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Clinical, Biological, Scannographic and Prognosis Characteristics of Severe Covid-19 According To the Extent of Lung Lesions on Chest CT Scan

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ABSTRACT

Introduction: COVID-19 caused by SARSCov-2 could be serious and fatal. The objective was to determine the correlation of clinical, biological, CT and prognosis of severe COVID-19 according to the extent of lung lesions on the chest CT scan.

Patients and method: This is a retrospective analytical study carried out in the department of pneumology University Hospital of the Joseph Raseta Befelatanana, Antananarivo, Madagascar for a three-month period from March to May 2021.

Results: 78 severe COVID-19 cases met the inclusion criteria, for an incidence of 66.7%. The mean age of our patients was 52.81 ± 16.64 years. Age did not differ for the three CT extension groups (p = 0.60). Male gender, dyspnea, C-Reactive protein elevation correlated with the extent of lung damage (p <0.05). On CT scan, the ground glass image and bilateral involvement were also associated with CT extension of lung lesions (p = 0.03, p = 0.04). The prognosis in terms of mortality was worse in severe COVID-19 patients with disease greater than 26%. The overall death was 6.41%.

Conclusion: Factors such as male gender, dyspnea, C-reactive protein, frosted glass and bilateral images of severe COVID-19 patients were correlated with the CT extent of lung lesions. Their understandings would make it possible to predict the unfavorable evolution of these lesions on a CT scan, thus reducing mortality.

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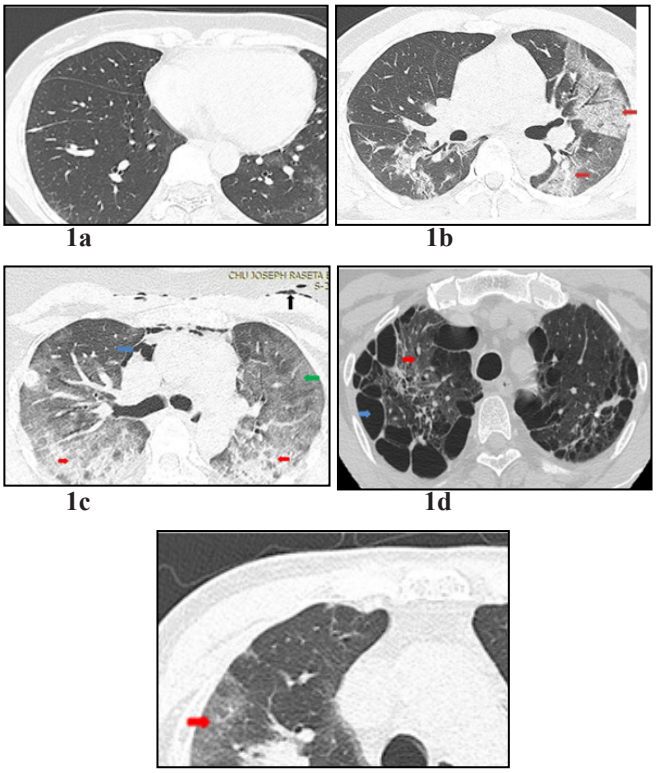
Introduction

COVID-19 caused by SARSCov-2 could be serious and fatal, it is responsible for millions of deaths worldwide. The disease is currently active due to the continued circulation of SARSCov-2 causing both economic and health impacts. In March 2020, since it became a pandemic, clinical, biological and radiological criteria were developed to categorize the best management of infected patients [1]. CT involvement of the lungs in SARSCov-2 infection is part of the COVID-19 severity criteria [2]. This chest scan remains the most reliable diagnostic tool due to the often typical images of COVID-19 [3]. It constitutes a prognostic factor in many studies [4]. Concerning the quantification of lung lesions on CT, the most used is that of the French Society of Radiology, which proposed four classifications according to the extension of lung lesions: mild (0-25%), moderate (25-50%), severe (50-75%) and critical (beyond 75%) [5]. On a global scale, the clinical, biological, and scannographic profiles and prognoses of patients with severe COVID-19 associated with the scannographic extent of lung lesions are poorly established in the studies realized. In Madagascar, this association has not been studied to our knowledge. The objective of this study was to identify, in severe COVID-19 patients, the clinical, biological, scannographic and prognostic aspects associated with the extent of lung lesions on CT.

Material and Methods

We conducted a retrospective, monocentric analytical study in the Pneumology Department of the Joseph Raseta Befelatanana University Hospital over a three-month period from March to May 2021. In effect, it was during this period that the peak of the COVID-19 epidemic occurred. The Pneumology Department of Befelatanana concentrates a large number of severe forms of COVID-19 coming from the emergency and triage department of this same institution. It is a service dedicated to the management of patients infected with SARSCov-2 during the successive waves of the COVID-19 epidemic in Madagascar. Quantification of lung lesions was performed visually by competent radiologists and pulmonologists. To better address our study, we categorized

the degree of involvement into three groups: ≤ 25% involvement, 26-50% involvement and > 50% involvement (Figure 1).



1a 1b 1c 1d 1e

Figure 1: Axial sections of CT scan according to the degree of involvement in the parenchymal window and without contrast injection :
Figure 1a: Involvement ≤25%, ground glass patches (arrow).
Figure 1b: Involvement between 26 - 50%, discretely reticulated and retractile condensations (arrows).
Figure 1c: Involvement >50%, frosted glass areas (green arrow) and diffuse bilateral retractive condensations (red arrows) with pneumomediastinum (blue arrow) and subcutaneous emphysema (black arrow).
Figure 1d: Ground glass plaques (red arrow) in a polyemphysematous man (blue arrow).
Figure 1e: Ground glass plaques (red arrows) with tubercular cavern (blue arrow) in a diabetic man.

The inclusion criteria were strictly based on CT images compatible with COVID-19, supported by laboratory confirmation of SARS-CoV-2 by a qualitative reverse transcriptase polymerase chain reaction test or SARS Cov-2 RT-PCR, and that the chest CT was performed in the vicinity of the tenth day after the onset of symptoms, in fact in this interval that the severe forms of COVID-19 develop [6]. Patients without RT-PCR and/or negative SARS Cov-2 RT-PCR test were excluded from the study.

We used the CRAN R ® software version 3.5.2 as a statistical analysis tool. Descriptive statistics consisted of calculating the mean and standard deviation of quantitative data. Proportions were used for categorical data. The Student's t test was used to compare means while the Chi-square test or the exact Fischer test compared proportions. Statistical significance was retained for a p value < 0.05 to reject the null hypothesis of no association between severe COVID-19 and scannographic extension of lung injury.

Results

Of a total of 117 COVID-19 hospitalized during the period of March to May 2021, 84 were severe cases of which 78 met the inclusion criteria or an incidence of 66, 7%. The mean age of our patients was 52.81 ± 16.64 years with extremes of 15 and 85 years, there was no significant difference for the three groups of lung lesion extension on CT scan (p=0.60). Male gender correlated with severity of lung involvement (p=0.003). There was more severe scannographic involvement in patients with a pathological history, but the association was not significant (Table 1). Clinically, dyspnea and asthenia were correlated with the degree of lung involvement (p=0.01; p=0.02, respectively). The association of vital parameters of severe COVID-19 patients with the extent of scannographic lesions is summarized in (Table 2). There was more inflammation in patients with more than 26% involvement, marked by elevated C-reactive protein (p = 0.02); but no significant correlation for other biological disturbances (Table 2). The ground glass image and bilateral lung parenchyma involvement were significantly correlated with the extension of the lung lesions (p = 0.03, p = 0.04) (Table 3). Therapeutically, patients with more than 26% extension received more oxygen therapy than those with less than 25% involvement with a significant difference (p < 0.05). The duration of hospitalization was similar for any extension of lesions on CT (p = 0.58). The prognosis in terms of mortality was worse in severe COVID-19 patients with more than 26% lung involvement. The all-inclusive death was 6.41% (Table 3).

Table 1: Distribution by demographic profile and disease history

	Extension of the lesions on the scanner			
	≤25% n=14(%)	**26 - 50% n=23(%)**	**>50% n=41(%)**	**p-value**
Age (years)	51,6 ± 21,4	55,2 ± 17,5	51,8 ± 14,4	0,60
Gender				
Femal	7 (50)	9 (39,1)	14 (34,1)	0,57
Male	7 (50)	14 (60,9)	27 (56,5)	0,003
Pathological history				
Arterial hypertension				
No	7 (50)	15 (65,2)	27 (58,5)	
Yes	7 (50)	18 (34,8)	14 (41,5)	0,65
Cardiac disease				
No	11 (78,6)	17 (73,9)	31 (75,6)	
Yes	3 (21,4)	6 (26,1)	10 (24,4)	0,95
Chronic bronchopneumopathy				
No	12 (85,7)	17 (73,9)	37 (90,2)	
Yes	2 (14,3)	6 (26,1)	4 (9,8)	0,21
Asthma				
No	11 (78,6)	21 (91,3)	37 (95,1)	
Yes	2 (14,3)	6 (26,1)	4 (9,8)	0,18
Tuberculosis				
No	13 (92,9)	23 (100)	37 (90,2)	
Yes	1 (7,1)	0	4 (9,8)	0,30
Diabetes				
No	11 (78,6)	18 (78,6)	32 (78)	0,24
Yes	3 (21,4)	5 (21,7)	9 (22)	0,94

Table 2: Distribution by clinical and biological parameters

	Extension of the lesions on the scanner			
	≤25% n=14(%)	26 - 50% n=23(%)	>50% n=41(%)	p-value
Dyspnea				
No	3 (21,4)	5 (21,7)	3 (7,3)	
Yes	11 (78,6)	18 (78,6)	38 (92,7)	0,01
Asthenia				
No	1 (7,1)	1 (4,3)	2 (4,9)	
Yes	13 (92,5)	22 (95,7)	39 (95,1)	0,02
Temperature (°C)	36,7 ± 0,8	36,9 ± 0,8	37,2 ± 1,1	0,62
Heart rate	91,7 ±	88,2 ± 15,8	90,4 ± 16	0,366
Respiratory rate	21 ± 3	15,8 ± 3,3	24,4 ± 3,3	0,17
PAOS in AA (%)	91,2 ± 5,9	85,7 ± 10,7	84 ± 11,7	0,24
C-RP (mg/L)	31,5 ± 28,3	38,9 ± 38,1	73,4 ± 58,4	0,02
Leukocytes (10^3/mm^3)	11,7 ± 7,8	9,1 ± 4	12,1 ± 5,7	0,06
NPC(10^3/mm^3)	10,3 ± 6,1	7,1 ± 3,6	12 ± 5,2	0,65
Lymphocytes (10^3/mm^3)	2 ± 2	2,2 ± 2,2	1,5 ± 1,8	0,62
Platelets (10^3/mm^3)	340,4 ± 166	322,1 ± 191,4	295,6 ± 103,3	0,37
D-Dimer (ng/L)	830 ± 768	2308 ± 3222	2068 ± 4078	0,32
ALT (UI/L)	51,7 ± 43,5	84,2 ± 127	62,3 ± 59,9	0,58
SGOT (UI/L)	31,5 ± 18	70,6 ± 57,8	65,5 ± 48,7	0,52
Creatininemia (µmol/l)	91,4 ± 19	87,3 ± 21,9	122 ± 174	0,34
Glucose (mmol/l)	8,3 ± 5,7	6,7 ± 2,8	8,1 ± 3,9	0,38

PAOS: Pulmonary Arterial Oxygen Saturation in ambient air **C-RP:** C-Reactive Protein. **NPC:** Neutrophilic Polynuclear Cell **SGOT:** Serum Glutamooxaloacetate Transferase. **ALT:** Alanine Aminotransferase

Table 3: Distribution by chest CT findings, oxygen therapy, length of hospital stay and mortality

	Extension of the lesions on the scanner			
	≤25% n=14 (%)	26 - 50% n=23 (%)	>50% n=41(%)	p-value
Ground glass				
No	0	1 (4,3)	0	
Yes	14 (100)	22 (95,7)	41 (100)	<0,01
Condensation				
No	8 (57,1)	14 (60,9)	27 (67,5)	
Yes	6 (42,9)	9 (39,1)	4 (32,5)	0,74
Bilateral				
No	1 (7,1)	0	0	
Yes	13 (92,9)	23 (100)	41 (100)	0,04
Pleuresis				
No	14 (100)	20 (87)	31 (75,6)	
Yes	0	3 (13)	10 (24,4)	0,09
O2 Standard				
No	5 (35,7)	2 (8,7)	1 (2,4)	
Yes	9 (64,3)	21 (91,3)	40 (97,6)	0,001
O2 broadband				
No	10 (71,4)	13 (56,5)	15 (36,6)	
Yes	4 (28,6)	10 (43,5)	26 (63,4)	0,05
Hospitalization duration (days)	11,4 ± 8,7	17 ± 20,8	14,7 ± 7,7	0,58
Deaths				
No	14 (100)	21 (91,3)	38 (92,7)	
Yes	0	2 (7,3)	3 (7,3)	0,54

Discussion

This study is the first to address the relationship between severe forms of COVID-19 and the degree of lung lesion extension on chest CT. The particularity of this study is to analyze the different parameters of severe COVID-19 patients according to the extent of the lesions. The study of their characteristics is important to deepen our understanding of the mechanism of severe radiological conditions in order to promote the most appropriate management. In this study, age did not differ for the three lesion extension groups. This is in accord with the study of Ruch et al in France, but the difference with our study concerns the population, the authors included all forms of COVID-19 [4]. The occurrence of these severe forms of COVID-19 in men is well known in published reviews; some have hypothesized the protective role of estrogens and progesterones in women, others stipulate the favoring role of androgens in men. Indeed, these androgens strongly express a receptor on pneumocytes 2 facilitating the penetration of the SARSCov-2 virus via the expression of the TMPRSS2 (transmembrane protease serine 2) gene [7,8]. However, its prognosis associated with the extent of pulmonary lesions is not yet established. In our study, male gender was significantly correlated with the degree of lesion extension on CT. Studies have been done on the prognosis of COVID-19 patients with one or more comorbidities, these patients have a fragile immune defense quality and would have had a worse prognosis compared to the general population. In our cases, these patients had a radiologically severe prognosis correlated to the extension of the pulmonary lesions, however, no significant difference was found. In fact, from a pathophysiological point of view, these secondary immune deficiencies alter the functions of pneumocytes and ciliaries, and would therefore be vulnerable to infection by SARSCov-2 via expression of the ACE2 receptor. The combined mechanism would cause a severe inflammatory response in the lungs of these patients [9]. This was demonstrated by a high proportion of SARS-Cov2 RNA in the lungs of an autopsy series of twelve patients [10]. Respiratory symptomatology such as dyspnea correlates with severe radiological damage in our patients with a significant difference but no difference in terms of hypoxia. It is related to severe alveolar damage. In some studies, despite the extent of the lesions on the CT scan, some patients present a radio-clinical discordance with moderate dyspnea and consequently a deep or silent hypoxemia occurs. One hypothesis is that of cytokine storming of autonomic nervous system afferents traveling through the vagus and glossopharyngeal nerves or their relay to the nucleus of the tractus solitarius in the bulb induced by SARSCov-2 [11,12].

The occurrence of these symptoms in these severe COVID-19 patients could therefore help clinicians to predict a possible unfavorable course of radiological involvement in terms of extension in clinical practice. On the biological side, only the elevation of C-reactive protein correlates significantly with the extent of lung damage. This elevated C-reactive protein, apart

from bacterial causes, could be used as an important index in the prediction of severe scannographic damage of the disease. Its elevation is related to the cytokine storm induced by lymphocytes. However, no study to date supports this association during severe forms of COVID-19. In the study of Ruch et al in France, where all forms of COVID-19 were included, elevated C-reactive protein, neutrophilic leukocytosis, lymphopenia and transaminases were significantly associated with a scannographic damage of more than 50% and that this elevated C-reactive protein constituted an independent poor prognostic factor for severe forms [4]. The study of the different scannographic images of COVID-19 is widely published, but their relationship with the extent of lesions on CT in severe forms of the disease is less described. In this study, we found that chest computed tomography (CT) findings showed a significant correlation of ground glass images, bilateral images with the extent of lung lesions on CT. Parenchymal density is also arguably an element of severity. In a review published by Lodé B et al in France, the ground glass image, parenchymal condensation and pleural effusion are markers of severity [3]. In clinical practice, this would allow us to predict the unfavorable evolution of these lesions in terms of extension in patients with severe forms of COVID-19. In terms of prognosis, we also showed a fatal evolution in severe COVID-19 with an involvement of more than 26%, especially in those with an involvement of 50% and more. This means that severe radiologically critical involvement is a poor prognostic factor for severe forms of COVID-19 in our study and also in the Ruch et al study [4]. In summary, the study of the different clinical, biological, scannographic parameters of severe COVID-19 patients according to the extent of lung lesions on CT scan can predict or assess the occurrence of severe scannographic involvement of the disease, which is of great importance for the diagnosis and follow-up of SARSCov-2 pneumonia. However, this study has some limitations, firstly we cannot generalize our results to the whole population due to the small number of our participants and the monocentric nature of the study, hence the interest of conducting a multicenter study. Secondly, the missing bibliographic data to compare our results, as this study is the first one dealing with the characteristics of severe forms of COVID-19 associated with the extent of scannographic lesions. Despite these limitations, our results should allow practitioners to reflect on their clinical practice in order to reduce the morbidity and mortality related to severe radiological COVID-19 lesions.

Conclusion

This study found an association between clinical, biological, and scannographic parameters and the extent of lung lesions on CT. The main predictive factors for the occurrence of severe CT lung lesions were male gender, dyspnea, elevated C-reactive protein, ground glass and bilateral CT images. The study of these factors would allow us, in clinical practice, to predict the unfavorable evolution of the pulmonary lesions in terms of extension, and thus to allow the management of patients at risk of radiological severity in the best time. All this in order to prevent and reduce mortality related to severe CT injury.

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Ethical approval: This article does not contain any personal identifying information; the name and date on the CT scan have been masked. The authors have included only the information necessary for scientific understanding.

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