Chest CT signs associated with pejorative evolution in COVID-19 patients

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Abstract

Background COVID-19 is a complex virus that has been spreading since December 2019. In this study, we aimed to assess the association between chest Computed Tomography (CT) signs and pejorative evolution, such as death, use of invasive endotracheal ventilation (IEV) and intensive care unit hospitalization (ICUH). We also evaluated the diagnostic performance of chest CT versus the diagnostic gold standard, RT-PCR. Methods This retrospective monocentric study included 349 patients who had a chest CT either for clinical suspicion of COVID-19 pneumonia with severe initial symptoms, or clinical deterioration in patients with suspected COVID-19 pneumonia, or clinical deterioration in RT-PCR positive patients. Principal judgement criteria for pejorative evolution were: death, IEV, and ICUH. Results Among the 109 RT-PCR positive patients, there were higher rates of bronchial distortion and total volume lung involvement [?] 50% in the dead, IEV and ICUH groups (p < 10-3). Vascular dilatation and a number of involved lobes [?] 4 were associated with IEV and ICUH (p < 10-3). Among the 349 patients, sensitivity, specificity, positive and negative predictive values of chest CT versus RT-PCR were respectively 93,6 % [95% CI 89-98,2], 85,8 % [81,4-90,2], 75 % [67,7-82,3], and 96,7 % [94,3-99,1]. Unlike previous studies, we found different kinds of CT signs patterns, rather than a stereotyped COVID-19 pneumonia pattern. Maximal lesion expansion was observed during the second week after the first symptoms. Conclusion Bronchial distorsion and lesion expansion seem to be correlated with death in COVID-19 patients. This study confirms chest CT major diagnostic value.

Title : Chest CT signs associated with pejorative evolution in COVID-19 patients

Short title : Chest CT prognostic value in COVID-19 patients

Author list

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Acknowledgments

Author contributions

The study was designed by RA, GD and P-AD. Data collection and analysis was performed by RA and GD. Statistical analysis was performed by P-AD and RA. First draft of the manuscript was written by RA, and all authors commented on previous versions of the manuscript. All authors have read and approved the final manuscript.

Abstract

Background

COVID-19 is a complex virus that has been spreading since December 2019. In this study, we aimed to assess the association between chest Computed Tomography (CT) signs and pejorative evolution, such as death, use of invasive endotracheal ventilation (IEV) and intensive care unit hospitalization (ICUH). We also evaluated the diagnostic performance of chest CT versus the diagnostic gold standard, RT-PCR.

Methods

This retrospective monocentric study included 349 patients who had a chest CT either for clinical suspicion of COVID-19 pneumonia with severe initial symptoms, or clinical deterioration in patients with suspected COVID-19 pneumonia, or clinical deterioration in RT-PCR positive patients. Principal judgement criteria for pejorative evolution were: death, IEV, and ICUH.

Results

Among the 109 RT-PCR positive patients, there were higher rates of bronchial distortion and total volume lung involvement [?] 50% in the dead, IEV and ICUH groups (p < 10^{-3}). Vascular dilatation and a number of involved lobes [?] 4 were associated with IEV and ICUH (p < 10^{-3}).

Among the 349 patients, sensitivity, specificity, positive and negative predictive values of chest CT versus RT-PCR were respectively 93,6 % [95% CI 89-98,2], 85,8 % [81,4-90,2], 75 % [67,7-82,3], and 96,7 % [94,3-99,1].

Unlike previous studies, we found different kinds of CT signs patterns, rather than a stereotyped COVID-19 pneumonia pattern. Maximal lesion expansion was observed during the second week after the first symptoms.

ConclusionBronchial distorsion and lesion expansion seem to be correlated with death in COVID-19 patients. This study confirms chest CT major diagnostic value.

Keywords : COVID-19, chest CT, invasive endotracheal ventilation, bronchial distortion, critical care.

Introduction

Coronavirus disease (COVID-19) has been spreading worldwide since December 2019 from Wuhan, Hubei Province.¹ The virus called SARS-Cov-2 belongs to the Betacoronavirus genus, is composed of a positive single-stranded RNA, and has a 50-200 nm diameter.^{2,3} Bats are the natural reservoir for coronaviruses.⁴ On April 26th 2020, more than 2 355 853 cases (of which 947 693 in Europe) and 164 656 deaths worldwide were reported due to this pandemic.⁵On March 16th 2020 in France, 124 114 cases were confirmed with 22 614 deaths (i.e. 18,6 % of mortality).⁶ Fever, cough, fatigue, diarrhoea, dyspnoea and myalgia are the most common symptoms but the patients' condition can deteriorate rapidly, requiring intensive medical care.^{7,8}Real time reverse-transcription polymerase chain reaction (RT-PCR) is the standard reference to detect viral nucleic acid but false-negative results have been reported and have led to a 66-80 % sensitivity due to multiple factors, notably the quality of sampling.⁹Compared to RT-PCR, chest computed tomography (CT) is an easy-to-use and a faster method to diagnose and assess an early pulmonary COVID-19 infection.¹⁰ Chest CT can also help to monitor the evolution and diagnose complications of COVID-19. Indeed, some authors have demonstrated the diagnostic value of chest CT in COVID-19 pneumonia describing compatible

radiological signs.^{11–13} Ai. *et al.* have evaluated chest CT diagnostic value in 1014 cases of suspected COVID-19 using RT-PCR as a reference, and determined a sensitivity of 97 % and negative predictive value of 83 %.¹⁰ Few authors have studied the prognostic value of chest CT. Yuan *et al*. have found in a small sample of 27 patients (of which 10 died) higher rates of consolidation and air bronchogram in the dead patients' group.¹⁴ In a retrospective study, Zhao *et al.* found pleural effusions and architectural distorsions to be CT signs potentially correlated with severe deterioration in a small population of severe or deceased patients (14/101 patients).¹⁵

In this study, our main objective was to assess whether some chest CT signs were associated with pejorative evolution (defined as requiring intensive care unit hospitalization, invasive endotracheal ventilation or a fatal outcome), for patients with COVID-19. Our secondary objective was to evaluate the diagnostic value of chest CT versus RT-PCR.

Patients and Methods

Study design

Ethical approval of this monocentric retrospective study was delivered by the review board of our hospital (Hospitals of Tours, Francois Rabelais University, France). From March 19th to April 28th 2020, we included 349 patients either suspected of COVID-19 infection or previous RT-PCR COVID-19 positive patients to whom a chest CT scan was performed in the radiology department.

Inclusion criteria were: clinical suspicion of COVID-19 infection with severe symptoms requiring hospitalization or other comorbidities listed below : patients previously hospitalized for another reason and suspected of COVID-19 infection, patients with initial negative RT-PCR presenting a clinical deterioration during their hospitalization.

Comorbidities were : age > 65 years, chronic respiratory disease, dialysis, cardiac insufficiency NYHA 3 or 4, history of cardiac diseases (arterial hypertension, coronaropathy, stroke, cardiac surgery), cirrhosis ([?] Child B), diabetes with complications or requiring insulin therapy, immunosupression (chemotherapy, biotherapy, immunosuppressive corticotherapy, uncontrolled HIV or CD4 < 200/mm³, metastatic cancer, all types of graft), BMI > 40, or pregnancy. Clinical severity scale was assessed according to the Chinese Center of Disease Control and Prevention : uncomplicated illness (upper respiratory tract damages, including mild fever, cough (dry), sore throat, nasal congestion, headache, myalgia, or malaise. Symptoms of a more serious disease, such as dyspnoea, are not present), moderate pneumonia with dyspnoea, severe pneumonia (Sp02 < 90 % in ambient air, tachypnoea > 30/min), and acute respiratory distress syndrome (clinical and ventilation criteria : mild acute respiratory distress syndrome (ARDS) = 200 mmHg < PaO2/FiO2 [?] 300 mmHg (positive PEEP or CPAP [?] 5 mmHg if not ventilated or non-invasive ventilation)), moderate ARDS = 100 mmHg < PaO2/FiO2 [?] 200 mmHg, and severe ARDS = PaO2/FiO2 [?] 100 mmHg).^{16,17}

RT-PCR test and clinical synthesis

RT-PCR and chest CT were performed for these patients. Coronavirus nucleic acid was collected with nasopharyngeal swab or/and bronchial aspiration. RT-PCR was performed using gene amplification RdRpE, and/or N (CNR Pasteur technic, AllPlex Seegene, Bosphore Anatolia; depending on availabilities). For patients who presented a high clinical probability of infection, two or three RT-PCR were performed if the previous results were negative, with a minimum of 48-72 hours between samples.

If one RT-PCR was positive, COVID-19 diagnosis was confirmed. In case of multiple chest CTs, we used the one that was closest, timewise, to the first RT-PCR. All patients were included whatever the time between RT-PCR and chest CT.

We also included the notion of highly probable COVID-19 infection, i.e. some cases had multiple RT-PCR negative results but the clinical (dyspnoea, fever, fatigue, cough), biological history (lymphopenia, high reactive C-protein, high D-Dimers and LDH), chest CT and epidemiology (contagion with a positive RT-PCR) arguments were consistent with a COVID-19 infection.¹⁰ There was a follow-up and additional chest

CTs to conclude if the patient was infected or not, based on clinical assessment and medical records.

Primary outcome

The primary outcome was pejorative evolution, a composite criterion which comprises use of invasive endotracheal ventilation, intensive care unit hospitalization (ICUH), or death.

Chest CT protocol

Images were obtained in supine position by one of the two following CT scanners : an Aquilion Prime 160 (Toshiba, Japan) or a Somatom Force CT VB10 (Siemens Healthinners, Germany). Mean scanning parameters were: tube voltage = 120 kV, automatic dose modulation (30-210 mAs), matrix 512 x 512, pitch 0,35-0,99, slice thickness = 0,5 mm, and a field of view = 500 mm x 500 mm. A 0,5 mm slice thickness was used after image reconstruction. When a pulmonary embolism was suspected, iodinated contrast media (300 mg/l) was intravenously injected (3 to 4 ml/s) according to patient weight, with bolus tracking in the main pulmonary artery. Images reconstructed were archived and transferred to the informatic network (PACS).

Chest CT images analysis

Three radiologists (18 years thoracic radiology specialist, 10 years general radiologist and 2 years radiologist resident) blinded to RT-PCR results reviewed CT images and concluded either to COVID-19 infection or not, according to the consensual signs described in COVID-19 chest damages⁷. Clinical history was available for interpretation.

Chest CT signs were analysed according to the Fleishner Society glossary¹⁸ : ground glass-opacities (patchy, nodular or mixed), crazy paving (thickened intralobular and interlobular lines in a ground glass opacity), subpleural curvilinear bands, consolidation areas, air bubble sign, vascular dilatation, bronchial distortion, reticular interlobular thickening, pleural effusion, pleural thickening, number of involved lobes, inferior predominance, laterality, lung localisation (subpleural, central or dual distribution), compatible CT aspect of ARDS) compatible CT aspect of organized pneumonia, compatible CT aspect of cardiac failure, lymphadenopathy, emphysematous lesions, bronchial thickening, endobronchial secretion, centrilobular nodule, and total lung volume involvement (0%, < 10%, 10-25%, 25-50%, 50-75%, > 75 %).

Compatible CT aspect of organized pneumonia included consolidation (nodular, linear, perilobular, or peribronchovascular), subpleural curvilinear bands, halo sign, and/or atoll sign.¹⁹Bronchial distortion is defined as bronchial dilatation, with irregular contours, focalized in the areas affected by the ground glass opacities, consolidation, or crazy paving.²⁰

Statistical Analysis

Statistical analysis was performed with Matlab(r) R2007b (MathWorks Inc., Natick, USA). Qualitative variables were reported with number, percentage and quantitative variables with mean and standard deviation.

We calculated sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and their respective 95 % confidence interval for the diagnosis of a COVID-19 infection with chest CT versus RT-PCR (reference).

The associations between the mortality or morbidity (invasive endotracheal ventilation or ICUH) and chest CT signs of COVID-19 infection (ground glass opacities, crazy paving, consolidation area, subpleural curvilinear bands, bronchial distortion, vascular dilatation, air bubble sign, interlobular thickening, total volume [50-100 % versus < 50%], compatible aspect of organized pneumonia, compatible CT aspect of ARDS, distribution [subpleural, central, and dual i.e. central and subpleural], inferior localization, number of involved lobes (0 to 3 VS 4 or 5 involved lobes) were evaluated using Chi2 tests when applicable (all theorical numbers superior to 5), and Fisher's exact test otherwise.

All test results with a p-value < 0.05 were considered statistically significant.

Results

Clinical and population characteristics

We included 349 patients suspected of COVID-19 who underwent chest CT. Their clinical and demographic characteristics are resumed in Table 1. There were 136 patients with compatible CT signs of COVID-19 infection and 109 were RT-PCR positive (Figure. 1). The two positive and negative RT-PCR groups were comparable in term of age, sex and comorbidity rate. 73 of 109 patients (67 %) with positive RT-PCR had severe symptoms (severe pneumonia or ARDS as described above), presenting high rates of ICUH (35,7 %), invasive endotracheal ventilation (25,7 %) and death (10,1 %). Mean time interval between chest CT and RT-PCR was inferior to 1,5 days. Patients generally had chest CT the same day or the day after hospitalization and 6,2 days mean time after the first symptoms. Table 2 presents the chest CT signs of the 109 COVID-19 patients who had positive RT-PCR.

There were 34 patients with compatible COVID-19 CT, i.e. patients with negative RT-PCR but compatible chest CT. Despite repeated RT-PCR tests, 14 were considered as probable COVID-19 infection by physicians at the end of hospitalization, based on clinical assessment. 6.4 % of RT-PCR positive patients did not show COVID-19 CT signs (normal CT or not compatible CT signs). Typical chest CT signs in the 109 positive RT-PCR COVID-19 patients are described according to the delay between first symptoms and the first CT (Days 0 to 6, 7 to 14, and > 14) in Figure. 2. Maximum peak of CT signs was during the second week after the beginning of symptoms, in relatively similar proportions.

CT signs and pejorative evolution

Associations between COVID-19 typical CT signs and intensive care unit hospitalization, use of invasive endotracheal ventilation and death are summarized in Table 3, with the calculated p-values, only for the 109 RT-PCR positive patients.

Bronchial distortion was significatively associated with mortality (p = 0,018), ICUH and invasive endotracheal ventilation (p < 10^{-3}). Vascular dilatation and a number of involved lobes [?] 4 were significatively associated with invasive endotracheal ventilation and ICU hospitalization (p < 10^{-3}). Total lung volume involvement [?] 50 % was also significatively associated with death, invasive endotracheal ventilation and ICUH (p < 10^{-3}). Air bubble sign (p = 0,039), interlobular (p = 0,026) and peribronchovascular thickening (p = 6.10^{-3}) were associated with invasive endotracheal ventilation.

Chest CT diagnostic value

With RT-PCR as the reference for the 349 patients included, sensitivity was 93,6 % [95% CI 89-98,2], specificity was 85,8 % [81,4-90,2], PPV was 75 % [67,7-82,3], NPV was 96,7 % [94,3-99,1], with a prevalence of 31,2 %.

Discussion

Among positive RT-PCR COVID-19 patients, bronchial distortion and total lung involvement volume [?] 50 %, are the only signs associated with a fatal outcome, as shown in Figures 3a, 3b and 4. We also found that vascular dilatation, bronchial distortion, lesional expansion (total lung involvement [?] 50 % or [?] 4 damaged lobes) are significantly associated with invasive endotracheal ventilation or ICUH. Maybe some of these signs are not correlated with death due to our sample size. Vascular dilatation, as shown in Figures 3b and 4, could be due to endothelial lesion with inflammatory vasodilatation or maybe to parenchymal retraction associated with fibrosis. The air bubble sign is more frequent in invasive endotracheal ventilation, it could correspond to a bronchioloalveolar dilatation linked with fibrosing damages or a previous existing cyst revealed by the diffuse infection. The significantly higher frequency of interlobular and peribronchovascular thickening in the invasive endotracheal ventilation group could be due to interstitial oedema observed in congestive heart failure (6/109 patients) and are not specific of COVID-19 infection. However, contrary to Zhao *et al.*, lymphadenopathy and pleural effusion were not associated with a pejorative evolution in our cohort.¹²

We also have observed a compatible pattern with organized pneumonia (OP) in more than 50 % of patients : an example is shown in Figure 3c. Association between OP and fibrosis lesions has been observed in

a pulmonary autopsy of one COVID-19 patient as a histologic pattern of acute fibrinous and organizing pneumonia, by Copin *et al.*, consistent with the CT aspect.²⁵

Frequency and type of chest CT signs are similar to other previous studies except for consolidation and bronchial distortion, more prevalent in our study probably due to the clinical severity of our patients.^{13,20–23} In a previous metanalysis, Salehi *et al.* have described 80 % of air bronchograms in COVID-19 lung damages.²⁴ Rather than air bronchograms, it seems more pertinent to use bronchial distortion as a typical sign of secondary fibrosing damage observed in severe COVID-19 pneumoniae.

All the CT signs must be analysed independently from each other: indeed, if the presence of ground glass opacities (frequent sign whatever clinical presentation) was not a pejorative evolution predictive sign, its expansion over 50 % of volume the lung was predictive of a pejorative evolution as shown in this study.^{20,24,26}

We have found that chest CT has a strong diagnostic value in COVID-19 infection comparing to RT-PCR, with a sensibility of 93,6 %, specificity of 85,8 %, PPV of 75 % and NPV of 96,7 %, as described in previous studies. Our sensibility was concordant with other studies, e.g. 97 % in Ai *et al.* ^{10,29} However, our specificity and PPV are better, perhaps due to the recruitment of our patients in terms of clinical severity.

Figure 2 shows that the proportion of different CT signs increases during the second week and decreases after, so it confirms that pulmonary extension is maximal around the $10^{\rm th}$ day.²⁷ Furthermore, we noted that all the typical COVID-19 CT signs were present during the first week in similar proportions. Contrary to Pan *et al.*, we haven't observed a relative predominance of ground glass opacities in the first week or consolidation predominance in the second week (perhaps due the exclusion of severe patients in these studies).²⁸Indeed, several kinds of CT patterns seem to exist in COVID-19 pneumonia, rather than a unique stereotyped chronological evolution, depending on the type and degree of histological damage.

This study has some limitations. It is a retrospective study. Only one CT scan was included per patient. No CT aspect evolution analysis was performed; however, the rapidity of symptoms evolution could be another predictive factor of pejorative evolution. Other futures studies should consider this point. It is possible that some signs are not associated with pejorative evolution because of a relatively small number of deaths.

Conclusion

Chest CT is a fast tool, with immediate results, which seems to have an excellent diagnostic value. CT also allows complication detection, differential diagnosis exclusion and seems to help assess the prognosis as described previously and in this study. This exam should be readily proposed for COVID-19 patients according to clinical criterias and local availabilities.

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Variable	Values	V
	RT-PCR COVID + (109 patients)	R
Age	64,6 (17,2)	64
Male sex	61 (55,6 %)	12
Comorbidity	81 (74 %)	18
Clinical severity		
No	12 (11 %)	12
Mild	24 (22 %)	64
Severe	46 (42,2 %)	49
Mild ARDS	1 (0,9 %)	0
Moderate ARDS	15 (13,7 %)	3
Severe ARDS	11 (10,1 %)	0
ICUH	39 (35,7 %)	12
Invasive endotracheal ventilation	28 (25,7 %)	6
Death	11 (10,1 %)	$\overline{7}$
Life status unknown at the end of the study	11 (10,1 %)	0
Number of unknown RT-PCR before CT	55 (50,5 %)	15
Average time between first symptom and CT (days)	$6,2 \pm 5,1$	6,
Average time between first symptom and CT among patients in ICUH (days)	$5,9 \pm 4,3$	7,
Average time between CT and RT-PCR (days)	$1,42\pm 2$	1,
Average time between RT-PCR and CT if RT-PCR results are not known (days)	$1,49 \pm 2,48$	1,
Average time between RT-PCR and CT if RT-PCR results are known (days)	$2,11 \pm 2,38$	1,
Average time between admission and CT (days)	$1,1 \pm 2,15$	1.

Table 1 - Clinical and demographic characteristics of the 349 patients included – Qualitative values are indicated as number and percentages. Quantitative values are indicated as mean and standard deviation. ARDS, Acute Respiratory Distress Syndrom; CT = Computed Tomography; ICUH, Intensive Care Unit Hospitalization; RT-PCR, Real Time Reverse-Transcription Polymerase Chain Reaction.

GGround glass opacities98 (89,9 %)Crazy paving65 (59,6 %)Not systematized consolidation area39 (35,8 %)Subpleural curvilinear bands63 (57,8 %)Bronchial distortion45 (41,3 %)Vascular dilatation25 (22,9 %)Air bubble Sign12 (11 %)Interlobular thickening14 (12,8 %)Compatible aspect of ARDS7 (6,4 %)Compatible aspect of organized pneumonia59 (54,1 %)Compatible aspect of cardiac additional6 (5,5 %)decompensation13 (11,9 %)Bronchial thickening13 (11,9 %)Endobronchial secretion7 (6,4 %)Centrilobular nodule7 (6,4 %)	<u></u>	77.1
Crazy paving $65 (59, 6 \%)$ Not systematized consolidation area $39 (35, 8 \%)$ Subpleural curvilinear bands $63 (57, 8 \%)$ Bronchial distortion $45 (41, 3 \%)$ Vascular dilatation $25 (22, 9 \%)$ Air bubble Sign $12 (11 \%)$ Interlobular thickening $14 (12, 8 \%)$ Compatible aspect of ARDS $7 (6, 4 \%)$ Compatible aspect of organized pneumonia $59 (54, 1 \%)$ Compatible aspect of cardiac additional $6 (5, 5 \%)$ decompensation $13 (11, 9 \%)$ Lymphadenopathy $13 (11, 9 \%)$ Bronchial thickening $13 (11, 9 \%)$ Centrilobular nodule $7 (6, 4 \%)$	Signs	Values
Not systematized consolidation area 39 ($35,8$ %)Subpleural curvilinear bands 63 ($57,8$ %)Bronchial distortion 45 ($41,3$ %)Vascular dilatation 25 ($22,9$ %)Air bubble Sign 12 (11 %)Interlobular thickening 14 ($12,8$ %)Compatible aspect of ARDS 7 ($6,4$ %)Compatible aspect of organized pneumonia 59 ($54,1$ %)Compatible aspect of cardiac additional 6 ($5,5$ %)decompensation 13 ($11,9$ %)Lymphadenopathy 13 ($11,9$ %)Bronchial thickening 13 ($11,9$ %)Endobronchial secretion 7 ($6,4$ %)Centrilobular nodule 7 ($6,4$ %)	Ground glass opacities	98~(89,9~%)
Subpleural curvilinear bands $63(57,8\%)$ Bronchial distortion $45(41,3\%)$ Vascular dilatation $25(22,9\%)$ Air bubble Sign $12(11\%)$ Interlobular thickening $14(12,8\%)$ Compatible aspect of ARDS $7(6,4\%)$ Compatible aspect of organized pneumonia $59(54,1\%)$ Compatible aspect of cardiac additional $6(5,5\%)$ decompensation $13(11,9\%)$ Bronchial thickening $13(11,9\%)$ Bronchial thickening $7(6,4\%)$ Centrilobular nodule $7(6,4\%)$	Crazy paving	65~(59,6~%)
Bronchial distortion $45 (41, 3 \%)$ Vascular dilatation $25 (22, 9 \%)$ Air bubble Sign $12 (11 \%)$ Interlobular thickening $14 (12, 8 \%)$ Compatible aspect of ARDS $7 (6, 4 \%)$ Compatible aspect of organized pneumonia $59 (54, 1 \%)$ Compatible aspect of cardiac additional $6 (5, 5 \%)$ decompensation $13 (11, 9 \%)$ Bronchial thickening $13 (11, 9 \%)$ Bronchial thickening $7 (6, 4 \%)$ Centrilobular nodule $7 (6, 4 \%)$	Not systematized consolidation area	$39 (35,\! 8 \%)$
Vascular dilatation $25(22,9\%)$ Air bubble Sign $12(11\%)$ Interlobular thickening $14(12,8\%)$ Compatible aspect of ARDS $7(6,4\%)$ Compatible aspect of organized pneumonia $59(54,1\%)$ Compatible aspect of cardiac additional $6(5,5\%)$ decompensation $13(11,9\%)$ Bronchial thickening $13(11,9\%)$ Endobronchial secretion $7(6,4\%)$ Centrilobular nodule $7(6,4\%)$	Subpleural curvilinear bands	63~(57,8~%)
Air bubble Sign $12 (11 \%)^{'}$ Interlobular thickening $14 (12,8 \%)$ Compatible aspect of ARDS $7 (6,4 \%)$ Compatible aspect of organized pneumonia $59 (54,1 \%)$ Compatible aspect of cardiac additional $6 (5,5 \%)$ decompensation $13 (11,9 \%)$ Lymphadenopathy $13 (11,9 \%)$ Bronchial thickening $13 (11,9 \%)$ Endobronchial secretion $7 (6,4 \%)$ Centrilobular nodule $7 (6,4 \%)$	Bronchial distortion	45 (41,3 %)
Interlobular thickening $14 (12,8 \%)$ Compatible aspect of ARDS $7 (6,4 \%)$ Compatible aspect of organized pneumonia $59 (54,1 \%)$ Compatible aspect of cardiac additional $6 (5,5 \%)$ decompensation $13 (11,9 \%)$ Lymphadenopathy $13 (11,9 \%)$ Bronchial thickening $7 (6,4 \%)$ Endobronchial secretion $7 (6,4 \%)$ Centrilobular nodule $7 (6,4 \%)$	Vascular dilatation	25~(22.9~%)
Compatible aspect of ARDS7 (6,4 %)Compatible aspect of organized pneumonia59 (54,1 %)Compatible aspect of cardiac additional6 (5,5 %)decompensation13 (11,9 %)Lymphadenopathy13 (11,9 %)Bronchial thickening13 (11,9 %)Endobronchial secretion7 (6,4 %)Centrilobular nodule7 (6,4 %)	Air bubble Sign	12 (11 %)
Compatible aspect of organized pneumonia59 (54,1 %)Compatible aspect of cardiac additional6 (5,5 %)decompensation13 (11,9 %)Lymphadenopathy13 (11,9 %)Bronchial thickening13 (11,9 %)Endobronchial secretion7 (6,4 %)Centrilobular nodule7 (6,4 %)	Interlobular thickening	14 (12,8 %)
Compatible aspect of cardiac additional6 (5,5 %)decompensation13 (11,9 %)Lymphadenopathy13 (11,9 %)Bronchial thickening13 (11,9 %)Endobronchial secretion7 (6,4 %)Centrilobular nodule7 (6,4 %)	Compatible aspect of ARDS	7 (6,4 %)
decompensationLymphadenopathy13 (11,9 %)Bronchial thickening13 (11,9 %)Endobronchial secretion7 (6,4 %)Centrilobular nodule7 (6,4 %)	Compatible aspect of organized pneumonia	59~(54,1~%)
Lymphadenopathy $13 (11,9 \%)$ Bronchial thickening $13 (11,9 \%)$ Endobronchial secretion $7 (6,4 \%)$ Centrilobular nodule $7 (6,4 \%)$	Compatible aspect of cardiac additional	6~(5,5~%)
Bronchial thickening13 (11,9 %)Endobronchial secretion7 (6,4 %)Centrilobular nodule7 (6,4 %)	decompensation	
Endobronchial secretion7 (6,4 %)Centrilobular nodule7 (6,4 %)	Lymphadenopathy	$13\ (11,9\ \%)$
Centrilobular nodule 7 (6,4 %)	Bronchial thickening	$13\ (11,9\ \%)$
	Endobronchial secretion	$7 \ (6,4 \ \%)$
Pneumothorax $2(1.8\%)$	Centrilobular nodule	$7 \ (6,4 \ \%)$
	Pneumothorax	2~(1,8~%)
Pulmonar embolism $6 (5,5 \%)$	Pulmonar embolism	6~(5,5~%)
Emphysematous lesions $5 (4,6 \%)$	Emphysematous lesions	5~(4,6~%)
Systematized consolidation $6 (5,5 \%)$	Systematized consolidation	6~(5,5~%)
Pleural effusion $17 (15,6 \%)$	Pleural effusion	$17 \ (15,6 \ \%)$
Pleural thickening $4 (3,7 \%)$	Pleural thickening	4 (3,7 %)
Bilateral $102 (9,3 \%)$	Bilateral	102~(9,3~%)
Unilateral $3(2,7\%)$	Unilateral	3~(2,7~%)
Subpleural localization $104 (95, 4\%)$	Subpleural localization	104 (95,4 %)
Central localization 48 (44 %)	Central localization	48 (44 %)
Dual distribution $52 (47,7 \%)$	Dual distribution	52~(47,7~%)
Inferior localization $75 (68,8 \%)$	Inferior localization	75~(68,8~%)
Number of involved lobes $4,2$ (1,4)	Number of involved lobes	4,2 (1,4)
Volume (total lung involvement) $0\%: 5 (4.6\%) < 10\%: 13 (11.9\%) 10-25 \%: 24$	Volume (total lung involvement)	0%: 5 (4.6%) < 10%: 13 (11.9%) 10-25 %: 24
(22%)25 -50 $%:31(28,4%)50-75%:(14,7%)$		$(22\ \%)\ 25\ \text{-}50\ \%:\ 31\ (28,4\ \%)\ 50\ -\ 75\ \%:\ (14,7\ \%)$
>75~%:~(18,4~%)		>75%: (18,4%)
No CT signs $4 (3,7 \%)$	No CT signs	4 (3,7 %)

Table 2 - First chest CT signs found for the 109 positive COVID-19 All signs are described with number and percentage, except the number of involved lobes which is described with mean and standard deviation. ARDS, Acute Respiratory Distress Syndrom; CT, Computed Tomography.

	ICUH	Invasive endotracheal ventilation	Death
	p-value	p-value	p-value
Ground glass opacities	-	-	-
Crazy paving	-	-	-
Not systematized consolidation area	-	-	-
Subpleural curvilinear bands	-	-	-

	ICUH	Invasive endotracheal ventilation	Death
Bronchial distortion	$< 10^{-3}$	< 10 ⁻³	0,018
Vascular dilatation	$< 10^{-3}$	$< 10^{-3}$	-
Air bubble sign	-	0,039	-
Interlobular thickening	-	0,026	-
Compatible aspect of ARDS	$< 10^{-3}$	$< 10^{-3}$	-
Subpleural localization	-	-	-
Central localization	0,019	-	-
Dual distribution	0,010	-	-
Inferior localization	-	-	-
Compatible aspect of organized pneumonia	-	-	-
Peribronchovascular thickening	-	6.10^{-3}	-
Number of involved lobes [[?]3 VS [?]4]	$3, 8.10^{-3}$	$4,25.10^{-3}$	-
Total lung volume involvement			
<50 VS [?] 50 %	$< 10^{-3}$	$< 10^{-3}$	$< 10^{-3}$

Table 3 - Association between CT chest signs and intensive care unit hospitalization, invasive endotrachealventilation and death among positive RT-PCR COVID-19 patients. Dashes correspond to p > 0.05. ARDS,Acute Respiratory Distress Syndrom; CT, Computed Tomography; ICUH, Intensive Care Unit Hospitalization.

Figure 1. Flow-chart of the 349 patients suspected of COVID-19 infection included in the study.

Figure 2. Main chest CT signs in the 109 COVID-19 positive RT-PCR cases according to the delay between first symptoms and the first chest CT. CT, Computed Tomography; RT-PCR, Real Time Reverse-Transcription Polymerase Chain Reaction.

Figure 3. Chest CT in positive RT-PCR COVID-19 cases - (a) A 74 years old man in ICU with endotracheal ventilation, 11 days after first symptoms, massive bronchial distortion (white arrow) in all the right lung, large areas of ground glass opacities and subpleural consolidation, with [?] 75 % of total lung involvement. Note a left anterior loculated pneumothorax and a left posterior pleural effusion drain. (b) A 57 years old man in ICU, 13 days after first symptoms, dual distribution areas (subpleural and central) of ground glass opacities in the lingula and the right inferior lobe with bronchial distortion (black arrow) and vascular dilatation (white arrow), with 50-75 % of total lung involvement. (c) A 67 years old man in ICU, 10 days after first symptoms, CT aspect of organized pneumonia (white arrow) with bilateral posterior subpleural curvilinear bands. CT, Computed Tomography; ICU, Intensive Care Unit; RT-PCR, Real Time Reverse-Transcription Polymerase Chain Reaction.

Figure 4. Chest CT of a 76 years old man in ICU, showed 10 days after first symptoms, bilateral, large and patchy ground glass opacities with crazy paving (white underlined dark arrow), bronchial distortion (white arrow) and vascular dilatation (dark arrow), with 50-75 % of total lung involvement. CT, Computed Tomography; ICU, Intensive Care Unit.







