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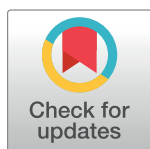


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RESEARCH ARTICLE

Low-dose chest CT for diagnosing and assessing the extent of lung involvement of SARS-CoV-2 pneumonia using a semi quantitative score

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Abbreviations: ARDS, acute respiratory distress syndrome; COVID19, coronavirus disease 2019;

Abstract

Objectives

The purpose is to assess the ability of low-dose CT (LDCT) to determine lung involvement in SARS-CoV-2 pneumonia and to describe a COVID19-LDCT severity score.

Materials and methods

Patients with SARS-CoV-2 infection confirmed by RT-PCR were retrospectively analysed. Clinical data, the National Early Warning Score (NEWS) and imaging features were recorded. Lung features included ground-glass opacities (GGO), areas of consolidation and crazy paving patterns. The COVID19-LDCT score was calculated by summing the score of each segment from 0 (no involvement) to 10 (severe impairment). Univariate analysis was performed to explore predictive factor of high COVID19-LDCT score. The nonparametric Mann-Whitney test was used to compare groups and a Spearman correlation used with $p < 0.05$ for significance.

Results

Eighty patients with positive RT-PCR were analysed. The mean age was 55 years \pm 16, with 42 males (53%). The most frequent symptoms were fever (60/80, 75%) and cough (59/80, 74%), the mean NEWS was 1.7 \pm 2.3. All LDCT could be analysed and 23/80 (28%) were normal. The major imaging finding was GGOs in 56 cases (67%). The COVID19-LDCT score (mean value = 19 \pm 29) was correlated with NEWS ($r = 0.48$, $p < 0.0001$). No symptoms were risk factor to have pulmonary involvement. Univariate analysis shown that dyspnea,

GGO, ground-glass opacity; LDCT, low-dose chest CT; NEWS, national early warning score; RT-PCR, real-time reverse transcription-polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

high respiratory rate, hypertension and diabetes are associated to a COVID19-LDCT score superior to 50.

Conclusions

COVID19-LDCT score did correlate with NEWS. It was significantly different in the clinical low-risk and high-risk groups. Further work is needed to validate the COVID19-LDCT score against patient prognosis.

Introduction

The outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), that began in Wuhan, China, spread worldwide, and is now in the ascending phase of the epidemic in Europe [1]. SARS-CoV-2 is responsible for coronavirus disease 2019 (COVID-19) pneumonia. Respiratory involvement has a wide variety of clinical features, ranging from simple nasal congestion to pulmonary failure [2]. Moreover, many patients remain asymptomatic but a vector of the disease, allowing the epidemic to spread easily.

The main problem of COVID-19 pneumonia is the risk of saturation of our health system due to an uncommonly massive inflow of patients requiring intensive care. Patient selection is therefore essential in order for health care practitioners to focus on patients with comorbidities and on severe cases. This selection is currently essentially based on clinical criteria.

Reverse-transcription polymerase chain reaction (RT-PCR) is currently the standard of reference for diagnosis of COVID 19 pneumonia. Chest x-ray might be replaced by low-dose computed tomography (LDCT) in COVID-19 to assess lung involvement. Thus, computed tomography (CT) has an important role in the management of patients, both for early screening and diagnosis and for establishing disease severity [3–5].

COVID-19 pneumonia lung lesions are now well characterized: they are typically asymmetric, with ground-glass opacity (GGO) lesions or, less commonly, pulmonary areas of consolidation, they have a peripheral distribution, and they preferentially affect the lower territories [6]. It seems that there is a continuum in the lung lesions visible on CT scans, first with GGO lesions; then reticulations appear with crazy-paving patterns, parenchymatous areas of consolidation and finally, healing [7, 8].

The objective is to evaluate the ability of (LDCT) to analyze well-known imaging abnormalities as well as to establish a COVID19-LDCT score reflecting disease severity and correlate it with clinical risk scores to allow better selection and follow-up of patients.

Material and methods

Study design

The first 80 patients with a diagnosis of COVID-19 pneumonia confirmed by RT-PCR method [9] were included in this single-centre retrospective study conducted from the 13th to the 20th of March 2020. The inclusion criteria and patient enrolment included all consecutive patients presenting to the department of infectious disease for 12 consecutive days with a diagnosis of COVID-19 confirmed by RT-PCR. All patients underwent LDCT. The protocol was approved by the local institutional review board: institut hospitalo-universitaire méditerranée-infection N°:2020–0012. The exclusion criteria was protocol refusal. For each patient, the following clinical parameters were recorded: age, sex, date of first symptoms, date of chest CT scan, delay between the first symptom and chest CT scan, fever, cough, dyspnea, diarrhea, myalgia,

rhinorrhea, abnormalities at lung auscultation, temperature, heart rate, blood pressure, respiratory rate, oxygen saturation, and oxygen needed. Medical history parameters were recorded as follows: heart disease, tobacco use, COPD, asthma, diabetes, obesity, sleep apnea syndrome, oncologic status and immunosuppression status. The National Early Warning Score (NEWS) was calculated for each patient using respiratory rate, oxygen saturation, supplemental oxygen needed, temperature, systolic blood pressure, heart rate, and AVPU score, as described previously [10]. The NEWS determines the degree of illness of a patient and prompts critical care intervention. According to previously published data, patients were divided into the following two groups based on the NEWS in order to compare the radiological data in these populations: low NEWS ($\text{NEWS} \leq 4$) and high NEWS ($\text{NEWS} > 4$) groups [10].

Equipment

All departments had to be reorganized in response to the increase in COVID-19 pneumonia, and CT scans were dedicated for this activity with a specific patient circuit. Technicians and workers in contact with COVID19 patients took all preventative means to protect themselves against transmission of the virus following the local institutional recommendations. A video was performed in our department to highlight the work of radiology technicians and available on https://youtu.be/mI-L_ZrL_U.

LDCT

All patients underwent LDCT on the same system (Revolution EVO—GE Healthcare). All LDCT scans were unenhanced in profound and maximal inspiration with the following parameters: detector collimation: 0.625 mm; field of view: 500 mm; matrix: 512x512; pitch: 1.375; gantry speed 0.35s; 120 KV; 45 mAs; and reconstructed slice thickness 1.2mm. All imaging data were reconstructed using high resolution and standard algorithms. LDCT data were sent directly to a picture archiving and communicating system. Monitors were used to view both mediastinal (width, 400 HU; level, 20 HU) and lung (width, 1500 HU; level, -2700 HU) windows. The pre-established top anatomic border was the lower part of the neck. The pre-established anatomic bottom boundary was the estimated location of the adrenal glands below the costophrenic angle.

All LDCT scans were analysed by a single chest radiologist with more than 25 years of experience in chest imaging (JYG). All abnormalities were described according to the Fleischner glossary [11]. The main features encountered during SARS-CoV-2 have been described elsewhere as GGOs, areas of consolidation, crazy paving patterns, and extension of these lesions might evolve dramatically to acute respiratory distress syndrome (ARDS). The type and distribution of the lesions were analysed [12, 13].

COVID19-LDCT score

LDCT scores were used to quantify the extent of lung abnormalities. The score was obtained by summing the notes attributed to each segment. The extent of the lesions of COVID-19 pneumonia was visually classified into 4 types for each segment: lack of lesions and minimal, intermediate and severe involvement. Lack of involvement was defined as a normal pattern and was equivalent to 0. Minimal involvement was defined as the presence of maximum 10 secondary lobules of any features and was equivalent to 1. Intermediate involvement was defined as less than 50% involvement of the segment by any features and was equivalent to 4. Severe involvement was defined as more than 50% involvement of the segment by any feature and was equivalent to 10. The score was obtained by summing the score of all segments for the right and left lungs, with the result ranking between 0

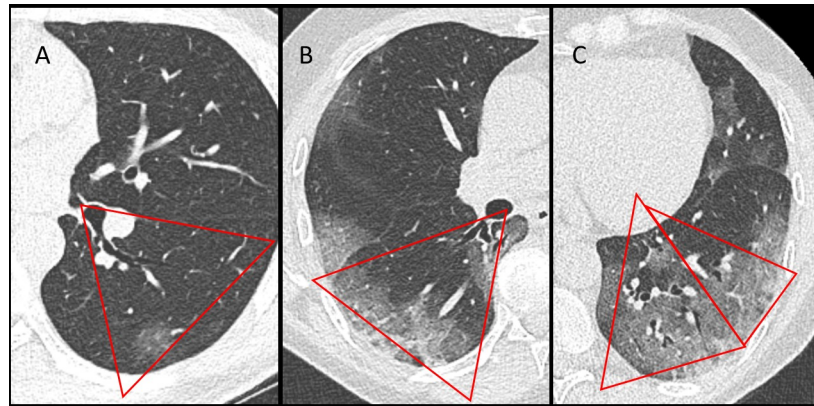


Fig 1. Illustration of how to calculate the COVID19-LDCT score. A. The triangle with red borders shows the 6th segment of the left lung with a unique GGO corresponding to minimal impairment. B. The triangle with red borders shows the 6th segment of the right lung with GGO inside involving 50% of the segment corresponding to intermediate impairment. C. Two triangles showing the 10th and the 9th segments of the left lung, where the extent of GGO was > 50% and 50%, corresponding to severe and intermediate impairment, respectively.

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corresponding to a normal chest CT and 200 if all segments had involvement of more than 50% of their volume (Fig 1). Chest-CT was considered with high impairment if the global score was superior to 50, we compared two groups to assess if clinical data could be predictor of severe involvement of lung parenchyma.

PCR assay

Virological diagnosis of SARS-CoV-2 infection was performed using a sample nasopharyngeal swabs with an hydrolysis probe-based real-time reverse transcription-PCR system that targets the envelope (E) protein-encoding gene [9, 14].

Statistical analysis

Quantitative data were expressed as mean, standard deviation and range. Qualitative data were expressed raw numbers, proportions and percentages. The differences between the variables were compared by the Chi 2 or Fischer test for qualitative variables and by U Mann-Whitney for quantitative variables. The relationship between quantitative parameters was examined with Spearman correlation test. Binary logistic regression analysis was used to test the relationships between COVID-LDCT score and clinically relevant variables. A value of $p < 0.05$ indicated a statistically significant difference. Statistical analysis was performed on XLSTAT v19.1 (Addinsoft, New York, USA).

Results

Patients

Between the 13th and the 20th of March 2020 the first 80 patients with positive RT-PCR results for COVID-19 were enrolled in a single center. All data could be recorded for all patients. The mean age of the population was 55 years \pm 16, with 42 males and 38 females (47%). For 75 of the patients (94%), the medical consultation was carried out following a symptom; for the others, it followed close contact with an affected case.

Clinical and LDCT Data

Initially the most frequent symptoms were fever in 60 patients (75%) and cough in 59 patients (74%). Myalgia, rhinorrhea, dyspnea and diarrhea were less frequent and were found in 35 (44%), 18 (23%), 11 (14%) and 11 (14%) patients, respectively. Lung auscultation abnormalities were found in only 14 patients (18%). Five patients needed resuscitation for an ARDS 5/80 (6%).

At the first examination before LDCT, the mean temperature was $37.5^{\circ}\text{C} \pm 0.9$, heart rate was $83 \text{ bpm} \pm 13$, systolic blood pressure was $134 \text{ mmHg} \pm 21$, diastolic blood pressure was $76 \text{ mmHg} \pm 14$, respiratory rate was $19/\text{min} \pm 5$ and oxygen saturation was $97\% \pm 2$. The mean NEWS was 1.7 ± 2.3 (Table 1).

The delay between the first symptom and the LDCT scan was 7 ± 4 days. The dose-length product mean was $41.7 \text{ mGy.cm} \pm 15.5$. All patients could have their images analysed 80/80

Table 1. Characteristics of the population and clinical data.

	<i>Total Population</i>
Number of patients	80
Demographic data	
Male	42/80; 53%
Female	38/80; 47%
Age (years)	55 ± 16 [17–89]
Delay between symptoms and CT (days)	7 ± 4 [2–21]
Symptomatic patients	75/80; 94%
Asymptomatic patients	5/80; 6%
Clinical data	
Fever, chills	60/80; 75%
Cough	59/80; 74%
Dyspnea	11/80; 14%
Myalgia	35/80; 44%
Diarrhea	11/80; 14%
Rhinorrhea	18/80; 23%
Auscultation abnormalities	14/80; 18%
Temperature ($^{\circ}\text{C}$)	37.5 ± 0.9 [36–40]
Heart rate (bpm)	83 ± 13 [53–110]
Systolic blood pressure (mmHg)	134 ± 21 [100–219]
Diastolic blood pressure (mmHg)	76 ± 14 [11–120]
Respiratory rate (/min)	19 ± 5 [8–36]
Oxygen saturation (%)	97 ± 2 [91–100]
Oxygen needed	10/80; 13%
Heart disease	9/80; 11%
Tobacco use	10/80; 12%
COPD	3/80; 4%
Asthma	8/80; 10%
Sleep apnea syndrome	6/80; 7%
Oncologic disease	6/80; 7%
Diabetes	8/80; 10%

Note: The qualitative variables are expressed as figures with percentages, and the continuous variables are expressed as the as mean values \pm SDs. $^{\circ}\text{C}$: Celsius degree; bpm: beat per minute; COPD: chronic obstructive pulmonary disease; CT: computed tomography; mmHg: millimeter of mercury.

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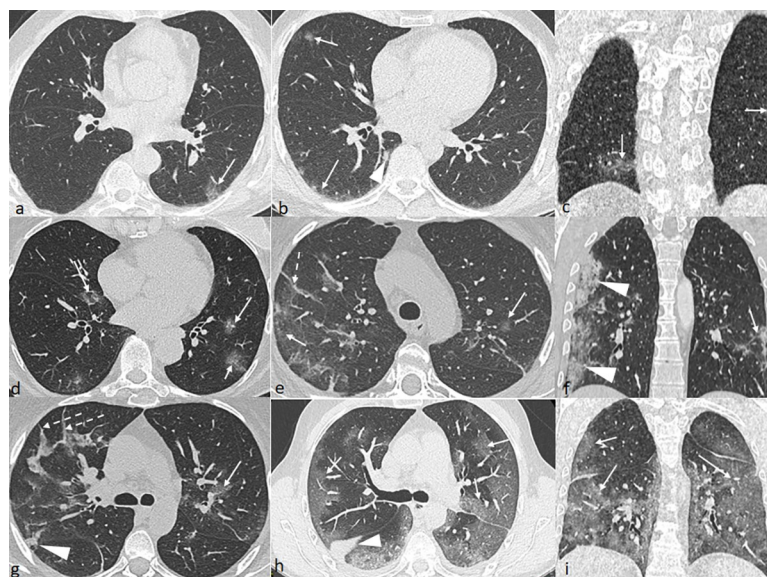


Fig 2. Chest CT of patients with laboratory-proven COVID-19 pneumonia and paucisymptomatic patients. Minimal form (a-c): Axial (a,b) and frontal reconstructions (c) of patchy ground-glass opacities (white arrows) with segmental parenchyma involvement of 1 to 3 patchy lesions. Intermediate form (d-f): Axial (d,e) and frontal reconstructions (f) of patchy ground-glass opacities (white arrows), band-like appearance (dotted arrow), and areas of consolidation (arrowheads) with involvement less than 50%. Severe form (g-i): Axial (g,h) and frontal reconstructions (i) of patchy ground-glass opacities (white arrows), band-like appearance (dotted arrow), and areas of consolidation (arrowheads) with an involvement greater than 50%.

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(100%). On LDCT 23 patients showed no abnormalities (28%), 56 patients demonstrated GGOs (67%), 21 patients had areas of consolidation (25%). An exclusive peripheral distribution was found in 33 patients (40%). Only 9 patients showed crazy paving patterns (11%) (Fig 2).

COVID19-LDCT-score

The mean COVID19-LDCT score was 19 ± 28 with a mean right lung score of 10 ± 15 and a mean left lung score of 8 ± 15 (Table 2). A significant correlation was found between the

Table 2. Imaging data.

	Total Population
Imaging data	
Dose x length product (mGy.cm)	41.7 ± 15.5 [30.1–100.1]
GGOs	56/80; 67%
Consolidation	21/80; 25%
Exclusively peripheral lesions	33/80; 40%
Crazy paving patterns	9/80; 11%
Normal imaging	23/80; 28%
Pleural effusions	4/80; 5%
Mediastinal nodes	4/80; 5%
COVID19-LDCT score	
Lung score	19 ± 29 [0–161]

Note: The qualitative variables are expressed as figures with percentages, and the continuous variables are expressed as the mean values \pm SDs. GGOs: ground-glass opacities; LDCT: Low-dose computed tomography.

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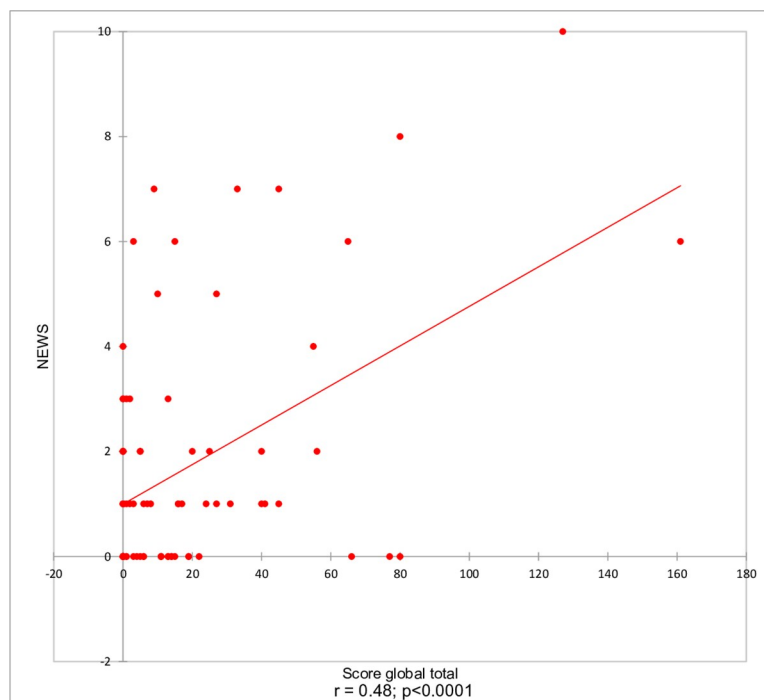


Fig 3. Correlation between the NEWS and COVID19-LDCT score. A significant correlation was found. Pearson coefficient = 0.48; $p < 0.001$.

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NEWS and the COVID19-LDCT score ($r = 0.48$, $p < 0.001$). The correlation was also significant for the right lung and the left lung (Fig 3).

No clinical symptoms were significant risk factors to find abnormalities on LDCT and especially cough was not a relevant clinical symptom to determine if patients had risk to have lung involvement on LDCT.

Mean pulse oxymetry show a tendency to decrease in patient with pneumonia on LDCT than without pneumonia: $97.6\% \pm 1.9$ [92.0–100.0] and $96.9\% \pm 2.1$ [91.0–100.0] respectively ($p = 0.07$). Dyspnea was found in 11/80 cases. Over 69 patients without dyspnea 47 have an abnormal LDCT and 22 were normal. Patients with normal LDCT showed a higher pulse oxymetry $98.0\% \pm 1.4$ [95.0–100.0] compared to patient with pneumonia on LDCT $97.2\% \pm 1.8$ [91.0–100.0] ($p = 0.028$) (Fig 4).

Score NEWS

Sixty-nine patients were classified as having low NEWS, and 11 patients had high NEWS. The COVID-LDCT score was 13 ± 19 in the low-NEWS group and was significantly higher in the high-NEWS group (52 ± 52 ; $p = 0.001$).

There was no significant difference between groups according to their symptoms or blood pressure at the time of admittance. Patients with a NEWS > 4 had a significantly higher temperature, heart rate, and respiratory rate and a lower oxygen saturation than patients with a low NEWS ($38.3^\circ\text{C} \pm 1.0$ versus $37.3^\circ\text{C} \pm 0.8$; $p < 0.0001$, $95 \text{ bpm} \pm 8$ versus $81 \text{ bpm} \pm 12$; $p < 0.0001$, $25/\text{min} \pm 9$ versus $18/\text{min} \pm 4$; $p < 0.0001$, $94\% \pm 2$ versus $98\% \pm 2$; $p < 0.0001$; respectively). Oxygen was needed in 7 of 11 patients (64%) in the high-NEWS group and in 3 of 69 patients (7%) in the low-NEWS group (Table 3). The clinical factors associated with high COVID19-LDCT Score in univariable analysis were diabetes (OR = 6.9 [1.32–36.2], $p = 0.02$),

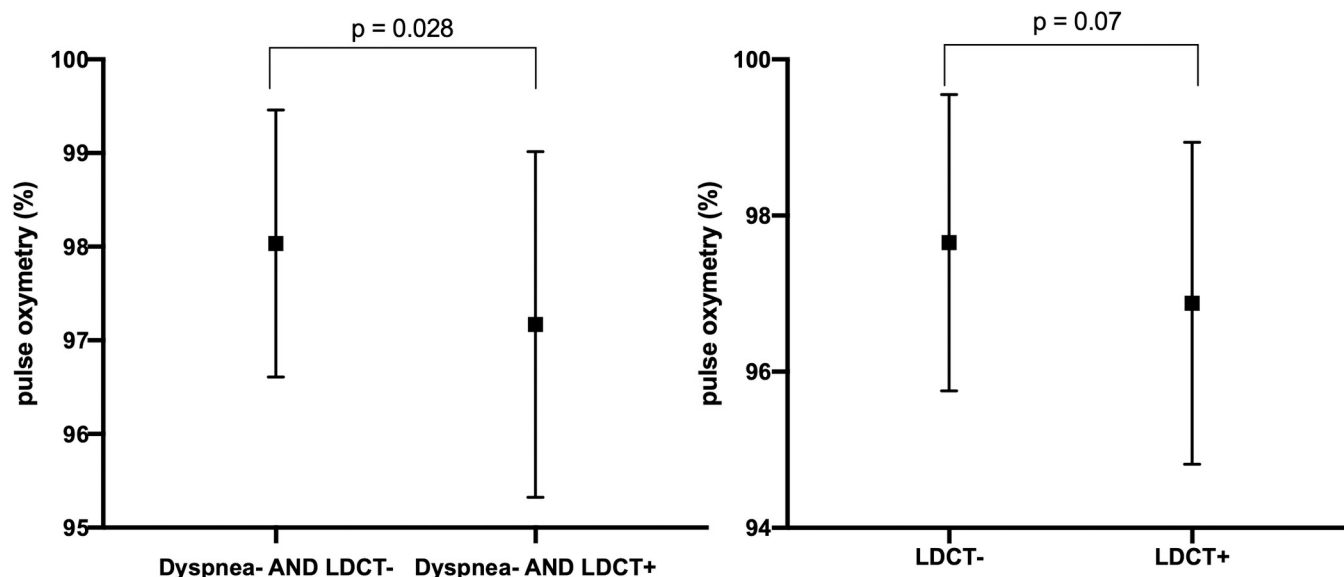


Fig 4. Pulse oxymetry according to LDCT and dyspnea. A significant difference was found between pneumonia and non pneumonia on LDCT concerning the oxymetry ($p = 0.07$) and between pneumonia and non pneumonia on LDCT among patient without dyspnea ($p = 0.028$). LDCT: low dose computed tomography.

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hypertension (OR = 7.20 [1.22–42.5], $p = 0.03$), dyspnoea (OR = 7.65 [1.66–35.3], $p = 0.01$) and respiratory rate (OR = 1.15 [1.03–1.30], $p = 0.02$). Because of the limited number of patients with high COVID19-LDCT score and the sample size, no multivariable analysis was performed.

Discussion

The main findings of the presented work are that 1) LDCT scans can depict the typical features of SARS-CoV-2 pneumonia with limited irradiation; and 2) the COVID19-LDCT score is correlated with the NEWS used routinely to assess disease severity and patient prognosis.

Table 3. Low- and high-risk groups.

	<i>Low-risk patients</i>	<i>High-risk patients</i>	
<i>Clinical data's</i>	NEWS 0–4 N = 69	NEWS >4 N = 11	
Symptoms	64/69; 93%	11/11; 100%	
Temperature (°C)	37.3 ± 0.8 [35.8–39.5]	38.3 ± 1.0 [36.5–40.0]	$p < 0.001$
Heart rate (bpm)	81 ± 12 [53–110]	95 ± 8 [80.0–105.0]	$p < 0.001$
Systolic blood pressure (mmHg)	134 ± 22 [100–219]	128 ± 18 [107–160]	$p = 0.501$
Diastolic blood pressure (mmHg)	77 ± 14 [11–120]	72 ± 13 [50–90]	$p = 0.440$
Respiratory rate (/min)	18 ± 4 [10–28]	25 ± 9 [8–36]	$p < 0.001$
Oxygen saturation (%)	98 ± 2 [92–100]	94 ± 2 [91–98]	$p < 0.001$
Oxygen need	3/69; 4%	7/11; 64%	$p < 0.001$
<i>COVID19-LDCT score</i>			
Lung score	13 ± 19 [0–80]	52 ± 52 [3–161]	$P = 0.001$

Note: The qualitative variables are expressed as figures with percentages, and the continuous variables are expressed as the mean values ± SDs. °C: Celsius degree; bpm: beat per minute; LDCT: low-dose computed tomography; mmHg: millimeter of mercury.

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Unenhanced chest CT was performed using a low-dose acquisition protocol. All the CT scans performed allowed optimal analysis of parenchyma involvement. Recently, recommendations have been made regarding the use of LDCT for COVID19 that indicate preference for LDCT [15]. They reported a mean dose-length product of 14.4 mGy.cm. A patient with COVID-19 pneumonia could have 3 to 6 chest CT scans in a short period of time, and a healthy patient could have 1 or 2 chest CT scans to ensure that they did not have COVID-19 [16]. Irradiation awareness is needed, especially for younger patients [17]. The present study showed that CT image quality using LDCT is sufficient for depicting all the typical features of COVID-19 pneumopathy. Acquisition parameters settings should be adapted to each patient to maintain good contrast-to-noise ratio and signal-to-noise ratio, allowing adequate quality of the lung parenchyma images [18]. Debray et al. have already shown in patients with lung transplantation that the use of LDCT could be interesting to decrease global irradiation because of repeated imaging for follow-up [19]. However, in patients with COVID-19 an enhanced chest CT scan might be required for patients with clinical worsening considering an over-risk of pulmonary embolism caused by inflammatory syndrome and bed rest.

As recently described, the clinico-radiological correlation is good, and diffuse lung involvement is frequently observed in severe forms [20, 21]. Lesions extent is higher in patients with a need for intensive care units than for ordinary units. In particular, lymph nodes and pleural effusion are highly frequent in severe patients. The present paper is in favor of a correlation between disease extent and clinical severity. There are some patients with a RT-PCR positive result and a normal chest CT 23 of 80 (28%), that is not consistent with the whole studies on CT scan sensitivity. We explained that because patients came from a screening center and some patients are tested because they are contact case with infected patients. The sensitivity of the CT scan depends on the level of pre-test risk of the population to present lung involvement. Disappointingly, we did not highlight any symptoms that could predict pulmonary involvement, particularly cough, which is generally one of the main symptoms of manifestations of alveolar involvement. It is in line with a recent publication from Yang et al. showing that patients could be COVID-19 infected and had few or no clinical symptoms with a normal chest CT and/or negative RT-PCR test [22].

The COVID19-LDCT score may provide the quantitative measurement of COVID-19 injury. Patients can be easily classified in various degrees of the disease. This type of CT score was first described in 2004 for severe acute respiratory syndrome (SARS). Investigators divided each lung into 3 parts (upper, middle and lower) and evaluated the involvement on a scale of 0–4: 0, <25%, 25–50 >50% and >75% involvement: the maximum possible score was 24 [23]. The present approach uses the simplest scale, comprising 3 kinds of impairment: minimal, intermediate, and severe. It focuses on the anatomical distribution of lesions based on segmental analysis. This scoring system is based on the decreased in lung function applied in thoracic surgery. It has been shown that wedge resection spare parenchyma loss more than segmentectomy and segmentectomy more than lobectomy [24]. We guess that a minimal involvement will have only few consequences on hematosi and more than 50% of segment involvement seems lead to a total shunt effect and we grade it 10. The score over 50/200 had been arbitrary chosen for severe involvement because that mean involvement of 50% of the lung corresponding to a lobectomy. Patients with comorbidities such as emphysema or former thoracic surgery have a higher risk of death in case of lobectomy [25]. We considered that a score > 50/200 could lead to death according to the comorbidities and need to classify patients in the severe group.

There are a few limitations in the present study. Our population was mainly paucisymptomatic patients which did not allow us to have a wide repartition of NEWS and CT scores for correlation, especially for high scores. This could be explained because we enrolled the 80 first

patients with COVID-19 pneumonia in our centre and the severe forms are not the most frequent. Another limit is the low number of patient that does not allowed us to perform a multivariate analysis and further studies are needed to establish this score a clinical prognosis tool.

Low-dose CT scan could depict the typical features of COVID-19 pneumonia. In this population of 80 COVID-19 patients detected positive by RT-PCR, there was a significant correlation between the clinical NEWS and the COVID19-LDCT score, showing the close relationship between signs and the extent of disease in the lung. More work is required to assess whether this score could add clinically relevant information to assess the prognosis of patients with COVID-19 pneumonia.

Supporting information

S1 File. IRB.

(PDF)

S1 Data.

(XLSX)

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Author Contributions

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Methodology: Philippe Parola.

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Writing – original draft: Thomas Leger, Paul Habert.

Writing – review & editing: Thomas Leger, Alexis Jacquier, Didier Raoult, Jean-Yves Gaubert, Paul Habert.

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