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COVID-19: Correlation between HRCT findings and clinical prognosis and analysis of parenchymal pattern evolution

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ABSTRACT

Objectives: Severe acute respiratory syndrome - coronavirus 2 (SARS-CoV-2) is a single-stranded positive ribonucleic acid virus of the coronaviridae family. The disease caused by this virus has been named by the World Health Organization coronavirus disease 19 (COVID-19), whose main manifestation is interstitial pneumonia. Aim of this study is to describe the radiological features of SARS-CoV-2 infection in its original form, to correlate the high-resolution computed tomography (HRCT) patterns with clinical findings, prognosis and mortality, and to establish the need for treatment and admission to the intensive care unit.

Material and Methods: From March 2020 to May 2020, 193 patients (72 F and 121 M) who were swab positive for SARS-CoV-2 were retrospectively selected for our study. These patients underwent HRCT in the clinical suspicion of SARS-CoV-2 interstitial pneumonia.

Results: Our results confirm the role of radiology and, in particular, of chest HRCT as a technique with high sensitivity in the recognition of the most peculiar features of COVID-19 pneumonia, in the evaluation of severity of the disease, in the correct interpretation of temporal changes of the radiological picture during the follow-up until the resolution, and in obtaining prognostic information, also to direct the treatment.

Conclusion: Chest computed tomography cannot be considered as a substitute for real-time - polymerase chain reaction in the diagnosis of COVID-19, but rather supplementary to it in the diagnostic process as it can detect parenchymal changes at an early stage and even before the positive swab, at least for patients who have been symptomatic for more than 3 days.

Keywords: Respiratory disease, Coronavirus disease 19, Severe acute respiratory syndrome - coronavirus 2, Radiology, Chest imaging, Computed tomography

INTRODUCTION

In the city of Wuhan in China, an epidemic by a new virus of unknown origin responsible for a new severe acute respiratory disease spread in December 2019.[1] On December 31, 2019, the Chinese health authority alerted the World Health Organization (WHO) for several cases of

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pneumonia of unknown etiology in Wuhan city[1] and on January 7, 2020, this virus was sequenced for the first time from the sample obtained from a patient's nasopharyngeal swab.[2] This virus was called Severe acute respiratory syndrome - coronavirus 2 (SARS-CoV-2), a positive single-stranded ribonucleic acid virus,[3] a member of the family coronaviridae, order nidovirales, and genus betacoronavirus. The disease caused by this virus has been named coronavirus disease 19 (COVID-19) by WHO.[4,5]

COVID-19 in its different variants that have emerged over the years has proven to be a highly contagious infectious disease, transmissible directly and indirectly, mainly through the respiratory droplets emitted by a symptomatic or asymptomatic infected patient. Mortality rate is variable depending on the patient and the different geographical distribution. The virus has a widespread tropism with greater predilection for the lower respiratory tract.[6,7] Clinical manifestations of SARS-CoV-2 infection present similarities with those determined by infection by the SARS-CoV virus, where the most common symptoms are fever (88% of cases), cough with or without sputum (57%), dyspnea (45%), ageusia and anosmia (40%), muscle pain and/or fatigue (27%), headache (14%), sore throat (10%), and gastrointestinal symptoms (9%).[6,7] Although the clinical picture is variable, non-specific, and shows great diversity in terms of disease severity and evolution, interstitial pneumonia is the predominant clinical manifestation of COVID-19.

Radiology plays a key role in the diagnosis, management, and follow-up of this disease, although X-ray and high-resolution computed tomography (HRCT) findings may vary depending on patient age, disease progression, immune status, comorbidities, and medical treatment.[8] The gold standard diagnosis is based on molecular nasopharyngeal swab, specifically real-time - polymerase chain reaction (RT-PCR) which amplifies a specific genetic sequence in the virus.[9]

Aim of our study was to describe the radiological features of SARS-CoV-2 infection in its original form, to correlate the HRCT patterns with clinical findings, prognosis and mortality, and to establish the need for treatment and admission to the intensive care unit (ICU). Moreover, we also evaluated the evolution of the parenchymal HRCT findings at short and medium time (45–90 days, respectively) from the COVID-19 diagnosis by nasopharyngeal swab.

MATERIAL AND METHODS

From March 2020 to May 2020, 193 patients (72 F and 121 M with a mean age of 63.6 years old, range 24–96 years) who were swab positive for SARS-CoV-2 were retrospectively selected for our study. These patients accessed the radiology department of santa maria delle croci hospital in ravenna, Italy, where they underwent HRCT in the clinical suspicion of SARS-CoV-2 interstitial pneumonia.

Chest HRCT was performed using a 64-layer computed tomography (CT) (Philips diamond select brilliance®) with the following acquisition parameters: - 100 kV for patients with body mass index (BMI) <19 kg/m^2, 120 kV for patients with BMI 19–24 kg/m^2, 140 kV for patients with BMI > 24 kg/m^2; - rotation speed: 0.75; - layer thickness: 1 mm. Study protocol for all patients was as follows: Patient in supine position, with the body in the center of the patient table and both arms raised above the head – those who had difficulty raising their arms left them along the sides of the body. Scanned area extended from the pulmonary apex to a plane under the base of the diaphragm.

All first 193 HRCT of the 193 swab-positive patients performed from March to May 2020 were retrospectively analyzed by a single radiologist (SGP), blinded to identity, and anamnestic data of all the patients. Subsequently, 57 follow-up HRCTs (second and/or third control CT) performed from April to September 2020, at least 45 days after the first CT examination, were retrospectively analyzed by the same radiologist. In both cases, the presence/absence of interstitial pneumonia was indicated and, in case of presence, the different patterns of interstitial pneumonia were reported.

The results obtained from CT images analysis were compared with data in the literature, especially with a recent review and a meta-analysis including a total of 52 studies. The two main papers we compared with showed that pulmonary involvement is more often bilateral (78.22%, 95% CI: 45–100%) and that most alterations have peripheral distribution (65.35%, 95% CI: 25.93–100%), followed by peripheral + central (31.12%, 95% CI: 1.96–74.07%) and central distribution (3.57%, 95% CI: 0.99–9.80%).[10,11]

The more frequent CT finding related to COVID-19 interstitial pneumonia was ground-glass opacity (GGO), which Salehi *et al*. found in 88% of cases.[11,12] In agreement with the meta-analysis and the more recent review, GGOs are the most frequent finding (58.05%, 95% CI: 16.67–100%), followed by GGO + parenchymal consolidation (52.99%, 95% CI: 19.05–76.79%) and parenchymal consolidation only (44.18%, 95% CI: 1.61–71.46%). In fact, GGO and parenchymal consolidation were reported in 94.5% (52/55) of the studies.[10] Other alterations reported in literature were: Crazy paving (23.57%, 95% CI: 3.13–91.67%), interlobular septa thickening (22.91%, 95% CI: 0.90–80.49%), pleural effusion (11.09%), and ilo-mediastinal lymphadenopathies (4.86%).[10]

Data analysis

All data collected during patient enrollment were transferred to a database on the Microsoft® Excel program. Anamnestic data collected were: Age, comorbidities, immune status,

and epidemiology as established or possible contact with SARS-CoV-2 positive subjects, symptomatology, and time interval from onset of symptoms. The time from symptom onset and HRCT was highly variable, ranging from 1 day to more than 10 days. The presence/absence of following CT signs suspicious for interstitial pneumonia was reported: GGO, parenchymal consolidation, crazy-paving, interstitial septa thickening, vascular tree-in-bud with or without associated efferent arterial vascular enlargement, and pleural effusion. In addition, the distribution of the CT signs was defined: Whether unilateral or bilateral, central, peripheral or diffuse, upper/lower lobes, or equally distributed.

The parenchymal involvement and the disease staging is generally evaluated using one of the CT severity score proposed in the international literature.[12-15] We preferred to report the total severity score (TSS) proposed by Li *et al*.[13] This score is calculated by giving each pulmonary lobe affected by the infectious process a value from 0 to 4 based on the percentage of parenchymal involvement: 0 = No involvement to a lobe (0%), 1 = minimal involvement to a lobe (1–25%), 2 = mild involvement to a lobe (26–50%), 3 = moderate involvement to a lobe (51–75%), and 4 = severe involvement to a lobe (76–100%) for a total of five lobes (right upper lobe, right lower lobe, middle lobe, left upper lobe + lingula, and left lower lobe). The overall score represents the sum of all five lung lobes scores, with a maximum of 20/20.[13]

Based on Li's score, and many others found in the international literature, the severity of lung involved on CT scan could be classified on a 4-point ordinal scale: Grade 0 corresponding to a score of 0 (no abnormality present on CT), Grade 1 score of 1–5, Grade 2 score of 6–10, Grade 3 score of 11–15, and Grade 4 score of 16–20.[16] For our study, we decided to use this 4-point grading system for the data analysis and in annexed tables.

RESULTS

The first HRCT: Findings and prognosis

Of the total of 193 patients enrolled in the study, 190 (98.4%) showed CT signs of interstitial pneumonia and only 3 patients (1.6%) showed no suggestive parenchymal alterations.

In the 190 patients with pulmonary COVID lesions, bilateral pulmonary involvement was demonstrated in 188/190 cases (98.9%), while in 2 patients (1.1%), it was unilateral, in line with what has been reported in the literature [Table 1].

A predominant distribution of parenchymal lesions to the lower lobes was demonstrated in 105/190 patients (55.3%), in 72/190 patients (37.9%) an equal distribution between upper and lower lobes and in 13/190 patients (6.8%) only to the upper lobes: These data were also consistent with those described in the literature [Table 1].

Table 1: HRCT findings distribution in the first computed tomography: Distribution of parenchymal alterations in terms of uni or bilateral involvement, lobar (lower lobes, upper lobes or equally to upper and lower lobes), and parenchymal localization (peripheral, peripheral, and central or diffuse).

HRCT findings distribution	*n*/N	%
Bilateral	188/190	98.9
Unilateral	2/190	1.1
Peripheral	112/90	59
Peripheral and central	77/190	40.5
Diffuse	1/190	0.5
Upper lobe	13/90	6.8
Lower lobe	105/190	55.3
Equal (upper and lower lobes)	72/190	37.9

HRCT: High-resolution computed tomography

Moreover, 112/190 patients (59%) showed a prevalent peripheral localization, 77/190 patients (40.5%) a peripheral + central localization, and 1/190 patients (0.5%) a diffuse distribution, without intervals of portions of healthy parenchyma or with portions of healthy parenchyma between the areas of lung alteration lower than 10% [Table 1].

Subsequently, different parenchymal lesions suggestive of interstitial pneumonia were analyzed, according to those most frequently reported in the literature (GGO, parenchymal consolidation, crazy-paving, interstitial thickening, vascular tree-in-bud with or without associated vascular enlargement, small airway abnormalities – such as bronchiectasis – and pleural effusion).

Based on the extent of the described alterations, parenchymal involvement was staged using the 4-point grading system reported and described in "Data analysis" section.[16]

Analyzing the first 193 HRCT and specially those of the 190 patients with specific CT findings, it was noted: GGO in 176/190 patients (92.6%), parenchymal consolidation in 65/190 patients (34.2%), GGO + parenchymal consolidation in 113/190 patients (59.5%), crazy-paving in 113/190 patients (59. 5%), interstitial thickening in 61/190 patients (32%), vascular tree-in-bud in 146/190 patients (76.8%), of which 100/146 patients (68.4%) with and 46/146 patients (31.6%) without associated arterial enlargement >3 mm, and in 17/190 patients (7.4%) pleural effusion (five of 14 cases bilateral, in 35% of cases) [Table 2].

TSS was calculated for each patient, resulting Grade 1 in 62/190 patients (32.6%) [Figure 1], Grade 2 in 81/190 patients (42.6%) [Figure 2], Grade 3 in 40/190 patients (21%) [Figure 3], and Grade 4 in 7/190 patients (3.8%) [Figure 4].

Finally, we should also mention the three patients without any type of parenchymal alteration suggestive of interstitial

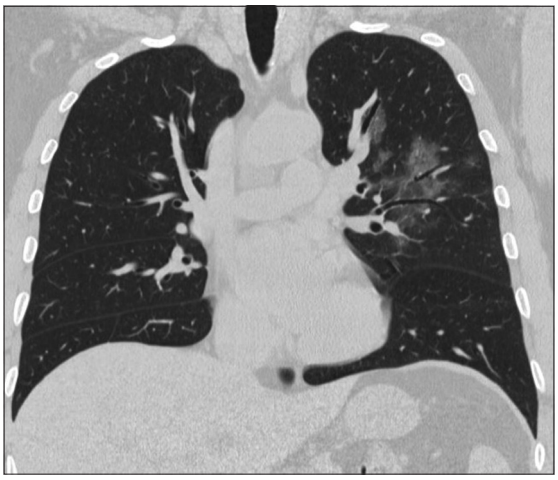

Figure 1: A 47-year-old man with coronavirus disease 19 pneumonia who presented with dyspnea and fever. High resolution computed tomography (CT) image on coronal plane shows crazy paving and ground-glass opacity with central distribution in the upper left lobe and in the lingula, with CT total severity score Grade 1.

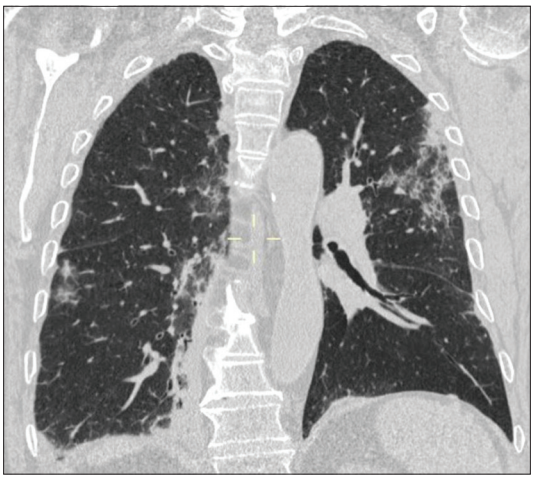

Figure 2: A 68-year-old man with coronavirus disease 19 pneumonia who presented with dyspnea and fever. High resolution computed tomography (CT) image on coronal plane shows bilateral ground-glass opacity with peripheral distribution, with interstitial thickening and parenchymal consolidation in the upper left lobe, with CT total severity score Grade 2.

Table 2: Frequency of the computed tomography findings specific for interstitial pneumonia analyzed in the first 190 HRCTs.

HRCT Specific findings	*n*/N	%
GGO	176/190	92.6
Consolidation	65/190	34.2
GGO+consolidation	113/190	59.5
Crazy paving	113/190	59.5
Interstitial thickness	61/190	32
Vascular tree-in-bud	146/190	76.8
(with vascular enlargement >3 mm)	100/146	68.4
(without vascular enlargement)	46/146	32.6
Pleural effusion	17/190	55.3

HRCTs: High-resolution computed tomographies, GGO: Ground-glass opacity

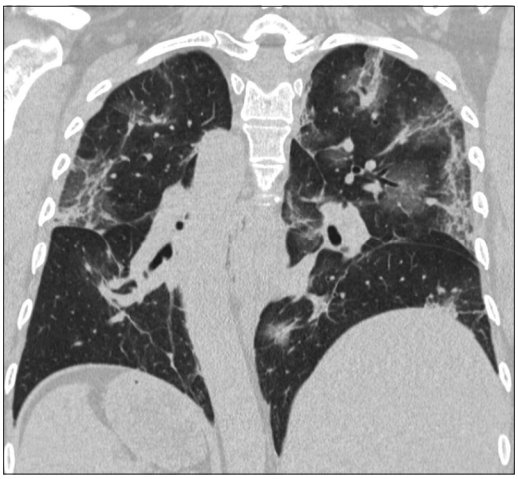

Figure 3: A 57-year-old woman with coronavirus disease 19 pneumonia who presented with severe dyspnea and fever. High resolution computed tomography (CT) image on coronal plane shows diffuse bilateral ground-glass opacity and interstitial thickening, especially in the upper lobes, with crazy paving pattern, with CT total severity score Grade 3.

pneumonia and therefore with TSS Grade 0, with 0% involvement of the global lung parenchyma.

In terms of prognosis, it was observed that 15/190 patients (7.9%) required.

ICU care and admission for respiratory support by assisted mechanical ventilation and other medical therapies, and 30/190 patients (15.8%) died with CT signs of interstitial pneumonia. Of the 30 patients who died, 10 were admitted to the ICU while the remaining 20 were admitted to other departments of the same hospital.

The 15/190 patients admitted to the ICU had the following features: 10 M and 5 F, age ranging from 50 to 96 years (mean 69.5 years), most without comorbidities (8/15, 56.7%), 5 patients (30%) with <2 comorbidities and only 2 patients (13.3%) with more than 2 comorbidities. Of these 15 patients, the TSS calculated was: Grade 1 in 3/15 patients (20%), Grade 2 in 3/15 patients (20%), Grade 3 in 6/15 patients (40%), and Grade 4 in 3/15 patients (20%).

The 30/190 patients (7.9%) who died with CT signs of interstitial pneumonia showed the following features: 22 M and 8 F, age ranging from 39 to 96 years (mean age 74.2 years), of whom 8/30 (26.6%) had no comorbidities, 14/30 (46.6%) had <2 comorbidities and 8/30 (26.6%) had more than 2 comorbidities.

Of these 30 patients, TSS observed was: Grade 1 in 9/30 patients (30%), Grade 2 in 7/30 patients (23.3%), Grade 3 in 11/30 patients (36.7%), and Grade 4 in 3/30 patients (10%).

Follow-up HRCT: Findings and prognosis

We examined how many patients who underwent a first HRCT with interstitial pneumonia diagnosis underwent follow-up CT scans, considering both the time interval since the first examination and the evolution of the parenchymal pattern. All the follow-up HRCTs performed at least 45 days after the first one were considered, assigning a numerical value for each interval: Interval of 45–60 days from the first CT examination (interval 1), of 61–75 days (interval 2), of 76–90 days (interval 3), of 91–105 days (interval 4), and of 106–120 days (interval 5), >120 days (interval 6).

Of the 190 patients who underwent an initial HRCT, 57 patients (30%) had at least one follow-up CT examination at a distance of at least 45 days: 6/57 (10.5%) during interval 1, 7/57 (12.3%) in the interval 2, 7/57 (12.3%) in the interval 3, 4/57 (7%) in the interval 4, 16/57 (28.1%) in the interval 5, and 17/57 (29.8%) during interval 6. Prognostically, 1/57 patients were admitted to the ICU and three died.

We then analyzed the main findings suggestive of interstitial pneumonia, including all those considered in the baseline HRCT and adding the presence of any fibrotic outcomes to be related to the evolution of the disease and any residual parenchymal damage. This analysis showed that: 26/57 (45.6%) patients were completely healed – without evidence of any parenchymal alterations – and 31/57 (54.4%) patients still had parenchymal alterations.

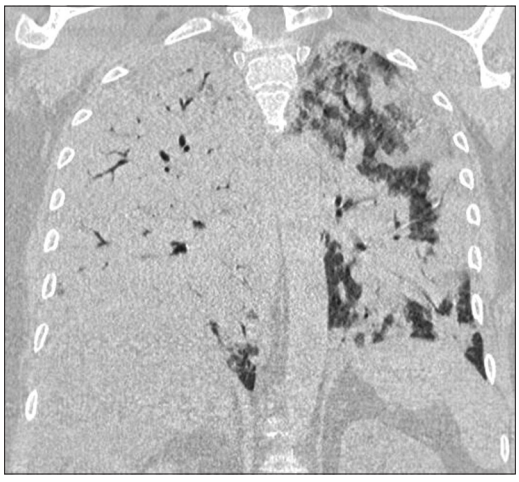

Figure 4: A 63-year-old woman with coronavirus disease 19 pneumonia who presented with severe dyspnea and fever. High resolution computed tomography (CT) image on coronal plane shows bilateral parenchymal consolidation occupying >75% of lung parenchyma, with CT total severity score Grade 4.

In the 31 patients with parenchymal alterations, it was observed that 28 patients (90.3%) showed bilateral lung involvement and only 3 patients (9.7%) unilateral, that 21/31 patients (67.7%), showed a predominance of lesions in the lower lobes, 10/31 patients (32.3%) an equal distribution between upper and lower lobes and no patients (0%) in the upper lobes. In addition, 25/31 patients (80.6%) had a peripheral localization, 6/31 patients (19.4%) peripheral + central, and no patient (0%) a diffuse distribution (without intervals of portions of healthy parenchyma or with portions of healthy parenchyma between areas of lung alteration <10%). The observed results, consistent with the international literature, are shown in [Table 3].

As specific findings, we reported: In 20/31 patients (64.5%) GGO, in 5/31 patients (16.1%) areas of parenchymal consolidation, in 3/31 patients (9.7%) areas of GGO plus areas of parenchymal consolidation, in 1/31 patients (3.2%) crazy-paving, in 21/31 patients (67.7%) interstitial thickening, and in 21/31 patients (67.7%) fibrosis [Table 4].

Furthermore, in this case, the TSS was calculated for each patient undergoing follow-up HRCT: 26/57 patients (45.6%) were classified as Grade 0 – they were radiologically healed, 19/57 patients (33.3%) as Grade 1, 9/57 patients (15.7%) as

Table 3: HRCT findings distribution in follow-up computed tomography: Distribution of parenchymal alterations in terms of uni or bilateral involvement, lobar (lower lobes, upper lobes, or equally to upper and lower lobes), and parenchymal localization (peripheral, peripheral, and central or diffuse).

HRCT Findings distribution	*n*/N	%
Bilateral	28/31	90.3
Unilateral	3/31	9.7
Peripheral	25/31	80.6
Peripheral and central	6/31	19.4
Diffuse	0/31	0
Upper lobe	0/31	0
Lower lobe	21/31	67.7
Equal (upper and lower lobes)	10/31	32.3

HRCT: High-resolution computed tomography

Table 4: HRCT findings specific for interstitial pneumonia analyzed in the follow-up computed tomography, in the 31 patients that still presented parenchymal alterations.

HRCT Specific findings	*n*/N	%
GGO	20/31	64.5
Consolidation	5/31	16.1
GGO+consolidation	3/31	9.7
Crazy paving	1/31	3.2
Interstitial thickness	21/31	67.7
Fibrosis	21/31	67.7

HRCT: High-resolution computed tomography, GGO: Ground-glass opacity

Grade 2, 2/57 patients (3.6%) Grade 3, and 1/57 patients (1.8%) as Grade 4.

HRCT comparison and parenchymal pattern evolution

We compared the results of CT image analysis of the first and subsequent HRCT, which showed: 48/57 patients (84.1%) improved from a higher to a lower TSS, 6/57 patients (10.6%) showed the same TSS, and 3/57 patients (5.3%) worsened from a lower to a higher TSS.

In the 48 patients who became better, it was observed that this data were independent of the time at which the follow-up examination was performed. In part, the data were also independent of the initial global score value, although more frequent improvement was noted in patients whose initial TSS was grade 1 and/or 2.

In particular: 14/48 patients (29.2%) went from a Grade 1 to 0, 10/48 patients (20.8%) went from a grade 2 to 0, 9/48 patients (18.8%) went from a Grade 2 to 1, 2/48 patients (4.2%) went from a Grade 3 to 0, 8/48 patients (16.6%) went from a Grade 3 to 1, 4/48 patients (8.3%) went from a Grade 3 to 2, and only one patient classified as a Grade 4 (2.1%) improved to a Grade 2. These results are explained more schematically in [Table 5] and visually showed in [Figure 5].

A total of 6/57 patients (10.6%) had shown no changes in the TSS from the initial one: 2 patients (33.3%) with a Grade 1, 3 patients (50%) of 2, and 1 patient (17.7%) of 4. Finally, we presented the 3/57 patients (5.3%) who worsened by moving from a lower to a higher TSS [Figure 6]: 1 patient (33.3%) moved from Grade 1 to 2, 1 patient from Grade 1 to 3, and 1 patient from Grade 2 to 3.

DISCUSSION

It is now evident that the SARS-CoV-2 virus infection in its original form has a particular tropism for the lower respiratory tract, specifically the lungs, through a pathogenetic mechanism determined by a severe autoimmune response with an important cytokine cascade and associated vasculitic and microthrombotic phenomena. All this determines as a predominant clinical manifestation the onset of interstitial pneumonia.

The diagnosis is based on the combination of epidemiological, clinical and radiological data, and on the results of the RT-PCR test, considered the diagnostic gold standard.[9] Although RT-PCR is highly specific, CT has a higher sensitivity in the diagnosis of SARS-CoV-2 interstitial pneumonia and therefore may play a key role in the diagnosis and treatment of the disease.[14,17,18]

By analyzing our case series, we were able to define tomographically the features of SARS-CoV-2 interstitial pneumonia both in terms of localization and predominance of lesions and for the evolution of the CT picture over time by subsequent controls.

From the analysis of the images of the first group of 193 patients with SARS-CoV-2 positive swab and undergoing the first HRCT, it was observed that 190 patients (98.4%) showed alterations in the CT picture compatible with interstitial pneumonia. In these 190 patients, it was noted that the distribution of alterations was predominantly

Table 5: Schematic representation of the reduction of the total severity score between the first HRCT and follow-up HRCT of the 48 improved patients.

Total severity score grading	*n*/N	%
1–0	14/48	29.2
2–0	10/48	20.8
2–1	9/48	18.8
3–0	2/48	4.2
3–1	8/48	16.6
3–2	4/48	8.3
4–0	0/48	0
4–1	0/48	0
4–2	1/48	2.1
4–3	0/48	0

HRCT: High-resolution computed tomography

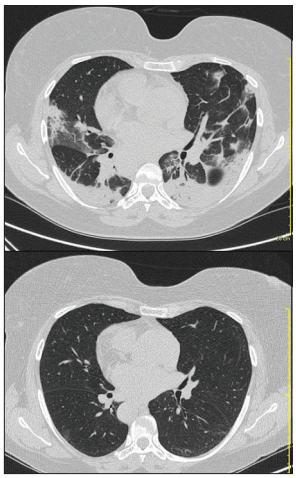

Figure 5: A75-year-old woman with coronavirus disease 19 pneumonia who presented with severe dyspnea and fever. High resolution computed tomography image on axial plane shows improvement after 120 days with total severity score reduction from Grade 3 (upper figure, showing consolidation + crazy-paving) to Grade 1 (lower figure, showing interstitial thickening).

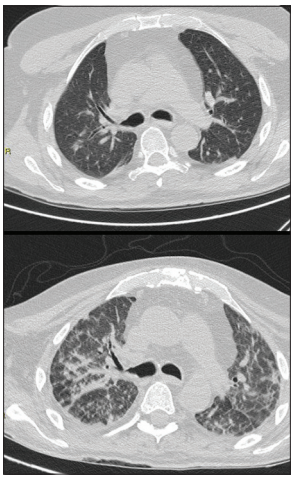

Figure 6: A 65-year-old man with coronavirus disease 19 pneumonia who presented with severe dyspnea and fever. High resolution computed tomography image on axial plane shows worsening after 130 days with total severity score increased from Grade 1 (upper figure, showing ground-glass opacity and interstitial thickening) to 3 (lower figure, showing nodular and linear consolidations + interstitial thickening + fibrosis).

bilateral (98.9%) at the lower lobes (55.3%) and peripheral (59%), according with international scientific literature.

In addition, in these 190 patients it was observed that the most frequent alteration was GGO (92.6%), followed by the copresence of GGO plus areas of consolidation (59.5%) and crazy-paving (59.5%), parenchymal consolidation (34.2%), and interstitial thickening (32%): Furthermore, these results showed a high correspondence with the data expressed in the scientific literature, with the only exception for the crazy-paving alteration that in our case series was shown to be the second most frequent alteration at the expense of pulmonary consolidation, in disagreement with what expressed in many scientific papers.

In this group of patients, we also observed a high percentage of vascular tree in bud (76.8%), that is, an associated arterial vascular enlargement >3 mm indicative of a vasculitic and microthrombotic pathogenetic process determined by the viral infection: This result is also consistent with the scientific literature.[19-23]

Even in our case series, it is confirmed that as the disease progresses the number of lesions can rapidly increase extending to central parenchymal areas and evolving from one type of alteration to another, that is, from GGO alone to GGO with or without crazy-paving up to true areas of parenchymal consolidation, with consequent progression of the TSS. In fact, consistently with the literature data, even in our case series, it has been observed that the highest grades[3,4] are mainly featured by crazy-paving alterations and diffuse areas of parenchymal consolidation.

These observations lead us directly to the prognostic data, which are influenced by multiple variables, easily assessable such as age, associated risk factors, comorbidities, immunodepression, or difficult to assess such as the subjective immune response of each patient. Basing on these variables, we confirmed that patients with multiple risk factors and comorbidities had a higher grade of TSS with a worse prognosis, in fact, 60% of patients admitted to the ICU were staged as grade of 3 or 4.

The most complex data in the elaboration of the results was about prognosis in terms of mortality, since, in addition to the mentioned variables, it is also necessary to consider the time interval elapsed before the patients came to medical attention, clinical manifestations, and therapy which they were subjected.

From this analysis, it emerged that the group of patients who presented the highest mortality rate had a high grade of TSS, especially the patients admitted to ICU (total mortality rate of 60%, 40% in patients with Grade 3–20% in patients with Grade 4, respectively).

The worse prognosis in patients with Grade 3 than in those with Grade 4, in terms of the need for ICU admission and of mortality rate, may find a reasonable explanation in the fact that patients with Grade 4, who were clinically more severe, died before accessing medical attention and appropriate care and undergoing a CT examination, because the clinical condition was such that it was not possible to move them and undergo HRCT. Therefore, these patients were excluded from our case series, as they were monitored by other imaging examinations (Chest X-ray and/or ultrasound).

Some patients underwent HRCT only after their clinical condition allowed it, with consequent downgrading of the grade from 4 to a lower value: This also explains the relatively low number of patients with TSS Grade 4 who came to our attention and therefore were not studied with HRCT.

Follow-up HRCT was performed in 57 of 190 patients, only 1/3 of the patients. This data may be explained by the fact that many patients decided not to undergo further radiological examinations, others were monitored only by X-ray and others decided to undergo HRCT in other hospitals closer to their residence.

Analysis of the 57 patients who underwent follow-up CT showed that 45.6% of them were radiologically healed

and no longer showed any type of parenchymal alteration, while 54.4% of patients still showed residual parenchymal alterations. In the group of 31 patients with residual parenchymal alterations, we noted that the distribution of the alterations remained predominantly bilateral (90.3%), in the lower lobes (67.7%), and peripheral (80.6%), consistent with the findings of the scientific literature.

The most frequent alterations were interstitial thickening (67.7%) and pulmonary fibrosis (67.7%), followed by more blurred and less distinct than at onset GGO (64.5%), parenchymal consolidation often with reticular or linear morphology (16.1%), copresence of GGO plus areas of consolidation (9.7%), and crazy-paving (3.2%): These results also showed a high correspondence with the data expressed in the scientific literature regarding follow-up at an average of about 3 months after the first CT examination.

Finally, comparing the initial and control TSS, it was observed that 84.1% of patients improved from a higher to a lower TSS grade, 10.6% showed a score equal to the initial one and only 5.3% worsened from a higher TSS, independently of the time variable between the two examinations. In the comparison of patients who improved from a higher to a lower grade, it was noted that this data were independent of the time of follow-up and of the initial TSS, even if the improvement was more frequent in those who started from an initial grade of 1 and 2, where 50% of patients reached a complete recovery, while only in about 4% of cases recovery was observed in patients with an initial grade of 3 and in no case with an initial grade of 4.

In the small group of only three patients who worsened from a lower to a higher TSS grade, upgrading occurred in 66.6% of cases for patients who started from an initial grade of 1 – up to Grade 2 and 3 – and in 33.3% of cases for one patient who went from Grade 2 to 3. The explanation for this data can be sought in an ineffectiveness of the set therapies, in an abnormal immune response, in associated comorbid conditions, and in a particularly high viral load.

CONCLUSION

We can affirm the importance of radiology and, in particular, of chest HRCT as a technique with high sensitivity in the recognition of the most peculiar features of COVID-19 pneumonia, in the evaluation of severity of the disease, in the correct interpretation of temporal changes of the radiological picture during the follow-up until the resolution, and in obtaining prognostic information, also to direct the treatment.

On the basis of the scientific evidence acquired so far, it is important to emphasize that CT of the chest cannot be considered as a substitute for RT-PCR in the diagnosis of COVID-19, but rather supplementary to it in the diagnostic process as it can detect parenchymal changes at an early stage and even before the positive swab, at least for patients who have been symptomatic for more than 3 days.

Ethic committee

Not applicable (retrospective study).

Authors contributions

SGP, GL, AC, DT, MC, GF, GC, and ADP meet the following article contributions (conceptualization, methodology, validation, formal analysis, investigation, data curation) and writing contributions (original draft preparation, review and editing). LG, PQ, AB, and MTM meet the following article contributions (formal analysis and data curation) and writing contributions (review).

Declaration of patient consent

Patient's consent not required as patient's identity is not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest.

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