Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Clinical Microbiology and Infection 26 (2020) 1417.e5–1417.e8

Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

Research note

CT lung lesions as predictors of early death or ICU admission in COVID-19 patients

Yvon Ruch [1,*], Charlotte Kaeuffer [1], Mickael Ohana [2], Aissam Labani [2], Thibaut Fabacher [3], Pascal Bilbault [4], Sabrina Kepka [4], Morgane Solis [5], Valentin Greigert [1], Nicolas Lefebvre [1], Yves Hansmann [1], François Danion [1]

[1] Department of Infectious Disease, Strasbourg University Hospital, Strasbourg, France
[2] Department of Radiology, Strasbourg University Hospital, Strasbourg, France
[3] Department of Biostatistics, Strasbourg University Hospital, Strasbourg, France
[4] Department of Emergency Medicine, Strasbourg University Hospital, Strasbourg, France
[5] Department of Virology, Strasbourg University Hospital, Strasbourg, France

ARTICLE INFO

Article history:
Received 15 May 2020
Received in revised form
16 July 2020
Accepted 19 July 2020
Available online 24 July 2020

Editor: M. Paul

Keywords:
Computed tomography
Coronavirus
COVID-19
Ground-glass opacities
Visual quantification

ABSTRACT

Objective: The main objective of this study was to investigate the prognostic value of early systematic chest computed tomography (CT) with quantification of lung lesions in coronavirus disease 2019 (COVID-19) patients.

Methods: We studied 572 patients diagnosed with COVID-19 (confirmed using polymerase chain reaction) for whom a chest CT was performed at hospital admission. Visual quantification was used to classify patients as per the percentage of lung parenchyma affected by COVID-19 lesions: normal CT, 0–10%, 11–25%, 26–50%, 51–75% and >75%. The primary endpoint was severe disease, defined by death or admission to the intensive care unit in the 7 days following first admission.

Results: The mean patient age was 66.0 ± 16.0 years, and 343/572 (60.0%) were men. The primary endpoint occurred in 206/572 patients (36.0%). The extent of lesions on initial CT was independently associated with prognosis (odds ratio = 2.35, 95% confidence interval 1.24–4.46; $p < 0.01$). Most patients with lung involvement >50% (66/95, 69.5%) developed severe disease compared to patients with lung involvement of 26–50% (70/171, 40.9%) and ≤25% (70/306, 22.9%) ($p < 0.01$ and $p < 0.01$, respectively). None of the patients with normal CT (0/14) had severe disease.

Conclusion: Chest CT findings at admission are associated with outcome in COVID-19 patients.

Yvon Ruch, Clin Microbiol Infect 2020;26:1417.e5–1417.e8

Introduction

Chest computed tomography (CT) has shown promise as a diagnostic tool for coronavirus disease 2019 (COVID-19) [1,2]. Initial studies have described a stereotypical time course with successive radiological stages, ground-glass opacities (GGOs) being the main initial lesion [3,4]. Quantitative CT lung analysis shows a good association with patient prognosis in those with non-COVID-19 acute respiratory distress syndrome [5]. From March 2020, patients admitted to the Strasbourg University Hospital with suspected COVID-19 were managed using a specific protocol, including reverse-transcription polymerase chain reaction (RT-PCR) on respiratory samples and a systematic chest CT to improve the triage of patients. We aimed to determine the early prognostic value of systematic chest CT with quantification of lung lesions in COVID-19 patients performed at the time of admission.

Methods

We conducted a retrospective study of prospectively collected data. We included patients with positive PCR and CT performed, this study was not interventional so the chest CT was not realized after inclusion in the study. All consecutive patients aged ≥18 years—hospitalized at the Strasbourg University Hospital in March 2020 with COVID-19 confirmed using RT-PCR and a chest

* Corresponding author. Yvon Ruch, Department of Infectious Disease, Strasbourg University Hospital, 1 Place de l'Hôpital, 67091, Strasbourg, Cedex. France.
E-mail address: yvon.ruch@chru-strasbourg.fr (Y. Ruch).

https://doi.org/10.1016/j.cmi.2020.07.030
1198-743X/

CT performed with quantitative evaluation of the lesions—were enrolled in this cohort study. Patients for whom the CT was realized ≥48 h after admission were excluded. Non-contrast-enhanced chest CT images were acquired on an 80-row scanner (Aquilion Prime SP, Canon Medical Systems), with parameters based on the patient's morphotype (tension 100–135 kV and maximum mAs 2–50) [6]. Images were reconstructed with a slice thickness of 1 mm in mediastinal and parenchymal windows using an iterative reconstruction algorithm (AIDR-3D, Canon Medical Systems) and read on dedicated workstations with multiplanar and maximum intensity projection reconstructions. CT angiography was performed secondarily for patients with suspected pulmonary embolism. Visual quantification of the lung lesions was performed at the time of the CT by two different radiologists who were blinded to the patients' clinical condition. Evaluations were made independently, but discrepancies were resolved by consensus. The CT images were classified as per the percentage of the whole lung parenchyma affected by COVID-19 lesions—GGO and/or consolidations—in the following six groups: normal CT (no lesion), minimal (0–10%), moderate (11–25%), important (26–50%), severe (51–75%), and critical (>75%) [7]. To simplify the analysis of the clinical data, the patients were divided into three subgroups: ≤25%, 26–50%, and >50%.

The primary endpoint was early severe disease, defined as death or intensive care unit (ICU) admission in the 7 days after hospital admission. Statistical analyses were performed using R software (version 3.5.2). This study was approved by the Ethics Committee of Strasbourg University Hospital (N°CE–2020–51). Oral informed consent was obtained from all the patients.

Results

During the study period, 572 patients were assessed out of 854 patients with positive RT-PCR (Supplementary Material Fig. S1). The mean patient age was 66.0 years (standard deviation 16.0; range 20–95 years), and 343/572 patients (60.0%) were men. Among all 572 patients, chest CT was normal in 14 patients (2.4%), and showed minimal, moderate, important, severe, and critical lesions in 68 (11.9%), 224 (39.2%), 171 (29.9%), 82 (14.3%), and 13 patients (2.3%), respectively. Most patients had bilateral involvement (524/572, 91.6%) and GGO (540/572, 94.4%). Consolidations were observed in 372/572 patients (65.0%).

There were no significant differences in the prevalence of comorbidities based on the extent of the lesions on CT (Table 1). Patients with lung involvement >50% had a significantly higher C-reactive protein (CRP) level and neutrophil count, lower lymphocyte count, and more consolidations on CT compared to those with lung involvement ≤25% ($p < 0.01$ for each comparison). Finally, 16/95 patients (16.8%) with lung involvement >50% were diagnosed with pulmonary embolism.

Table 1
Baseline characteristics of the 572 COVID-19 patients according to the extent of lesions on CT

	Extent of lesions on CT			p
	≤25% ($n = 306$)	26–50% ($n = 171$)	>50% ($n = 95$)	
Age, mean ± SD (years)	66.5 ± 16.2	65.2 ± 16.2	65.6 ± 14.9	0.69
Male sex	153 (50.0)	114 (66.7)	76 (80.0)	<0.01
Body mass index, mean ± SD (kg/m^2)	28.7 ± 6.0 ($n = 265$)	29.0 ± 5.9 ($n = 151$)	29.6 ± 4.3 ($n = 86$)	0.13
Comorbidity				
Diabetes	76 (24.8)	44 (25.7)	25 (26.3)	0.95
Hypertension	161 (52.6)	87 (50.9)	49 (51.6)	0.93
Chronic heart failure	30 (9.8)	21 (12.3)	5 (5.3)	0.18
Chronic lung disease	58 (19.0)	23 (13.5)	18 (18.9)	0.28
Immunodepression	8 (2.6)	5 (2.9)	3 (3.2)	0.94
Active malignancy	20 (6.5)	9 (5.3)	4 (4.2)	0.66
Clinical findings				
Fever	224 (73.2)	146 (85.4)	67 (70.5)	<0.01
Dyspnea	180 (58.8)	140 (81.9)	82 (86.3)	<0.01
Cough	192 (62.7)	126 (73.7)	58 (61.1)	0.03
Chest pain	28 (9.2)	17 (9.9)	7 (7.4)	0.78
SpO_2 (%)	94 ± 4 ($n = 302$)	92 ± 6 ($n = 166$)	90 ± 8 ($n = 95$)	<0.01
Maximal oxygen level (L/min)	2 ± 3 ($n = 288$)	4 ± 5 ($n = 159$)	9 ± 12 ($n = 80$)	<0.01
Time between symptom onset and CT performance (days)	6 ± 6	7 ± 6	7 ± 4	<0.01
Imaging findings				
Bilateral involvement	260 (85.0)	169 (98.8)	95 (100.0)	<0.01
Ground-glass opacities	277 (90.5)	169 (98.8)	94 (98.9)	<0.01
Consolidations	174 (56.9)	127 (74.3)	71 (74.7)	<0.01
Micronodules	20 (6.5)	4 (2.3)	7 (7.4)	0.10
Pulmonary embolism[a]	7 (2.3)	6 (3.5)	16 (16.8)	<0.01
Laboratory findings				
C-reactive protein (mg/L)	59 ± 85 ($n = 300$)	104 ± 84 ($n = 169$)	154 ± 114 ($n = 91$)	<0.01
Neutrophil count (cells/mm^3)	4000 ± 2877 ($n = 302$)	5100 ± 2900 ($n = 169$)	6375 ± 4592 ($n = 94$)	<0.01
Lymphocyte count (cells/mm^3)	900 ± 527 ($n = 302$)	930 ± 590 ($n = 169$)	740 ± 475 ($n = 95$)	<0.01
Serum creatinine (μmol/L)	74 ± 35 ($n = 301$)	77 ± 35 ($n = 170$)	84 ± 47 ($n = 95$)	0.2
Aspartate aminotransferase (U/L)	37 ± 26 ($n = 242$)	47 ± 31 ($n = 143$)	58 ± 42 ($n = 84$)	<0.01
Lactate (mmol/L)	0.9 ± 0.5 ($n = 186$)	1.1 ± 0.7 ($n = 123$)	1.2 ± 0.9 ($n = 83$)	<0.01
Outcome				
Severe disease on day 7[b]	70 (22.9)	70 (40.9)	66 (69.5)	<0.01
Severe disease on day 30[b]	82 (26.8)	74 (43.3)	71 (74.7)	<0.01
Death on day 7	19 (6.2)	20 (11.7)	16 (16.8)	<0.01
Death on day 30	33 (10.8)	29 (17.0)	27 (28.4)	<0.01

Data are given in *n* (%) or median ± interquartile range, otherwise specified. The inferential analysis for the categorical data was performed using the χ^2 test or Fisher's exact test (2 × 3 comparison), as per the theoretical size of the samples. Continuous data were compared using a non-parametric test (Kruskal–Wallis test).
COVID-19, coronavirus disease 2019; CT, computed tomography; SD, standard deviation; SpO_2, peripheral oxygen saturation.
[a] Only 10/29 pulmonary embolisms were diagnosed at admission.
[b] Defined as intensive care unit admission or death.

Overall, 206/572 patients (36.0%) met the criteria for early severe disease, including 55/572 (9.6%) who died. The extent of lesions on the initial CT was associated with severe disease (Fig. 1A). Among the 14 patients with normal chest CT at admission, none developed severe disease. Most patients with lung involvement >50% were admitted to the ICU or died (66/95, 69.5%), and this rate was lower in patients with lung involvement of 26–50% (70/171, 40.9%) and ≤25% (70/306, 22.9%) (Table 1). In multivariate analysis, lung involvement >50% was significantly associated with early severe disease (odds ratio 2.35, confidence interval 1.24–4.46; $p < 0.01$) (Supplementary Material Table S1). Survival analysis showed a significantly reduced 30-day event-free survival in patients with lung involvement of 26–50% and >50% ($p < 0.001$) (Supplementary Material Fig. S2).

The median time between the onset of the symptoms and CT was 7 days (interquartile range 6.0). This duration was shorter in patients with normal CT or minimal lesions (Fig. 1B). None of the patients with minimal lesions and symptoms for more than 10 days has developed severe disease, while 10/12 (83.3%) of those with minimal lesions and severe disease presented with symptoms for ≤5 days (Fig. 1C).

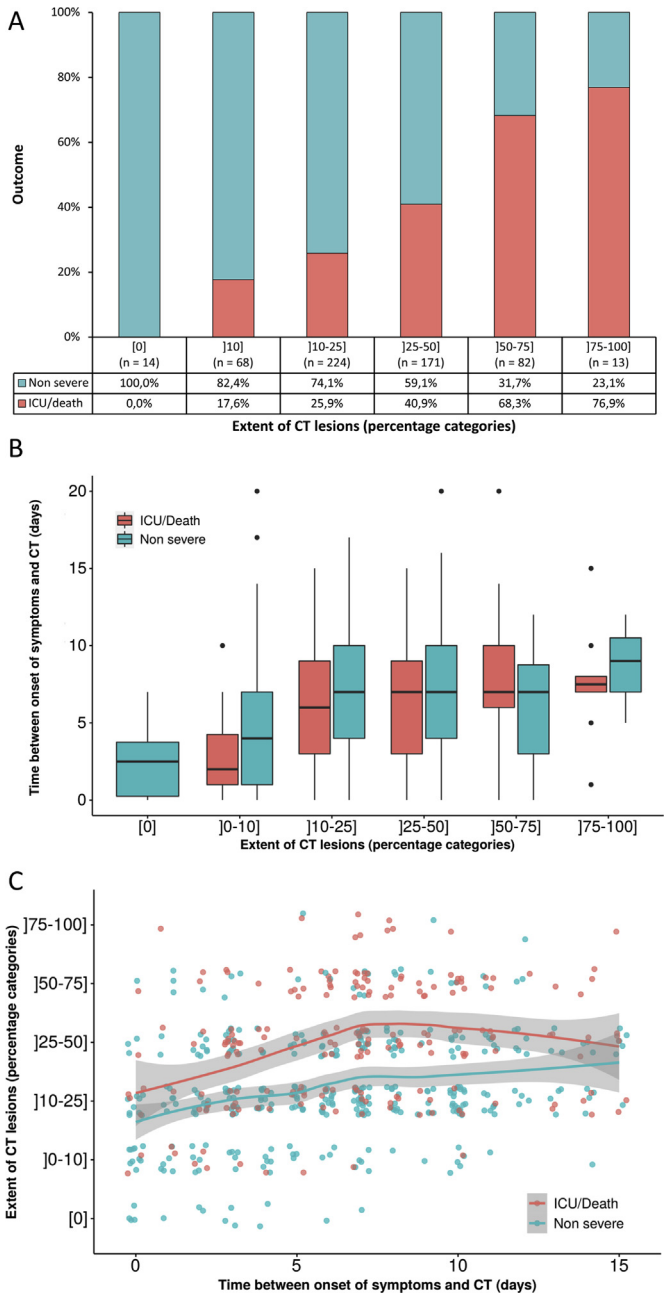

Fig. 1. Outcome and time from onset of symptoms as per the quantification of lesions on computed tomography (CT). (A) Histogram showing the outcome according to the extent of lesions on CT. (B) Box plot showing the time between symptom onset and CT performance as per the extent of lesions on CT. (C) Scatter plot showing the extent of lesions on CT as per the time between symptom onset and CT performance. In order to ease visualization, noise was randomly added to each point. Curves were fitted through points with the locally weighted scatterplot smoothing (LOESS) method using the 'ggplot 2' R package. Shaded area represents the standard error.

Discussion

Our study has shown that visual quantification of CT lung lesions is associated with early death or ICU admission in hospitalized patients, especially in patients with lung involvement >50%.

Several risk factors for severe COVID-19 have been reported, such as older age, male sex, and chronic diseases [8,9]. The chest CT has shown benefit in the diagnosis of COVID-19 pneumonia; however, its relevance as a prognostic factor remains unclear [1]. Based on a study of 134 COVID-19 patients, Liu et al. showed that CT quantification of pneumonia lesions can predict early progression to severe illness [10].

Although our study has employed one of the largest cohorts on COVID-19 imaging, it has some limitations. We chose to evaluate early prognosis with the outcome on day 7; a longer endpoint may have increased the number of patients with severe disease. However, most deaths and ICU admissions occurred within 7 days after admission in our study, and peak lung involvement was reached before 2 weeks of evolution in previous studies [3,11]. Furthermore, we performed visual quantification, while other studies have used dedicated software to quantify lung lesions [10,11]. Although this makes our evaluation dependent on the experience of radiologists, this facilitates its generalization to centres that are not equipped with such software.

Four radiological stages have been described, with progressive extent of GGO and the secondary onset of consolidations [3,12]. The higher CRP level, neutrophilia and lymphopenia in our severe patients suggested an inflammatory profile that appears to be associated with lung consolidations and subsequent worsening of their respiratory condition [13]. Consolidations are associated with poor outcome, as previously described [14]. Patients with lung involvement >50% were significantly more often diagnosed with pulmonary embolism. This higher risk of thrombosis in patients with severe COVID-19 has been reported, although the pathophysiology remains unclear and may possibly involve several mechanisms [15].

The timing between the onset of symptoms and the performance of CT was lower for patients with lung involvement ≤25%, indicating that these patients could have presented at an earlier disease stage. However, this difference was only 1 day, raising a question about its clinical relevance. Fourteen patients (2.4%) had no lesions on the initial chest CT, and among these 10/14 had symptoms for ≤3 days, as has previously been reported [1,2]. None of these patients died or was admitted to the ICU, suggesting that normal CT at the time of hospital admission could predict a good prognosis.

In conclusion, in addition to its diagnostic value, chest CT could predict severe COVID-19 pneumonia as visual quantification of the lesions appears to be associated with early prognosis. Whether this strategy should be systematically implemented remains to be evaluated in further studies.

Author contributions

All authors have made substantial contributions to this work and have approved the final manuscript. Concept and design: YR, CK, FD, MO and AL. Acquisition and interpretation of imaging data: MO and AL. Collection of clinical data: YR, CK, FD, YH, NL, VG, PB and SK. Virological analysis: MS. Analysis and interpretation of clinical data: YR, CK and FD. Statistical analysis: YR, TF, FD and VG. Writing of the original draft: YR and FD.

Transparency declaration

The authors report no conflicts of interest. MO reports personal fees from Canon Medical Systems, outside the submitted work. This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cmi.2020.07.030.

References

[1] Ai T, Yang Z, Hou H, Zhan C, Chen C, Lv W, et al. Correlation of chest CT and RT-PCR testing in coronavirus disease 2019 (COVID-19) in China: a report of 1014 cases. Radiology 2020:200642. https://doi.org/10.1148/radiol.2020200642.

[2] Fang Y, Zhang H, Xie J, Lin M, Ying L, Pang P, et al. Sensitivity of chest CT for COVID-19: comparison to RT-PCR. Radiology 2020:200432. https://doi.org/10.1148/radiol.2020200432.

[3] Pan F, Ye T, Sun P, Gui S, Liang B, Li L, et al. Time course of lung changes on chest CT during recovery from 2019 novel coronavirus (COVID-19) pneumonia. Radiology 2020:200370. https://doi.org/10.1148/radiol.2020200370.

[4] Li M, Lei P, Zeng B, Li Z, Yu P, Fan B, et al. Coronavirus disease (COVID-19): spectrum of CT findings and temporal progression of the disease. Acad Radiol 2020;27:603–8. https://doi.org/10.1016/j.acra.2020.03.003.

[5] Nishiyama A, Kawata N, Yokota H, Sugiura T, Matsumura Y, Higashide T, et al. A predictive factor for patients with acute respiratory distress syndrome: CT lung volumetry of the well-aerated region as an automated method. Eur J Radiol 2020;122:108748. https://doi.org/10.1016/j.ejrad.2019.108748.

[6] Ludes C, Labani A, Severac F, Jeung MY, Leyendecker P, Roy C, et al. Ultra-low-dose unenhanced chest CT: prospective comparison of high kV/low mA versus low kV/high mA protocols. Diagn Interv Imaging 2019;100:85–93. https://doi.org/10.1016/j.diii.2018.11.012.

[7] Revel M-P, Parkar AP, Prosch H, Silva M, Sverzellati N, Gleeson F, et al. COVID-19 patients and the radiology department—advice from the European society of radiology (ESR) and the European society of thoracic imaging (ESTI). Eur Radiol 2020. https://doi.org/10.1007/s00330-020-06865-y.

[8] Zhang J, Wang X, Jia X, Li J, Hu K, Chen G, et al. Risk factors for disease severity, unimprovement, and mortality in COVID-19 patients in Wuhan, China. Clin Microbiol Infect 2020;26:767–72. https://doi.org/10.1016/j.cmi.2020.04.012.

[9] Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. JAMA Intern Med 2020. https://doi.org/10.1001/jamainternmed.2020.0994.

[10] Liu F, Zhang Q, Huang C, Shi C, Wang L, Shi N, et al. CT quantification of pneumonia lesions in early days predicts progression to severe illness in a cohort of COVID-19 patients. Theranostics 2020;10:5613–22. https://doi.org/10.7150/thno.45985.

[11] Huang L, Han R, Ai T, Yu P, Kang H, Tao Q, et al. Serial quantitative chest CT assessment of COVID-19: deep-learning approach. Radiol Cardiothorac Imaging 2020;2:e200075. https://doi.org/10.1148/ryct.2020200075.

[12] Shi H, Han X, Jiang N, Cao Y, Alwalid O, Gu J, et al. Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study. Lancet Infect Dis 2020;20:425–34. https://doi.org/10.1016/S1473-3099(20)30086-4.

[13] Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall RS, Manson JJ, et al. COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet 2020;395:1033–4. https://doi.org/10.1016/S0140-6736(20)30628-0.

[14] Yuan M, Yin W, Tao Z, Tan W, Hu Y. Association of radiologic findings with mortality of patients infected with 2019 novel coronavirus in Wuhan, China. PloS One 2020;15:e0230548. https://doi.org/10.1371/journal.pone.0230548.

[15] Helms J, Tacquard C, Severac F, Leonard-Lorant I, Ohana M, Delabranche X, et al. High risk of thrombosis in patients with severe SARS-CoV-2 infection: a multicenter prospective cohort study. Intensive Care Med 2020:1–10. https://doi.org/10.1007/s00134-020-06062-x.