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Research note

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

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Keywords

Computed tomography; coronavirus; COVID-19; ground-glass opacities; visual quantification

1 **Abstract**

2 Objective

3 The main objective of this study was to investigate the prognostic value of early systematic
4 chest computed tomography (CT) with quantification of lung lesions in coronavirus disease
5 2019 (COVID-19) patients.

6 Methods

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

13 Results

14 The mean patient age was 66.0 ± 16.0 years, and 343/572 (60.0%) were men. The primary
15 endpoint occurred in 206/572 (36.0%) patients. The extent of lesions on initial CT was
16 independently associated with prognosis (odds ratio = 2.35, 95% confidence interval 1.24–
17 4.46; $p < 0.01$). Most patients with lung involvement >50% developed severe disease (66/95,
18 69.5%), compared to patients with lung involvement of 26%–50% (70/171, 40.9%) and $\leq 25\%$
19 (70/306, 22.9%) ($p < 0.01$ and $p < 0.01$, respectively). None (0/14) of the patients with normal
20 CT had severe disease.

21 Conclusion

22 Chest CT findings at admission are associated with bad outcome in COVID-19 patients.

23 **Introduction**

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

34

35 **Methods**

36 We conducted a retrospective study of prospectively collected data. All consecutive patients
37 aged ≥ 18 years, with COVID-19 confirmed using RT-PCR and a chest CT performed with
38 quantitative evaluation of the lesions, hospitalised at the Strasbourg University Hospital in
39 March 2020 were enrolled in this cohort study. Patients for whom the CT was realised ≥ 48
40 hours after admission were excluded. Non-contrast enhanced chest CT images were acquired
41 on an 80-row scanner (Aquilion Prime SP, Canon Medical Systems), with parameters based on
42 the patient's morphotype (tension 100-135kV and maximum mAs 2-50) [6]. Images were
43 reconstructed with a slice-thickness of 1 mm in mediastinal and parenchymal windows using
44 an iterative reconstruction algorithm (AIDR-3D, Canon Medical Systems) and read on
45 dedicated workstations with multiplanar and maximum intensity projection reconstructions.
46 CT angiography was performed secondarily for patients suspected of pulmonary embolism.
47 Visual quantification of the lung lesions was performed at the time of the CT by two different

48 radiologists who were blinded to the patients' clinical condition. Evaluations were made
49 independently, but discrepancies were resolved in consensus. The CT images were classified as
50 per the percentage of the whole lung parenchyma affected by COVID-19 lesions– GGO and/or
51 consolidations– in the following six groups: normal CT (no lesion), minimal (0%–10%),
52 moderate (11%–25%), important (26%–50%), severe (51%–75%), and critical (>75%) [7]. To
53 simplify the analysis of clinical data, the patients were divided into three subgroups: ≤25%, 26–
54 50%, and >50%.

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

59

60 **Results**

61 During the study period, 572 patients were assessed out of 854 patients with positive RT-PCR
62 (Supplementary material, Figure S1). The mean patient age was 66.0 years [standard deviation
63 16.0; range 20–95 years], and 343/572 (60.0%) patients were men. Among all 572 patients,
64 chest CT was normal in 14 (2.4%) patients, and showed minimal, moderate, important, severe,
65 and critical lesions in 68 (11.9%), 224 (39.2%), 171 (29.9%), 82 (14.3%), and 13 (2.3%) patients,
66 respectively. Most patients had bilateral involvement (524/572, 91.6%) and GGO (540/572,
67 94.4%). Consolidations were observed in 372/572 (65.0%) patients.

68 There were no significant differences in the prevalence of comorbidities based on the extent of
69 the lesions on CT (Table 1). Patients with lung involvement >50% had significantly higher C-
70 reactive protein (CRP) level and neutrophil count, lower lymphocyte count, and more
71 consolidations on CT compared to those with lung involvement ≤25% ($p < 0.01$, for each

72 comparison). Finally, 16/95 (16.8%) patients with lung involvement >50% were diagnosed with
73 pulmonary embolism.

74 Overall, 206/572 (36.0%) patients met the criteria for early severe disease, including 55/572
75 (9.6%) who died. Extent of lesions on the initial CT was associated with severe disease (Figure
76 1, A). Among the 14 patients with normal chest CT at admission, none developed severe
77 disease. Most patients with lung involvement >50% were admitted to the ICU or died (66/95,
78 69.5%), and this rate was lower in patients with lung involvement of 26%–50% (70/171, 40.9%)
79 and ≤25% (70/306, 22.9%) (Table 1). In multivariate analysis, lung involvement >50% was
80 significantly associated with early severe disease (odds ratio 2.35, confidence interval 1.24–
81 4.46; $p < 0.01$) (Supplementary material, Table S1). Survival analysis showed a significantly
82 reduced 30-days event-free survival in patients with lung involvement of 26%–50% and >50%
83 ($p < 0.001$) (Supplementary material, Figure S2).

84 The median time between the onset of the symptoms and CT was 7 days (interquartile range
85 6.0). This duration was shorter in patients with normal CT or minimal lesions (Figure 1, B).
86 None of the patients with minimal lesions and symptoms for more than ten days have
87 developed severe disease, while 10/12 (83.3%) of those with minimal lesions and severe
88 disease presented with symptoms for five days or less (Figure 1, C).

89

90 **Discussion**

91 Our study has shown that visual quantification of CT lung lesions was associated with early
92 death or ICU admission in hospitalised patients, especially in patients with lung involvement
93 >50%.

94 Several risk factors for severe COVID-19 have been reported, such as older age, male sex, and
95 chronic diseases [8,9]. The chest CT has shown benefit in COVID-19 pneumonia diagnosis;

96 however, its interest as a prognosis factor remains unclear [1]. Based on a study on 134 COVID-
97 19 patients, Liu and al. showed that CT quantification of pneumonia lesions can predict early
98 progression to severe illness [10].

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

108 Four radiological stages have been described, with progressive extent of GGO and the
109 secondary onset of consolidations [3,12]. The higher CRP level, neutrophilia and lymphopenia
110 in our severe patients suggested an inflammatory profile that appears to be associated with
111 lung consolidations and subsequent worsening of their respiratory condition [13].

112 Consolidations were associated with poor outcome, as previously described [14]. Patients with
113 lung involvement >50% were significantly more diagnosed with pulmonary embolism. This
114 higher risk of thrombosis in patients with severe COVID-19 has been reported, even if the
115 pathophysiology remains unclear with several mechanisms possibly involved [15].

116 The timing between the onset of the symptoms and performance of CT was lower for patients
117 with lung involvement $\leq 25\%$, indicating that these patients could have presented at an earlier
118 disease stage. However, this difference was only of 1 day, raising a question about its clinical
119 relevance. Fourteen patients (2.4%) had no lesions on the initial chest CT, among whom 10/14
120 had symptoms for three days or less, as previously reported [1,2]. None of these patients died

121 or was admitted to ICU, suggesting that normal CT at the time of hospital admission could
122 predict good prognosis.

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

127

128 **Conflict of interests**

129 There are no reported conflicts of interest. MO reports personal fees from Canon Medical
130 Systems, outside the submitted work.

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134 **Author contributions**

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

140

141 **References**

- 142 [1] Ai T, Yang Z, Hou H, Zhan C, Chen C, Lv W, et al. Correlation of Chest CT and RT-PCR
143 Testing in Coronavirus Disease 2019 (COVID-19) in China: A Report of 1014 Cases.
144 Radiology 2020:200642. <https://doi.org/10.1148/radiol.2020200642>.
- 145 [2] Fang Y, Zhang H, Xie J, Lin M, Ying L, Pang P, et al. Sensitivity of Chest CT for COVID-19:
146 Comparison to RT-PCR. Radiology 2020:200432.
147 <https://doi.org/10.1148/radiol.2020200432>.

- 148 [3] Pan F, Ye T, Sun P, Gui S, Liang B, Li L, et al. Time Course of Lung Changes On Chest CT
149 During Recovery From 2019 Novel Coronavirus (COVID-19) Pneumonia. *Radiology*
150 2020;200370. <https://doi.org/10.1148/radiol.2020200370>.
- 151 [4] Li M, Lei P, Zeng B, Li Z, Yu P, Fan B, et al. Coronavirus Disease (COVID-19): Spectrum of
152 CT Findings and Temporal Progression of the Disease. *Acad Radiol* 2020;27:603–8.
153 <https://doi.org/10.1016/j.acra.2020.03.003>.
- 154 [5] Nishiyama A, Kawata N, Yokota H, Sugiura T, Matsumura Y, Higashide T, et al. A
155 predictive factor for patients with acute respiratory distress syndrome: CT lung
156 volumetry of the well-aerated region as an automated method. *Eur J Radiol*
157 2020;122:108748. <https://doi.org/10.1016/j.ejrad.2019.108748>.
- 158 [6] Ludes C, Labani A, Severac F, Jeung MY, Leyendecker P, Roy C, et al. Ultra-low-dose
159 unenhanced chest CT: Prospective comparison of high kV/low mA versus low kV/high mA
160 protocols. *Diagn Interv Imaging* 2019;100:85–93.
161 <https://doi.org/10.1016/j.diii.2018.11.012>.
- 162 [7] Revel M-P, Parkar AP, Prosch H, Silva M, Sverzellati N, Gleeson F, et al. COVID-19 patients
163 and the radiology department - advice from the European Society of Radiology (ESR) and
164 the European Society of Thoracic Imaging (ESTI). *Eur Radiol* 2020.
165 <https://doi.org/10.1007/s00330-020-06865-y>.
- 166 [8] Zhang J, Wang X, Jia X, Li J, Hu K, Chen G, et al. Risk factors for disease severity,
167 unimprovement, and mortality in COVID-19 patients in Wuhan, China. *Clin Microbiol*
168 *Infect Off Publ Eur Soc Clin Microbiol Infect Dis* 2020.
169 <https://doi.org/10.1016/j.cmi.2020.04.012>.
- 170 [9] Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, et al. Risk Factors Associated With Acute
171 Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019
172 Pneumonia in Wuhan, China. *JAMA Intern Med* 2020.
173 <https://doi.org/10.1001/jamainternmed.2020.0994>.
- 174 [10] Liu F, Zhang Q, Huang C, Shi C, Wang L, Shi N, et al. CT quantification of pneumonia
175 lesions in early days predicts progression to severe illness in a cohort of COVID-19
176 patients. *Theranostics* 2020;10:5613–22. <https://doi.org/10.7150/thno.45985>.
- 177 [11] Huang L, Han R, Ai T, Yu P, Kang H, Tao Q, et al. Serial Quantitative Chest CT Assessment
178 of COVID-19: Deep-Learning Approach. *Radiol Cardiothorac Imaging* 2020;2:e200075.
179 <https://doi.org/10.1148/ryct.2020200075>.
- 180 [12] Shi H, Han X, Jiang N, Cao Y, Alwalid O, Gu J, et al. Radiological findings from 81 patients
181 with COVID-19 pneumonia in Wuhan, China: a descriptive study. *Lancet Infect Dis*
182 2020;20:425–34. [https://doi.org/10.1016/S1473-3099\(20\)30086-4](https://doi.org/10.1016/S1473-3099(20)30086-4).
- 183 [13] Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall RS, Manson JJ, et al. COVID-19:
184 consider cytokine storm syndromes and immunosuppression. *Lancet Lond Engl*
185 2020;395:1033–4. [https://doi.org/10.1016/S0140-6736\(20\)30628-0](https://doi.org/10.1016/S0140-6736(20)30628-0).
- 186 [14] Yuan M, Yin W, Tao Z, Tan W, Hu Y. Association of radiologic findings with mortality of
187 patients infected with 2019 novel coronavirus in Wuhan, China. *PloS One*
188 2020;15:e0230548. <https://doi.org/10.1371/journal.pone.0230548>.
- 189 [15] Helms J, Tacquard C, Severac F, Leonard-Lorant I, Ohana M, Delabranche X, et al. High
190 risk of thrombosis in patients with severe SARS-CoV-2 infection: a multicenter
191 prospective cohort study. *Intensive Care Med* 2020:1–10.
192 <https://doi.org/10.1007/s00134-020-06062-x>.
- 193

Table 1

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

	Extent of lesions on CT			p value
	≤25% (n = 306)]25%–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
Dyspnoea	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

COVID-19: coronavirus disease 2019; CT: computed tomography; SD: standard deviation;

SpO₂: peripheral oxygen saturation.

^aOnly 10/29 pulmonary embolisms were diagnosed at admission; ^bDefined as intensive care unit admission or death.

The inferential analysis for the categorical data was performed using the χ^2 test or Fisher's exact test (2x3 comparison), as per the theoretical size of the samples. Continuous data were compared using a nonparametric test (Kruskal–Wallis test).

Fig. 1. Outcome and time from symptoms onset as per the quantification of lesions on 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.

CT, computed tomography; ICU, intensive care unit

In order to ease visualisation, noise was randomly added to each point. Curves were fitted through points with the locally weighted scatterplot smoothing (LOESS) method using the 'ggplot2' R package. Shaded area represents the standard error.



