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Tomographic scale for the assessment of COVID-19 severity at the National Respiratory Diseases Institute

Escala tomográfica para evaluar la gravedad de COVID-19 en el Instituto Nacional de Enfermedades Respiratorias

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ABSTRACT. Introduction: The pandemic of SARS-CoV-2 (COVID-19) has caused high rates of morbidity and mortality. The use of adequate diagnostic methods to identify the evolution of this disease is necessary; computerized tomography (CT) is of the main tools by image, with sensitivity of 96-99%. Different studies have created scales to evaluate the extent and severity of lung disease from COVID-19, with a variability in the results. **Objective:** To evaluate the use of a tomographic scale (TS) to determine the severity of lung affectation in COVID-19. **Material and methods:** Analytical cross-sectional study including patients with confirmed diagnosis of COVID-19 and initial CT. ATS was used to evaluate the lung affectation, to identify pulmonary pattern and to establish the state of the disease. Statistical analysis consisted in descriptive and analytical statistics (ROC curve). **Results:** 151 patients, mean age 50 years. The predominant pulmonary pattern was «crazy paving» (46%), identified in the phase of progression. The area under the ROC curve was 0.831 (95% CI: 0.764-0.898), with a cut-off value of 16.5 to discriminate the severe from non-severe affectation, with sensitivity 84% and specificity 74%. **Conclusion:** The use of TS in initial CT showed an acceptable sensitivity to identify the severity of the disease.

Keywords: Severity, tomographic scale, lung, COVID-19, respiratory disease.

RESUMEN. Introducción: La pandemia por SARS-CoV-2 (COVID-19) provocó altas tasas de morbimortalidad. Es necesario el uso de métodos diagnósticos para la identificación o evolución de este padecimiento; la tomografía computarizada (TC) es una de las principales herramientas por imagen con sensibilidad de 96-99%. Diferentes estudios han elaborado escalas para evaluar la extensión y gravedad de la enfermedad pulmonar por COVID-19 con variabilidad en sus resultados. **Objetivo:** Evaluar la utilidad de una escala tomográfica (ET) para determinar la gravedad de la afectación pulmonar en COVID-19. **Material y métodos:** Estudio transversal analítico; se incluyeron pacientes con diagnóstico confirmado de COVID-19 con TC inicial en la cual se aplicó la ET para evaluar la afectación pulmonar, identificar el patrón pulmonar y establecer el estadío. El análisis estadístico fue descriptivo y analítico, con cálculo de curva ROC. **Resultados:** 151 pacientes con edad media de 50 años. El patrón pulmonar predominante fue el «empedrado» (46%) identificado en fase de progresión; el área bajo la curva fue 0.831 (IC95%: 0.764-0.898) con punto de corte 16.5 para discriminar la afectación grave, con sensibilidad de 84% y especificidad de 74%. **Conclusión:** El uso de la ET en TC inicial mostró una sensibilidad aceptable para identificar la gravedad de la enfermedad.

Palabras clave: Gravedad, escala tomográfica, pulmón, COVID-19, enfermedad respiratoria.

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INTRODUCTION

The SARS-CoV-2 virus is responsible for the COVID-19 disease, causing the current pandemic and a global public health emergency; the clinical manifestations of this condition can progress from mild symptoms to acute respiratory distress syndrome.[1-3] High morbidity and mortality rates have placed Mexico as one of the countries with the greatest affectation;[4] this could be due to different risk factors[5] and comorbidities (obesity, hypertension and

diabetes *mellitus*) that affect our population,[6] because they have an important role in the progression and evolution of COVID-19 diseases.[7-9]

Among the diagnosis methods used, chest CT has emerged as the main diagnosis tool, with a sensitivity between 96 and 98%.[10-12] There is controversy about the usefulness of CT as a standard method, experts point out that it is useful for assessing the severity of the disease.[13-15] Typical tomographic lung patterns (TLP) associated with COVID-19 are: ground glass opacity (GGO), «crazy-paving» pattern and consolidation, these are associated with disease progression;[16] these TLP have also been identified in the Mexican population.[17] In the evolution of the disease, the pattern of organizing pneumonia (OP) has been described,[18] characterized by the presence of different TLP such as consolidation, GGO, bronchiectasis, bronchioloectasis, nodules, halo sign, pulmonary parenchymal bands, and perilobular consolidation.[19]

Several studies have proposed semi-quantitative staging methods such as the creation of scales to assess the extent and severity of the damage to the lung tissue. The scales proposed by Chang, *et al*. evaluated the tomographic changes in the recovered population of severe acute respiratory syndrome (SARS), it was found that the CT score was correlated with clinical and laboratory parameters.[20] Likewise, Yang, *et al*. developed a CT scale to determine the severity, they evaluated 20 pulmonary segments to identify the status of parenchyma in severe COVID-19, using the amount of tomographic affectation as a substitute of the load of COVID-19 disease;[21] however, these scales require a domain of pulmonary segmental anatomy that in daily practice are a limitation due to the complexity it represents, since more time in the analysis and interpretation of the findings is needed, it is not compatible with the high demand for care in the health system.

The objective of this study is to develop and evaluate a tomographic scale to determine the severity of COVID-19, that allows us to know the predominant TLP and the stage of disease evolution; the proposal of this scale is characterized by an evaluation by lobes of the lungs, simplifying the interpretation of the imaging study.

MATERIAL AND METHODS

This work was approved by the Ethic Committee of the National Institute of Respiratory Diseases (INER), approval code: C37-20. Cross-sectional study carried out from March to June of 2020; patients who went to the emergency service of INER with a diagnosis of COVID-19, > 18 years, both sexes and confirmed positive result with polymerase chain reaction in real time (RT-PCR) (GeneFinder™ COVID-19 Plus RealAmp Kit) were selected. Imaging studies were selected consequently during the indicated period and only patients who had a chest CT scan at admission or within the first 24 hours after hospitalization were included. The outcome variable to carry out the cut-off point of the scale in the statistical analysis (ROC curve) it was the presence of severe disease defined by the need for intubation and/or death.

Imaging technique

It was used a multidetector scanner SIEMENS brand (SOMATON Sensations model, 64 detectors); A Siemens-branded multidetector tomograph (SOMATON sensations model, 64 detectors) was used; the studies were performed with volumetric acquisition in supine decubitus during maximum inspiration in pulmonary and mediastinal window. All images were reconstructed with high spatial resolution algorithm and B70 lung filter with window amplitude of -600/1,200; for the mediastinum, B30 filter with window width of 50/350 was used.

The images were blinded in random order and independently evaluated by two thoracic radiologists with more than 17 years of experience, obtaining a Cronbach's alpha of 0.912 in the interobserver evaluation. The final decision was reached by consensus with adjudication if there were disagreements in the interpretation.

Table 1: Description of sociodemographic, clinical and tomographic characteristics in patients with COVID-19. N = 151.

Variables	n (%)
Age (years)	50 ± 14
Male	94 (62)
Duration of the disease	9 ± 5
Oxygen saturation percentage	77 ± 14
Presence of comorbidities • Diabetes • Hypertension • Obesity	95 (63) 42 (28) 34 (23) 43 (29)
Score on tomographic scale	18 ± 6
Category • Non-severe (< 16.5 points) • Severe (≥ 16.5 points)	 53 (35) 98 (65)
Tomographic pattern • Ground glass opacity • «Crazy-paving» pattern • Consolidation	 64 (42) 69 (46) 18 (12)
Organizing pneumonia Intubation Death	136 (90) 84 (56) 54 (36)

Qualitative variables were expressed in frequencies (%); quantitative variables were expressed in means ± standard deviation (SD).

Table 2: Comparison of clinical aspects between three groups according to tomographic patterns.

Variables	Tomographic patterns			p
	Ground glass opacity	«Crazy-paving» pattern	Consolidation	
	N = 64 n (%)	N = 69 n (%)	N = 18 n (%)	
Age (years)	49 ± 14	52 ± 13	44 ± 17	0.061
Male	38 (60)	45 (65)	11 (61)	0.787
Duration of the disease (days)	8 ± 5	9 ± 4	8 ± 4	0.531
Oxygen saturation percentage	80 ± 12	76 ± 14	67 ± 17	**0.001**
Presence of comorbidities	39 (63)	44 (65)	12 (71)	0.842
Score on tomographic scale	15 ± 6	19 ± 4	20 ± 5	**< 0.001**
Organizing pneumonia	53 (39)	66 (48)	17 (13)	**0.038**
Intubation	26 (41)	44 (64)	14 (78)	**0.004**
Death	20 (31)	27 (39)	7 (39)	0.616

Qualitative variables were expressed in frequencies (%); quantitative variables were expressed in means ± standard deviation (SD). For the comparison of proportions, the χ^2 and ANOVA tests were used for analysis of variance.

Determination of tomographic scale (TE) score

To assess lung involvement using the scale, the percentage of affected tissue in each lobe was determined. The TLP were defined based on what is stablished in the Glossary of the Fleischner Society.[22]

Severity scale description

The proposed TE is an adaptation of the scale developed by Chang *et al.* for patients with SARS, in which findings such as GGO, consolidation and air entrapment are identified and correlated with clinical and laboratory parameters.[20] The present scale evaluated the extent of structural changes in each lobe, resulting in a score of zero to five points for each lobe. Based on the score, a value of zero indicates no involvement, one indicates involvement of less than 5% of the lobe, two indicates > 5-25%, three indicates > 25-50%, four indicates > 50-75% and five indicates > 75%. The total sum of the score obtained for each lobe varies from zero to 25 points. The scores are divided into two groups according to the cut-off values obtained with the ROC curve, where a cut-off point of 16.5 points indicates severe disease.

For the qualitative evaluation of the TLP, the main findings in viral pneumonia are GGO (category A, initial stage of involvement), «crazy-paving» pattern (category B, stage of progression) and consolidation (category C, advanced stage).[16,23]

Statistical analysis. A descriptive analysis was performed as well as a χ^2 test for differences between proportions, and a Student's t test for mean comparisons. ANOVA was used for comparisons between TLP. ROC curve analysis was developed to determine the usefulness of the scale among patients with severe and non-severe COVID-19. Logistic regression was performed to determine variables associated with the scale score. A value $p \leq 0.05$ was considered significant.

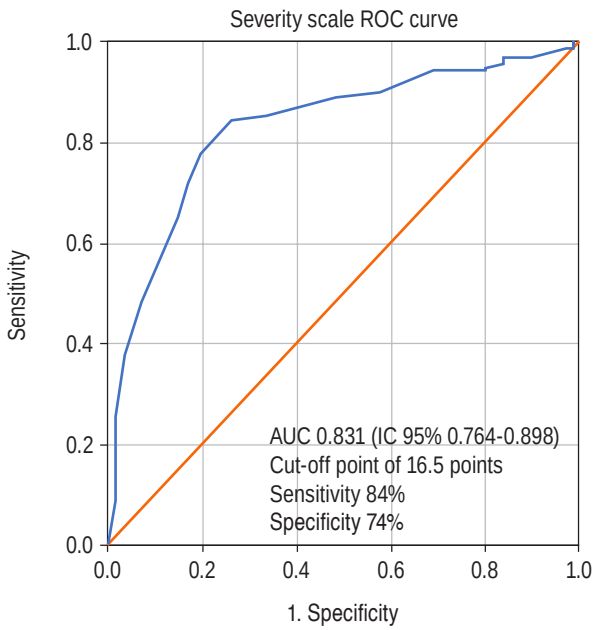

Figure 1: ROC curve cut-off on the tomographic scale to assess its utility in discriminating between severe and non-severe COVID-19 patients.

RESULTS

151 patients with COVID-19 pneumonia were included. *Table 1* describes the sociodemographic, clinical and tomographic characteristics; 62% were men, with a mean age of 50 years and a mean disease duration of nine days. The total score obtained in the TE was 18 points, therefore, 65% had severe disease and 35% non-severe disease. The observed TLP were: 46% «crazy-paving» pattern, 42% GGO and 12% consolidation; 90% had a NO pattern. Overall, 56% of patients required intubation and 36% died.

In data not shown in tables, the comparison of clinical characteristics between patients with severe and non-severe COVID-19, severe patients were older (52 years of age vs. 45 years of age, p = 0.008). Oxygen saturation was significantly lower in patients with severe disease (71 vs 87%, p < 0.001), the same patients obtained a higher punctuation in the TE (21 points vs 11 points, p < 0.001). Finally, the presence of NO was higher in severe patients (97 vs 77%, p < 0.001).

Table 2 compares the clinical characteristics among the three groups stratified by TLP. The groups were age, duration of disease, distribution of comorbidities, and mortality rates similar. Patients with consolidation had a lower mean percentage of oxygen saturation (67 vs 76% in patients with the «crazy-paving» pattern and 80% in those with GGO, p = 0.001). The score on the scale was significantly higher in patients with consolidation than in patients with other patterns (mean of 20 points vs. 19 points in patients with the «crazy-paving» pattern and 15 points in those with GGO, p < 0.001). The presence of NO was higher in patients with a «crazy-paving» pattern compared to the other TLP (p = 0.038). There was a need of intubation in patients with consolidation findings (p = 0.004).

Figure 1 shows the results of the analysis to determine the cut-off point in the tomographic scale base on the ROC curve to identify severe and non-severe disease in patients with COVID-19. The area under ROC curve was 0.831 (IC de 95%: 0.764-0.898) for the cut-off value of 16.5 (sensitivity, 84%; specificity, 74%).

Table 3 shows the results of the linear regression analysis that was performed to determine the clinical variables associated with severe disease, according to the scale score; the selection of the variables was included by biological plausibility. After adjusting for age, it was observed that the longer the duration of the disease (p = 0.02) the lower the oxygen saturation (p < 0.001) and the need for intubation or death (p < 0.001); a higher score result will be obtained in the TE.

The different TLP identified in the study: a) GGO pattern, b) «crazy-paving» pattern, and c) mixed pattern are shown in the *Figure 2*. According to the qualitative assessment of

Table 3: Linear regression to evaluate the association of clinical variables with the tomographic scale. N = 151.

Patients with COVID-19	Method: Enter		Method: Stepwise	
	β	p	β	p
Age	0.01	0.651	–	–
Duration of the disease	0.17	**0.027**	0.17	**0.027**
Oxygen saturation percentage	-0.18	**< 0.001**	-0.18	**< 0.001**
Severity (intubation/death)	2.88	**0.001**	2.93	**0.001**

Dependent variable: scale score. The covariates included this analysis were the qualitative and quantitative variables with biological plausibility that explain severity.

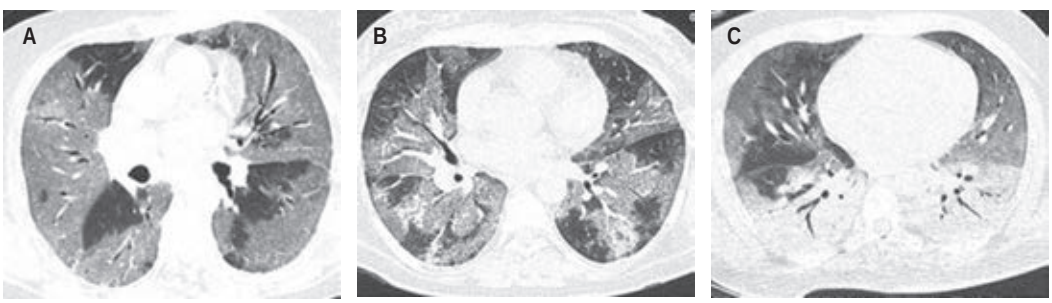

Figure 2: Axial chest tomography images with window for lung parenchyma in three different patients to demonstrate the different patterns. **A)** Ground glass opacity pattern, diffuse distribution, bilateral with subpleural predominance. **B)** Predominantly central-peribronchial «crazy-paving» pattern. **C)** Mixed pattern, mid-lobeglass ground glass opacity pattern and lingula associated with a consolidation pattern in lower lobes.

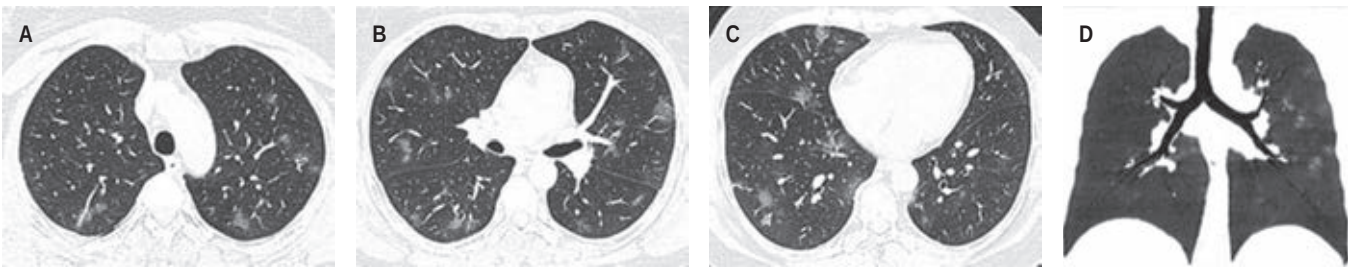

Figure 3: A-C) Thoracic axial tomography images with window for pulmonary parenchyma. **D)** MiniP coronal reconstruction. Ground glass with random distribution in patches, score of 5/25 points, category A, non-severe disease.

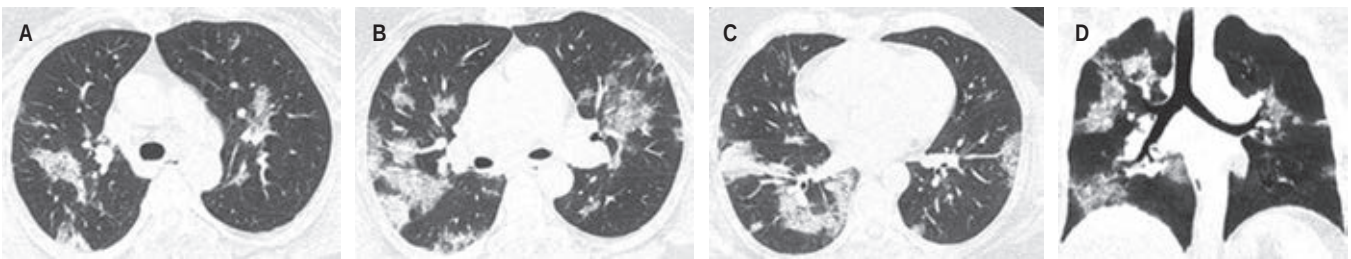

Figure 4: A-C) Thoracic axial tomography images, with window for pulmonary parenchyma. **D)** MiniP coronal reconstruction. Predominant «crazy-paving» pattern with consolidation focal areas with subpleural and peribronchial distribution, score of 13/25 points, category B, non-severe disease.

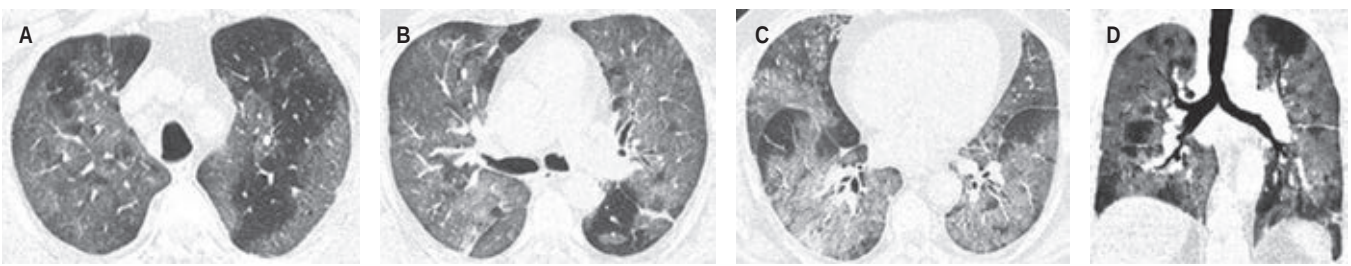

Figure 5: A-C) Thoracic axial tomography images with pulmonary parenchyma window. **D)** MiniP coronal reconstruction. Predominant pattern of bilateral, diffuse ground glass with areas of «crazy-paving» pattern in posterior and inferior segments, score of 24/25 points, category A, severe disease.

the predominant TLP of the disease it was given category A (initial stage of involvement) identifying a mean score in the TE of 15 points, with 48% of severe disease *(Figure 3)*; category B (stage of progression) showed a mean score on the scale of 19 points, with a severe disease at 77% *(Figure 4)*; and category C obtained a mean score of 20 points, with 78% of severe disease (advanced stage). However, we found a higher frequency of severe disease according to the score obtained in the TE *(Figure 5)*, regardless the stage of disease progression.

DISCUSSION

This paper proposes the adaptation of a semi-quantitative TE for the evaluation of pulmonary involvement in patients with COVID-19. The analysis of the ROC curve, the area under the curve was of 0.831 (95% CI: 0.764-0.898), with a sensitivity of 84% and specificity of 74%, using a cut-off point of 16.5, for the prediction of serious disease.

Yang, *et al.* applied a semi-quantitative TE to evaluate 20 segments, with a total score between zero and 40, with a cut-off point of 19.5, the scale could identify a serious disease with a sensitivity of 83.3% and specificity of 94%.[21] Compared to the scales used in the present study, the scale described above had higher cut-off and diagnostic value; however, the reproducibility of the assessment with a lung segment scale is reduced in staff with less experience in the thoracic area.

Francone *et al.* in a longitudinal study evaluated a TE in patients with COVID-19 through the assessment of the initial

CT, with the aim to predict mortality by obtaining a score on the scale equal to or greater than 18 points. In this study we did not follow up patients but a regression analysis was proposed to identify clinical variables that were associated as predictors of severity of severe disease based on the proposed TE score.[15]

Pan *et al.* identified the TLP and described the stage of disease assessment.[16] In this study, the «crazy-paving» pattern was the most common corresponding to the stage of disease progression, attributable to the date of acquisition of the tomography, which on average was performed on the ninth day of set of symptoms. In addition, individuals with consolidation were observed to have higher initial severity scores and lower oxygen saturation ($p = 0.01$), a figure that is consistent with that reported in the study by Pan *et al.*[16] y Sabri *et al.*[24] in which they identified the greatest severity of the disease is observed with the consolidation pattern. According to the TLP identified in the present study, a pattern similar to those described in patients with SARS and MERS is evident.[23,25]

The mortality rate identified was similar between patients with a «crazy-paving» patterned those with consolidation; a higher risk of mortality has been observed in patients with comorbidities, initially described in China; this association was not significant in our study.[26] The mortality rate in our study was 36%, similar to that reported by Yuan M. *et al* 37%,[9] however, these authors related elderly age and underlying diseases (hypertension, diabetes and heart disease), with the presence of this event; despite the high percentage of patients with comorbidities in our population, this finding was not significant ($p > 0.05$).

CONCLUSION

The application of TE in the initial CT as a diagnostic test demonstrated a good sensitivity to identify the severity of the disease in the population served in the institute; it is useful to know the predominant TLP and the stage of the evolution of the disease, therefore, it is proposed to implement the use of this scale in the evaluation of initial TC of patients with COVID-19.

The limitations of this research include the lack of follow up, which does not allow the scale to be applied to other CT scans performed at different stages of the disease; therefore it is necessary to carry out longitudinal studies to evaluate the effectiveness of the scale and its contribution in clinical decision-making.

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