2019, when the first COVID-19 outbreak started, no upper limit for the search was chosen.

The following search keywords were used: “COVID-19” [all fields] AND “computed tomography” [all fields] AND “evolution” [all fields]. The reference lists of the included articles and reviews/meta-analyses on our research topic were also reviewed to identify additional relevant papers.

Study selection and eligibility criteria

Retrospective studies, prospective studies and case reports describing the evolution of COVID-19 pneumonia on CT scan were included. Only English language articles were considered eligible. Studies with insufficient radiological data were excluded. We planned qualitative analysis only, forecasting a high heterogeneity between the eligible studies, likely preventing quantitative analyses.

Data extraction and synthesis

The study characteristics (first author, year of publication, type of study, number of patients included, CT scan follow-up, dynamic evolution and main CT manifestations) were extracted from the included articles by a single author (Casartelli C). Two reviewers (Perrone F and Casartelli C) initially performed the data extraction, and then it was independently reviewed by an additional reviewer (Bersanelli M).

Any doubt or disagreement was discussed with a fourth investigator (Buti S) and resolved with all investigators’ consensus.

RESULTS

General description

The study selection led to the inclusion of 16 reports: 13 retrospective studies[9-21], 1 prospective study[22] and 2 case series[23,24]. The outline of the search is reported in [Figure 1](#).

These reports (more specifically, 15 from China[9-23], 1 from Italy[24]) have analyzed several cases of pneumonia caused by SARS-CoV-2 diagnosed through CT without contrast ([Table 1](#)).

Most of the reports have considered moderate/common pneumonia; if pneumonia was not explicitly classified, most of the articles included patients with a good and defined prognosis, who were ultimately discharged from the hospital, while patients with severe/critical pneumonia were generally excluded.

Four studies have also included a minority group of patients showing severe/critical pneumonia[10,14,17,20]; the 11 patients described by Sun Q *et al*[23] case series had severe pneumonia[23].

Scoring system

The most common score used to evaluate dynamic CT evolution was a semi-quantitative scoring system, which considered the total area of involvement of the lesions. The nature of the semi-quantitative scoring system was similar in the studies considered, even with some adjustments and discrepancies among them.

For example, Liang *et al*[11] assigned a 0-4 score based on the percentage of each lung lobe involvement; in agreement with this, the overall lung total severity score was reached by summing up the five lobe scores, with a possible range from 0 to 20.

Zhou *et al*[12] divided each lung into six zones, and the total score, given by the sum of the different lung regions, could reach a maximum of 48.

Zhang *et al*[15] used yet another adaptation of the system based on the lung segments involved, assigning a score based on the percentage of ground glass opacities (GGOs) and consolidation, with a possible range from 0 to 36.

The study from Liu *et al*[17], analyzing the CT of discharged patients, focused the score on non-GGO lesions since extended GGO areas were defined as a basic manifestation of convalescence, which could lead to an overestimation of the CT score.

Other authors, considering the limited accuracy and sensitivity of the semi-quantitative score based mainly on visual evaluation, proposed evaluating dynamic evolution by quantitative techniques.

Table 1 Characteristics and findings of the studies included in the systematic review

Ref.	Type of study	Patients included	Mean age in yr, range	CT scan follow-up	CT evaluation, scoring system
Han <i>et al</i> [9], 2020	Retrospective	17 surviving and discharged patients with COVID-19 pneumonia	40 ± 6	4 wk (4 weekly CT scan during hospitalization)	Semi-quantitative
Wang <i>et al</i> [10], 2020	Retrospective	63 patients with asymptomatic/mild, 378 with moderate, 43 with severe/critically COVID-19 pneumonia	47 (33-57)	From symptoms onset to beyond day 15	Quantitative
Liang <i>et al</i> [11], 2020	Retrospective	88 patients with mild COVID-19 pneumonia	42.7 (4-82)	3 wk after disease onset	Semi-quantitative
Sun <i>et al</i> [23], 2021	Case series	11 patients with severe COVID-19 pneumonia	52 (33-75)	CT scan during hospitalization (not well defined, at least 3 wk during hospitalization)	Qualitative
Zhou <i>et al</i> [12], 2020	Retrospective	100 patients with COVID-19 pneumonia (without ARDS)	52.3 ± 13.1 (27-80)	CT during hospitalization (from symptoms onset to beyond day 21)	Semi-quantitative
Wang <i>et al</i> [13], 2020	Retrospective	126 patients with COVID-19 pneumonia, (severe and critical cases excluded)	41.2 ± 10.8	CT scan during hospitalization (mean days of hospitalization 22 ± 5 d (12-40))	Qualitative
Wang <i>et al</i> [14], 2020	Retrospective	79 patients with non-severe (mild/common) COVID-19 pneumonia, 27 with severe pneumonia	48.0 ± 15.4	CT scan during hospitalization (mean days of hospitalization 25) + CT scan at 2-4 wk after discharge	Semi-quantitative
Zhang <i>et al</i> [15], 2020	Retrospective	33 patients with moderate COVID-19 pneumonia	49.0 ± 15.5	CT scan during hospitalization (mean days of hospitalization 20.8, range 18-37)	Semi-quantitative
Feng <i>et al</i> [16], 2020	Retrospective	19 patients with COVID-19 pneumonia	43.6 ± 15.5 (10-67)	0-34 d after symptoms onset	Quantitative
Liu <i>et al</i> [17], 2020	Retrospective	149 discharged patients with COVID-19 pneumonia (142 pneumonia, 7 severe pneumonia, no critical patients included)	43 (36-56)	Basal CT scan at discharge and at 1 st , 2 nd and 3 rd week after discharge	Semi-quantitative
Pan <i>et al</i> [18], 2020	Retrospective	105 patients with COVID-19 pneumonia (severe pneumonia excluded)	48.6 ± 13.1 (23-72)	1-47 d after symptoms onset	Semi-quantitative
Zhuang <i>et al</i> [19], 2021	Retrospective	22 patients with COVID-19 pneumonia with solitary pulmonary lesion	40.7 ± 10.3 (23-54)	CT scan during hospitalization (mean days of hospitalization 19 d, range: 11-44) + first CT scan after discharge	Semi-quantitative
Urciuoli and Guerriero [24], 2020	Case series	6 patients with mild COVID-19 pneumonia	59.5	First CT on admission and 4 mo after symptoms onset	Qualitative
Zhang <i>et al</i> [20], 2020	Retrospective	53 patients with common COVID-19 pneumonia, 20 patients with severe COVID-19 pneumonia	45 ± 14 common pneumonia, 50 ± 15 severe pneumonia	0-30 d after symptoms onset	Quantitative
Pan <i>et al</i> [21], 2020	Retrospective	21 patients with COVID-19 pneumonia (severe pneumonia excluded)	40 ± 9 (25-63)	0-26 d after symptoms onset	Semi-quantitative
Wang <i>et al</i> [22], 2020	Prospective	90 patients with COVID-19 pneumonia	45 ± 14 (5-43)	0-24 d after symptoms onset	Semi-quantitative

ARDS: Acute respiratory distress syndrome; COVID-19: Coronavirus disease 2019; CT: Computed tomography.

For example, Feng *et al*[16] measured the total volume (V_T) and mean CT value (CT), and from these, they calculated the mass (m): $V_T \times (CT + 1000)$ [16].

In the report from Wang *et al*[10], quantitative CT measurements of pulmonary opacities, including volume, density and location, were extracted through deep learning algorithms.

In another report, quantitative CT features were automatically calculated using intelligent artificial algorithms, giving back the percentage of GGO volume, consolidation volume and total lesion volume[15].

Other reports described the evolution of lung lesions qualitatively[13,23,24].

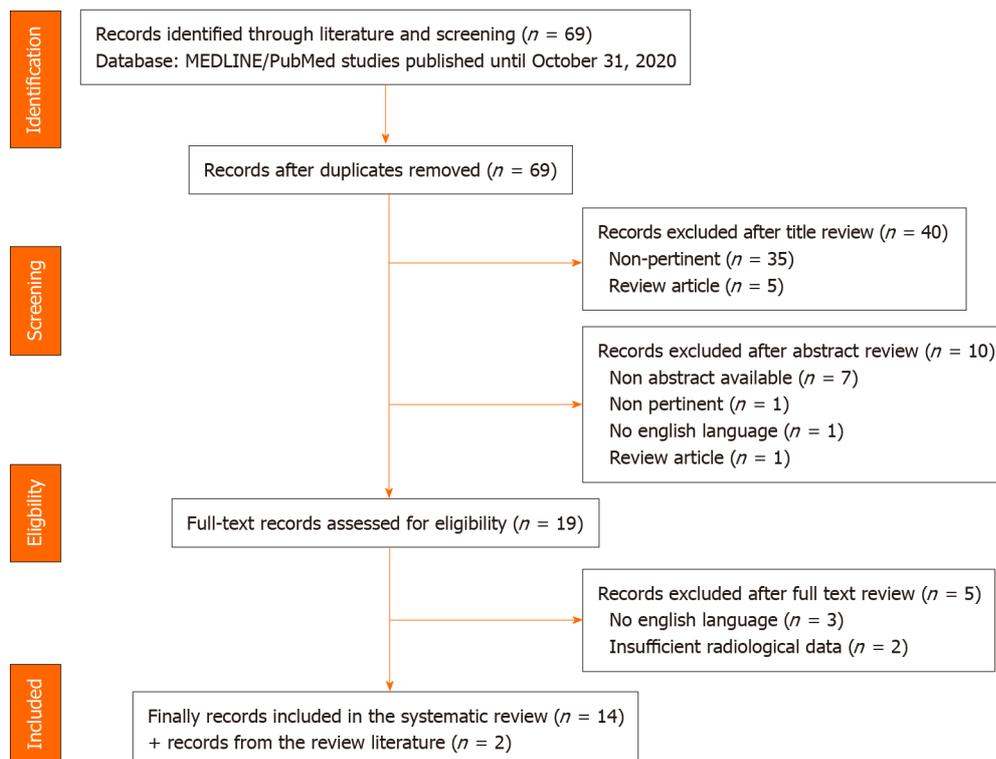


Figure 1 PRISMA flow diagram.

Radiological dynamic evolution: Severity and timing

Almost all the reports present a short-term radiological follow-up, focusing on the first few weeks from the symptoms appearance and studying serial CT scan approximately in the first 4 wk during hospitalization (Table 1).

It has been observed that the initial CT features and dynamic evolution of COVID-19 pneumonia have specific characteristics and regularity.

Several reports identify well-defined stages, from the onset of the symptoms to radiological recovery.

The most common pattern of radiographic evolution found is as follows. First, there is a progressive rapid radiographic deterioration, during which the lesions keep growing until they reach a peak; once this peak is reached, the lesions stop growing and are gradually reabsorbed and repairing signs appear. Almost all the studies found that the peak was reached roughly within 2 wk after the symptoms appearance, and after that lung abnormalities started to decrease.

There are some exceptions. Zhang *et al*[15] found an earlier peak, 8 d after symptoms onset, and lung lesions improved after 11 d. Wang *et al*[22] discovered a similar peak at around 6-11 d; in this case, though, a significant extent of lung lesions was found for longer times after the peak, showing a slower recovery.

Specific patterns of temporal evolution and relative peaks are shown in Table 2.

When severe pneumonia was considered separately, the disease seemed to have a slightly longer evolution, showing the peak later than for moderate pneumonia cases.

In the report from Zhang *et al*[20], severe pneumonia exhibited a peak approximately 17 d after symptoms onset (compared to moderate pneumonia, which peaked at 12 d in the same study). In the report from Wang *et al*[10], the opacity volume kept increasing even after 15 d in the severe/critical group. Four reports had taken into account a longer CT follow-up, considering CT scan after discharge[14,17,19,24].

Zhuang *et al*[19] considered both CT during hospitalization and the first CT after discharge (22-51 d after symptoms onset). During the latter phase, further absorption of the lung lesions compared with the previous radiological exam was observed, but not all patients showed a complete resolution.

Liu *et al*[17] studied the radiological evolution during the first few weeks after discharge, in particular 1, 2 and 3 wk after discharge. The aim was to determine the cumulative percentage of complete radiological resolution at each time point. They discovered that lung lesions could be entirely absorbed with no sequelae, and they suggested that the optimal time point for an early radiological estimation might be 2

Table 2 Computed tomography scan features of lung lesions according to the follow-up timing of coronavirus disease 2019 pneumonia

Ref.	Short-term follow-up, dynamic evolution during hospitalization period: Severity and timing	Main CT features at short-term follow-up	Late follow-up, dynamic evolution after hospital discharge	Main CT features at late follow-up
Han <i>et al</i> [9], 2020	Initial deterioration to a peak at the 2 nd week followed by improvement in the 3 rd and 4 th week	GGO decreased from 1 st week to 2 nd week, then increased in 3 and 4. Consolidation and a mixed pattern noted in 2 wk. Crazy paving pattern had the highest frequency in 2 nd week	N/A	N/A
Wang <i>et al</i> [10], 2020	Severe/critically ill group: Opacity volume continued to increase beyond 15 d. Moderate group: Peak on days 13-15 (the opacity density began to drop from day 10 to day 12). Asymptomatic/mild group: Highest opacity volume on days 1-3 and almost resolved after 15 d	GGO in the early stages, followed by appearance of consolidations. In the severe/critically ill group: Decreasing trend of GGO, increasing trend of consolidation over time	N/A	N/A
Liang <i>et al</i> [11], 2020	Total severity score showed an increasing trend in the first 2 wk, followed by a slight decrease in the 3 rd week	GGO was the most common finding over time, consolidation decreased 2 wk after symptom onset. Reticulations and linear opacities and fibrosis became increasing prevalent later in the disease course	N/A	N/A
Sun <i>et al</i> [23], 2021	Improvement in the first 3 wk after hospitalization	Decrease in consolidation and GGO overtime and appearance of fibrous-like stripes	N/A	N/A
Zhou <i>et al</i> [12], 2020	3 stages: Early rapid progressive stage (1-7 d from symptom onset); > advanced stage with peak levels of abnormalities on CT at 8-14 d; > improvement after 14 d (particularly, after 21 d the absorption was more obvious)	GGO, GGO + reticular pattern/consolidation in the rapid progressive stage. ↑ GGO + reticular pattern and consolidation in the advanced stage. ↓ GGO + reticular pattern and consolidation and ↑ subpleural line, bronchus distortion, and fibrotic strips in the absorption stage	N/A	N/A
Wang <i>et al</i> [13], 2020	3 stages: Progression process; > absorption process; > stage of discharge	↑ GGO with consolidation (↑ crazy paving pattern, ↑ vascular thickening sign ↑ air bronchogram sign) in the progression process. Absorption of consolidation displayed as inhomogeneous partial GGOs with fibrosis shadows, occurrence of the fishing net on trees sign, ↑ fibrosis sign, ↑ subpleural line sign in the absorption process. Further absorption of GGOs, consolidation and fibrosis shadows and no appearance of new lesions in the stage of discharge	N/A	N/A
Wang <i>et al</i> [14], 2020	Radiological aggravation (< 2 wk) and improvement (> 2 wk)	GGO decreased while mixed GGO and consolidation increased from 1 wk to 2 wk after onset; linear opacity increased from 2 wk to 3 wk after onset	1-2 mo after symptom onset (median day 38): In 1/3 of cases complete absorption of lesions. Patients with more severe lesions at day 8-14 (> consolidations, CT score > 4, > 3 lobes involved) were more prone to have pulmonary residuals	Mainly linear opacities
Zhang <i>et al</i> [15], 2020	4 stages: Early stage (0-5 d); > peak stage (6-10 d); > absorption stage (11-15 d); > recovery stage (≥ 16 d)	Mainly GGO, (vascular thickening, bronchial wall thickening, and consolidation were also noted) in the early stage. ↑ GGO, vascular and bronchial thickening, and consolidation (mean peak at 8 d) in the peak stage. GGO and consolidation were predominantly present, with ↑ bronchial wall thickening and vascular thickening in the absorption stage. GGO and consolidation were partially absorbed, and bronchial wall thickening and vascular thickening ↓ (residual GGO and subpleural parenchymal bands) in the recovery stage	N/A	N/A
Feng <i>et al</i> [16], 2020	3 stages: Progressive stage (0-5 d); > peak stage (5-15 d). The greatest severity showed	GGO and interlobular/intralobular septal thickening were the most frequent CT manifestation	N/A	N/A

	approximately 7-8 d from onset; > absorption stage (15-30 d)			
Liu <i>et al</i> [17], 2020	N/A	N/A	At 3 wk follow up CT scan: Complete absorption of lesions in more than half of the patients	Gradually decrease of GGO and fibrous stripe (GGO during the first and fibrous stripe the 3 rd week after discharge). "Tinted" sign and bronchovascular bundle distortion
Pan <i>et al</i> [18], 2020	5 stages: 0-3, 4-7, 8-14, 15-21, and > 21 d from symptoms onset (stages A-E, respectively). The total CT score of lung involvement was significantly higher in Stage C. The lung lesions in most patients improved after 14 d since initial symptom onset	Proportion of GGO was similar in each stage, consolidation gradually ↑ from Stage A to C and gradually ↓ from Stage C to E	N/A	N/A
Zhuang <i>et al</i> [19], 2021	Lung involvement peak at approximately 11 d, then lung lesions improved significantly	Mainly GGO in the first scan (0-4 d), crazy-paving pattern and consolidation in scan-2 (4-22 d), lesions were gradually absorbed and tended to be stable and linear opacities were noted in the scan-3 (before discharge, 6-41 d)	1 st CT scan after discharge (22-51 d): Further absorption of lung lesions	Various presentations: negative CT scan, GGO, consolidation, linear opacities
Urciuoli and Guerriero [24], 2020	N/A	N/A	Persistence of lung abnormalities in 5/6 cases even if all the patients completely asymptomatic	Various presentations: 1 negative CT scan; in 2 patients, persistence of mixed pattern (GGO and fibrous streaks); in 1 patient fibrotic stripes, in 1 patient mixed pattern (interlobular septal thickening and patchy GGO); in 1 patient fibrotic pattern
Zhang <i>et al</i> [20], 2020	5 stages: Stage 1 (0-3 d), stage 2 (4-7 d), stage 3 (8-14 d), stage 4 (15-21 d), and stage 5 (22-30 d). PTV peaks at 12 d in common pneumonia, at 17 d in severe pneumonia	Common pneumonia: No significant differences in the PTV, PGV and PCV between stages 1-4 (percent of lesions was reduced in stage 5 compared with stage 4). Severe pneumonia PTV, PGV and PCV ↑ from stage 2 to stage 4 and ↓ in stage 5	N/A	N/A
Pan <i>et al</i> [21], 2020	4 stages: Early stage (0-4 d); progressive stage (5-8 d); peak stage (10-13 d); and absorption stage (≥ 14 d). Peak at 10 d after symptoms onset. CT signs improvement at approximately 14 d	GGO in the early stage, ↑ crazy-paving pattern and consolidation in the progressive stage, consolidation in the peak stage, progressive resolution of consolidation in the absorption stage	N/A	N/A
Wang <i>et al</i> [22], 2020	Lung abnormalities increased quickly after the onset of symptoms, peaked around 6-11 d, and were followed by persistence of high levels in extent for a long duration (slow absorption of the lesions)	GGOs trend: "first falling then rising". Consolidation was the second most common feature seen in the first 11 d. Mixed pattern: The second most predominant pattern since illness days 12-17	N/A	N/A

CT: Computer tomography; GGO: Ground glass opacity; N/A: Not applicable; PCV: Percentage of consolidation volume; PGV: Percentage of ground glass opacity volume; PTV: Percentage of total lesion volume.

wk after discharge. In their analysis, the cumulative percentage of the complete radiological resolution was 8%, 42%, 50% and 53% at discharge and during the 1st, 2nd and 3rd week after discharge, respectively[17].

Wang *et al*[14] conducted a study including both common and severe pneumonia, showing that approximately 1/3 of cases had complete absorption of lesions in the first 1-2 mo after symptom onset (median day 38). In their study, patients with more severe lung involvement at days 8-14 (peak) were more prone to have pulmonary residuals.

Urciuoli and Guerriero[24] considered a longer follow-up, with the study of CT up to 4 mo after the onset of the symptoms; the sample of this report was relatively small, as it considered only 6 patients with mild pneumonia. Interestingly, the follow-up CT scan revealed the persistence of lung abnormalities in 5 cases out of 6, even if all patients were completely asymptomatic at that point[24].

CT scan features of lung lesions at follow-up

The main features of lung lesions in the retrieved reports were multiple, bilateral, with a peripheral subpleural distribution.

In the short-term follow-up some features recurred. Consolidations and GGOs were always described, and often a mixed pattern was noted. Consolidations were more frequent during the peak, sometimes with accompanying signs such as a “crazy paving pattern” or “vascular thickening sign;” after the peak, they were gradually absorbed.

GGOs were described mainly in the early phase, but they could be observed also in later stages. In fact, in the report from Pan *et al*[18] the proportion of GGOs was similar in each stage. In those from Wang *et al*[22], the observed trend of GGOs was described as “first falling then rising” as they were present both in the first phase and in the last CT scan.

After the peak, besides GGOs, repairing CT signs, such as linear opacities, fibrous stripes, subpleural line sign and fibrosis shadows, were noted. Wang *et al*[13] proposed, in the absorption process, a particular sign called “fishing net on trees.” This sign “indicated that the pulmonary lesions were in the stage of obvious absorption but not complete absorption. CT showed that the large area of consolidation was reduced, the density was reduced, the edge had shrunk, and there were significantly more bands and incomplete absorption of fibrosis shadows. The area was similar to a fishing net hanging on a branch that was not fully spread under the background of the increased bronchovascular bundle”[13].

In the longer-term follow-up, CT scans showed various presentations. Zhuang *et al* [19] observed in the first CT scan after discharge further absorption of the lung lesions. Also, GGOs, consolidations and linear opacities were still found in some patients. In the case series of Urciuoli and Guerriero[24], 2 patients presented persistence of a mixed pattern with GGO and fibrous streaks, 1 patient fibrotic stripes, 1 patient a mixed pattern with interlobular septal thickening and patchy GGOs and 1 patient fibrotic pattern[24].

Wang *et al*[22], who followed the CT scan until 4 wk after discharge, found mainly linear opacities. Liu *et al*[17] still observed in some patients GGOs and fibrous stripes even at the 3 wk radiological follow-up, even with a decreasing trend (GGO during the 1st week and fibrous stripes during the 3rd wk). Two additional signs were found during the evolution: “tinted” sign and bronchovascular bundle distortion. The “tinted” sign was demonstrated to coincide with an extension of the GGO area and a decrease in its density. According to the authors, the appearance of this pattern probably implied the gradual resolution of inflammation with re-expansion of alveoli. The bronchovascular bundle may be caused by inflammatory distraction or subsegmental atelectasis[17].

DISCUSSION

Current evidence of the temporal evolution of COVID-19 pneumonia derives from studies evaluating a relatively short follow-up period, and data about long-term radiological (and clinical) sequelae are still awaited[17,22,25,26]. The hallmark of early COVID-19 pneumonia includes bilateral, peripheral GGOs and consolidation often showing features resembling organizing pneumonia, such as a perilobular distribution and “reversed halo” sign (*i.e.* a focal, rounded area of ground-glass surrounded by a ring or arc of denser consolidation)[27,28]. These findings are non-specific and variably comprise foci of edema, organization and diffuse alveolar damage that are not too far removed from patients with other acute injuries, even noninfectious[29,30]. Notably, up to 56% of patients have been reported to demonstrate no abnormalities in the first 3 d after onset of symptoms, while conversely patients with no symptoms may show abnormal CT findings[31]. Moreover, still in the initial phase of the disease, pulmonary opacities may be unilateral and lack the characteristic peripheral distribution, possibly reducing diagnostic confidence in differentiating COVID-19 from potential mimickers such as heart failure and other infections[21,32].

The severity of acute COVID-19 manifestations is likely to peak within 2 wk from the disease onset, though reported temporal evolution varies depending on the studied population[12,13,18,21,31]. In this phase, patients may show an increasing extent of pulmonary consolidation, which parallels lung injury evolution. With the awareness of the heterogeneous studies included in the present analysis and intrinsic individual variation of the disease course, patients have been found to enter the so-called absorption stage roughly 14 d from the disease onset[12,13,18,21]. During this

period, consolidation tends to wane, while other findings such as linear opacities, parenchymal bands and reticulation possibly emerge, sometimes leading to a “fibrotic-like” appearance[26]. Even in this last case, it remains unclear whether residual abnormalities truly represent irreversible disease or will solve over time as no studies with a follow-up period greater than 6 mo have been performed so far[26,33]. Remarkably, most studies examined CT patterns in isolation at various time points rather than temporal changes of each pulmonary finding, providing valuable information about the overall disease evolution but missing the opportunity to examine regional linkages between patterns. Future studies are needed to explore how underlying pathogenetic pathways such as diffuse alveolar damage and an auto-inflammatory response would determine imaging features of COVID-19. In this regard, the role of baseline risk factors such as vascular thrombosis and interstitial lung abnormalities remains poorly investigated.

Besides providing clues to assess COVID-19 morphological changes, CT has been used to enrich clinical and laboratory findings to quantify disease severity in the acute setting and longitudinal evolution[12,18,21]. Various methods have been employed to assess CT lung involvement in COVID-19, including qualitative, semi-quantitative and software-based quantitative scoring systems[12,18,21,34-37]. In the included works, most CT scores were based on semi-quantitative methods, while only two studies used artificial intelligence techniques. Several parameters such as symptoms, oxygenation status and laboratory measures of infection and inflammation have been found to correlate with parenchymal involvement at CT, highlighting the potential role of imaging in predicting the clinical course of COVID-19 and optimizing patient care[38-40]. However, further evidence is needed to demonstrate CT scoring usefulness to manage COVID-19 and its actual impact on clinical decision-making in the acute and follow-up setting.

Clinical compendium: Pulmonary sequelae of COVID-19

The clinical counterpart of long-term radiological outcomes of COVID-19 pneumonia is a topic of growing interest. After the first wave of COVID-19, the awareness of patients suffering from residual symptoms, persistent beyond the acute phase of the disease, became very common, leading to the description of a post-COVID syndrome or Long-COVID[41]. However, the type and severity of respiratory impairment or functional sequelae are still unknown.

The current knowledge gained from the previous coronavirus outbreaks (SARS-CoV-1 in 2002-2004 and Middle East respiratory syndrome coronavirus in 2012) and the general understanding about outcomes in the acute distress respiratory syndrome suggest that some COVID-19 survivors might experience impaired lung function and exercise limitation, and some of them develop interstitial lung disease in the mid-long term[42-44].

Up until recently, only a few retrospective studies, including small samples, showed that patients might experience a reduction of forced vital capacity (13 patients at 6 wk) [45] and of forced vital capacity, forced expiratory volume in the first second, total lung capacity (TLC) and diffusion lung carbon monoxide (DLCO) (55 patients at 3 mo) [46].

In one of the largest cohorts studied to date describing the medium-term consequences of the infection (767 patients, follow-up at median time of 81 d after discharge), 51.4% of the patients reported being still symptomatic, with fatigue (55.0%), exertional dyspnea (45.8%) and post-traumatic psychological consequences (30.5%) as the most reported symptoms. Impaired lung function was found in 19% of the patients (reduced DLCO with or without restrictive pattern)[47].

Anastasio *et al*[48] recently published a study on 379 patients evaluated 4 mo after the diagnosis of COVID-19. Almost 69% of the patients reported almost one residual symptom. Patients who had pneumonia showed lower SpO₂ at rest and during the six-minute walking test and TLC compared with patients without prior pneumonia. Furthermore, the authors found an association between SpO₂/FiO₂ ratio and the pneumonia severity index during the acute phase, and mid-term alteration in SpO₂ at rest and during six-minute walking test, TLC, residual volume and forced vital capacity[48].

In an Italian study with 238 patients enrolled, DLCO was reduced less than 80% of the predicted value in more than half of the patients at 4 mo follow-up, and in 15.5% of the cases were less than 60%. More than 50% of the patients showed functional impairment assessed with Short Physical Performance Battery and 2-minute walk test [49].

In another large cohort of 647 patients evaluated at 3 mo follow-up, patients reported ongoing symptoms, in particularly fatigue (13%), palpitation (10%) and

dyspnea (9%). Those symptoms were significantly higher in patients who experienced severe COVID-19 compared to non-severe patients. In this cohort, only 81 patients were assessed with lung function test. More than half of the patients showed reduced DLCO. Similarly to symptoms, an impaired DLCO was more frequently associated with severe cases than non-severe (68% *vs* 42%). On a multivariate analysis, a CT total severity score > 10.5 and acute distress respiratory syndrome were significantly associated with impaired DLCO[50].

Similar results were found in a smaller cohort of 22 patients at 3 mo follow-up. Furthermore, on multivariate analysis, low TLC was associated with the need for mechanical ventilation and low forced expiratory volume in the first second with a high APACHE II score[51].

In a cohort of 119 patients who survived severe COVID-19 evaluated at 2 mo after discharge, respiratory symptoms (breathlessness 32%, cough 7%) were less frequent than persistent fatigue (68%), sleep disturbance (57%), anxiety and depression (22% and 18%, respectively) and post-traumatic stress disorder (25%). Despite radiological resolution in 87% of the patients, 41% reported persistent limitations in everyday life, and 44% had a Modified British Medical Research Council Questionnaire grade above the pre-COVID19 baseline[52]. A similar study on 134 patients found breathlessness as the most commonly reported symptoms (68%) followed by myalgia (51.5%), extreme fatigue (39.6%), low mood (37.3%) and sleep disturbance (35.1%)[53].

Long-term follow-up will help understand the impact of COVID-19 pneumonia on lung pathophysiology. Therefore, it is advisable to schedule serial follow-up in patients that still present lung function impairment or exercise limitation.

CONCLUSION

At present, the available literature focus on the acute phase of radiological follow-up of COVID-19 pneumonia and describes well-defined stages in the first few weeks after the onset of the symptoms.

The most common finding seems to be a peak of lung involvement reached roughly within the first 2 wk, characterized mainly by the growth of GGOs and consolidations. After that peak, these manifestations are gradually absorbed, and repairing signs, such as linear opacities, fibrous stripes, subpleural line sign and fibrosis shadows, tend to appear.

When considering later follow-up, up to 4 mo, lesions are usually not completely absorbed. A longer follow-up is definitely needed, especially to check whether the later signs are reversible and how they affect patients' conditions. Following CT scan evolution over time could help physicians better understand the clinical impact of COVID-19 pneumonia and manage the possible sequelae.

ARTICLE HIGHLIGHTS

Research background

Pneumonia is the main manifestation of severe acute respiratory syndrome coronavirus 2 infection. Chest computed tomography is an effective way to detect and keep track of coronavirus disease 2019 pneumonia cases over time.

Research motivation

As of now, few studies evaluated serial computed tomography scan temporal changes during the course of severe acute respiratory syndrome coronavirus 2 pneumonia.

Research objectives

This systematic review describes the dynamic evolution of coronavirus disease 2019 pneumonia, considering the available literature on this topic.

Research methods

A systematic review according to PRISMA guidelines was performed. Pertinent keywords on PubMed were used.

Research results

Different and well-defined stages characterized the first few weeks after the onset of

the symptoms.

Research conclusions

A peak of lung involvement within the first 2 wk, followed by the gradual absorption of the lesions and the advent of repairing signs was observed. Later follow-up showed that lesions were usually not completely absorbed, at least up to 4 mo.

Research perspectives

Longer follow-up is needed to check whether the later signs are reversible and how they affect patients' conditions.

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