Role of Chest Tomography Combined With Prognostic Indices for Severity Classification in Patients With SARS-CoV2 Pneumonia. Beyond Vaccination There Are Disease.

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Research

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Abstract

The initial evaluation of patients with COVID-19 represents a challenge to regulate a decision in preventive and timely management. There are various proposals as support tools that deserve to be evaluated.

Aim. Evaluation of Chest CT Score performance and prognostic indices in COVID-19 patients to predict progress to critical illness.

Methods. This was a retrospective study run from April to December 2020. Patients of any age and gender and who required hospitalization due to a confirmed diagnosis of COVID-19 by RT-PCR and Chest CT, were included. Demographic, characteristics prognosis indexes and laboratory were analyzed. Patients with acute coronary ischemic syndrome (ACS), acute heart failure, those who developed critical illness in the first 24 hours, and those with no RT-PCR result were excluded. Critical illness was defined by the need for supplemental oxygen and / or death during the hospitalization.

Results. 109 patients were included. The mean age was 53.88 ± 13.51 years. In 75% of them, there was at least one comorbidity and 30% developed critical illness. In 49.5% there was a CORADS-5 on admission, and in 50% there was a peripheral distribution of the interstitial infiltrate in the left lower lobe. The risk factors were FiO_2 , CT Score > 18 and the NRL index. The combination of the High risk qCSI plus CT score > 18 indices was the best prediction index for development of a critical condition. Average mortality was 10%.

Conclusion. The combined use of indices in patients infected with SARSCoV2 shows diagnostic accuracy and predicts severity.

Introduction

Chest computed tomography (chest CT) has shown great utility in the diagnosis of infection with SARS-CoV-2. Its complementary use with the reverse transcription polymerase chain reaction (RT-PCR) test to assess subjects infected with SARS-CoV2 allows timely medical intervention and accurate therapeutic decision in COVID-19. (1)

The most common COVID-19 findings in Chest CT are ground glass opacities (GGO), which are isolated or in combination with areas of focal consolidation. This areas show predominantly a bilateral distribution and subpleural predominance (2– 4). In patients with SARS-CoV2 infection, chest CT provides relevant data that are currently part of the diagnostic tools (5,6) and might be further implied in prognosis (7,8).

In March 2020, the Dutch Society of Radiology developed a standardized evaluation scheme for the lung condition due to COVID-19 whose acronym is CO-RADS. It was derived from the COVID-19 Reporting and Data System. This system proposed a level of suspicion of pulmonary involvement in COVID-19, based on the findings of the chest CT. It divided the suspicion ranging from very low CO-RADS 1 to very high CO-RADS 5 with two additional categories taking into account a technically deficient study CO-RADS 0 and the existence of a positive reverse transcription polymerase chain reaction (RT-PCR) test for SARS-CoV-2 before CT CO-RADS 6 (9).

It is also possible to evaluate the severity of lung damage and extension caused by COVID-19 through chest CT in a semi-quantitative way (10), and there is an adequate correlation between the severity and the degree of affection (11). One of these methods is the CT score, which is an index that has shown an adequate correlation with age and inflammation. A CT score value ≥ 18 predicts short-term mortality in the follow-up of patients with COVID-19 (11).

The use of predictive clinical indexes facilitates medical judgment and leads to an improvement in the therapeutic and clinical decisions determining whether the patient with SARS-CoV2 infection can be cared for at home or requires hospitalization. These indexes are easy to obtain and are useful in the risk stratification of complications, respiratory deterioration and the prognostic determination of mortality.

Of all these tools, one of the scores proposed to evaluate the risk of critical illness in hospitalized patients is COVID-GRAM. Its use predicts the risk of a patient to be admitted to the critical care unit (ICU), the requirement of invasive ventilation and of death (8). Similarly, the Quick COVID-19 severity index (qCSI) predicts the risk of critical respiratory disease in 24 hours, in patients admitted from the emergency department (13).

On the other hand, other indexes were created with laboratory parameters obtained after patient admission, such as the neutrophil-lymphocyte ratio (NLR), which predicts the level of physiological stress (14). It allows for the early detection of sepsis and helps in decision making regarding the requirement for admission to the ICU (15). Therefore, many of these indexes allow a comprehensive evaluation of the underlying problem in the patient at the time they seek care. The objective of this work was to evaluate the prognostic performance of clinical indexes and chest CT in patients with COVID-19 who progress to critical illness.

Methods

Source of data

This was a retrospective and observational study run between April and December 2020 at the Ignacio Chávez National Institute of Cardiology in Mexico City, Mexico. This study was carried out under the rules of the Declaration of Helsinki. It was evaluated and accepted by the ethics and research committee of the INC (number 20-1177) and registered at www.clinicaltrials.gov (NCT04577105). Informed consent was obtained and signed by the patient or his legal representative.

Participants

Patients of any age who required hospitalization at the third level of care due to a confirmed diagnosis of COVID-19 by RT-PCR (16–19) were included. Patients had undergone chest CT on admission. The patients received standard treatment according to the recommendations available at the date of admission by the American Infectious Diseases Society (IDSA) and the panel of the National Institutes of Health (NIH) (20,21). Patients with a diagnosis of acute coronary ischemic syndrome (ACS), acute heart failure, patients who were admitted to another clinical trial, those who developed critical illness in the first 24 hours after admission or did not have a RT-PCR result were excluded.

Outcome

Critical illness was defined as the need for supplemental oxygen (> 10 L / min by low-flow device, high-flow device, non-invasive, or invasive ventilation) and / or death during patient hospitalization (8,22).

Predictors

Data from the electronic medical record were collected. Upon admission to the emergency service, a clinical questioning and a physical examination were performed. Oxygen saturation was quantified by pulse oximetry (%) in ambient air and the FiO_2 administered was calculated using the O_2 flow rate, L / min. The device used varied from a nasal cannula, a mask with or without reservoir and a high-flow cannula (23,24).

Model development

A univariate analysis of the clinical variables and of the laboratory and chest CT characteristics was performed. The significant results were included in a multiple logistic regression model. Clinical data, including 77 non-serious and 35 severe cases, were randomly selected. The diagnosis of COVID-19 was achieved according to the interim guidelines of the World Health Organization (WHO) 2019 (25) and the diagnosis and treatment guidelines of COVID-19 in China (26).

Non-serious patients met early-onset epidemiological characteristics (27) epidemiological history, (28) fever or other respiratory symptoms, (29) and typical abnormalities of the CT scan of pneumonia virus. (30) Critically ill patients also met at least one of the following conditions: Difficulty breathing, $RR \geq 30$ times / min, (2) Oxygen saturation (resting state) $\leq 93\%$, (3) PaO_2 /

$FiO_2 \leq 300$ mmHg. COVID-19 patients were confirmed by a positive result of high-throughput sequencing or real-time reverse transcriptase polymerase, positive RT-PCR result for SARS-CoV RNA- from nasal and pharyngeal swab samples (1). Only laboratory confirmed cases were included in the analysis. The imperative of informed consent was waived in light of anonymity.

Anthropometric and demographic characteristics, history of comorbidities such as systemic arterial hypertension (31), type 2 diabetes mellitus (32), dyslipidemia (33) and chronic renal failure (34) were determined. Arterial blood gas was performed by puncture of the radial artery (35) and PaO_2 (mmHg) was quantified. Levels of hemoglobin (g / L), neutrophil cell count ($\times 10^3$ / L), lymphocyte count ($\times 10^3$ / L), creatinine (mg / dL), blood urea nitrogen (mg / dL), C-reactive protein (mg / L), D-dimer level (mg / mL), hsTnI (pg / mL), NT-proBNP (pg / mL), CK-MB fraction (U / L), ferritin (ng / mL), fibrinogen (g / L), alkaline phosphatase (U / L) and LDH (U / L) were obtained at the moment of admission.

Subsequently, prognostic scores and indexes were calculated with clinical and laboratory characteristics from the first hospital medical evaluation. Web-based risk calculators were used, for COVID-GRAM available at <http://118.126.104.170/> [8] and qCSI available at <https://covidseverityindex.org/> (13) and for the neutrophil-lymphocyte ratio calculated with the following formula: $NLR = (\text{absolute neutrophil count, cells} / \mu\text{l}) / (\text{absolute lymphocyte count, cells} / \mu\text{l})$ (14).

TOMOGRAPHY

Images were acquired with a Siemens 256-slice multidetector tomograph (Somatom® Definition Flash 128x2, Siemens Healthcare, Forchheim, Germany) following the recommended parameters for low-dose simple chest tomography. The chest scout was acquired using 35 mA, 100 Kv and 6 mm slices, and then the chest tomographic slices maintaining inspiration in a cephalocaudal direction with 80 mA, 100 Kv, a duration of 2.24 seconds, a pitch of 1 and slices of 1 mm, with a total of 110 DLP, with which a total of 1.5 mSv is calculated with the conversion factor for thorax. Multiplanar reconstructions were performed with Kernel filters B26f and B50f for the mediastinum and lung, respectively, at 1 mm slices.

The CT score was calculated by 2 experts as follows: a value of 0 to 5 was assigned in each lung lobe for a total of 5 lobes (assigning 0 points with involvement was 0%, 1 point with involvement less than <5 %, 2 points with involvement of 5-25%, 3 points with involvement of 26-50%, 4 points with involvement of 51-75% and 5 points with involvement of > 75%) obtaining a severity score by tomography of 0 -25 points (11). There was a strong agreement between raters (0.89).

Sample Size and Missing Data

A sample size of 30 patients was estimated with an alpha of 0.05, a power of 0.80, a R^2 0.35 and 5 tested covariates. Variables with more than 5% missing values were excluded.

Statistical Analysis Methods

The categorical variables were expressed in frequencies and percentages, the continuous ones as mean $\pm$ SD or mean or interquartile range, depending on their distribution. Comparisons of proportions between groups were made with the chi-square test or Fisher's exact test and Student's T test or Mann-Whitney U according to the number and distribution. A logistic regression analysis was performed by the backward elimination approach (36) to select and estimate the association between the severity of patients with COVID-19 and the variables (clinical or Chest CT) that were relevant based on prior knowledge and statistically significant in univariate binary logistic regression analysis. Variables with $p < 0.10$ were included in the multivariate model in the univariate analysis to select the predictors. We report the area under the receptor operating characteristic (ROC), sensitivity, specificity, OR, positive (PPV) and negative (NPV) predictive value. Results are presented as odds ratios (OR) with 95% confidence intervals (95% CI) and p-values. Statistical analysis was performed with STATA version 16.0 software (StataCorp LLC).

Results

Participants

Eighty-six patients were excluded due to lack of clinical data, delayed RT-PCR or Chest CT results, and 3 patients were also excluded who required endotracheal intubation within 24 hours of admission. Therefore, 109 patients were included. Table 1 shows the characteristics and demographics of the included patients. The mean age was 53.88 ± 13.51 years, 69 (63.3%) were men. 74 patients (75%) had at least one comorbidity, 32 (29.9%) patients developed critical disease and the average mortality was 10.14%.

Table 1
Clinical and Demographic characteristics at Hospital admission in patients diagnosed with COVID-19

Variable	Critical Illness			p
	Total (n = 109)	No (n = 77)	Yes (n = 32)	
Age, years	53.88±13.51*	52.02±13.21*	57.90±13.37*	0.02 [†]
Male gender	69 (63.3)	46 (59.74)	23 (71.88)	0.23 [‡]
Smoking	22 (20.18)	18 (23.38)	4 (12.50)	0.19
Admission measurements				
Symptom onset-hospitalization, days	6 (3–9)	6 (3–9)	7 (2–9.5)	0.94 [§]
Respiratory rate, breaths/min	20 (18–26)	19 (18–22)	25 (22.5–32)	0.00
Heart rate, beats/min	93 (80–105)	90 (80–104)	95.5 (82.5–110)	0.17
Temperature, °C	36.6 (36–37.3)	36.5 (36–37.2)	37 (36.3–37.8)	0.08
MAP, mean (SD), mmhg	91.96±13.24*	92.27±11.86*	91.21±16.28*	0.70 [†]
Symptoms, No. (%)				
Fever	93 (85.32)	66 (85.71)	27 (84.38)	0.53 [¶]
Shortness of breath	81 (74.31)	56 (72.73)	25 (78.12)	0.85 [†]
Dry cough	93 (85.32)	64 (83.12)	29 (90.62)	0.24 [¶]
Headache	53 (48.62)	38 (49.15)	15 (46.88)	0.81 [†]
Sore throat	56 (51.38)	39 (50.65)	17 (53.12)	0.81
Myalgia/arthralgia	77 (70.64)	55 (71.43)	22 (68.75)	0.78
Diarrhea	20 (18.35)	14 (18.18)	6 (18.75)	0.94
Comorbidities, No. (%)				
No. of Comorbidities				
0	35 (32.11)	27 (35.06)	8 (25)	0.30
1	34 (24.68)	19 (25.00)	15 (46.88)	0.02
2	23 (21.10)	18 (23.38)	5 (15.62)	0.02 [¶]
3	9 (8.26)	9 (11.69)	0	0.03
4	5 (4.59)	3 (3.9)	2 (6.25)	0.46
5	3 (2.75)	1 (1.30)	2 (6.25)	0.20
Obesity	27 (24.77)	17 (22.08)	10 (31.25)	0.31 [†]
Hypertension	52 (47.71)	37 (48.05)	15 (46.88)	0.91
Diabetes	31 (28.44)	20 (25.97)	11 (34.38)	0.37
Dyslipidemia	30 (27.52)	21 (27.27)	9 (28.12)	0.92

Critical Illness				
Cardiovascular disease	16 (14.68)	10 (12.99)	6 (18.75)	0.30 [¶]
COPD	2 (1.83)	2 (2.60)	0	0.49
Cerebrovascular disease	3 (2.75)	0	3 (9.38)	0.02
Malignancy	1 (0.92)	1 (1.30)	0	0.70
Chronic kidney disease	10 (9.17)	8 (10.39)	2 (6.25)	0.39
Values are expressed in number (percentage), median (interquartile range).				
°C = degree Celsius, COPD = chronic obstructive pulmonary disease, MAP = mean arterial pressure, SD = standard deviation,				
* media (Standard deviation), [†] Student's <i>t</i> -test, [‡] Chi-squared test, [§] Mann–Whitney U test, [¶] Fisher's exact test				

Table 2 shows the laboratory findings and the differences observed according to the severity of the disease.

Table 2
Laboratory findings on admission in patients with COVID-19

Variable	Critical Illness			p
	Total (n = 109)	No (n = 77)	Yes (n = 32)	
PaO ₂ , mmHg	63.5 (51.5–80.5)	68 (55.5–85)	51.5 (46–64)	0.00 ^{\$}
FiO ₂ , %	41 (29–50)	33 (21–41)	60 (41–60)	0.00
Horowitz Index (P/F ratio)	166.6±97.08	221.95± 92.14	96.56±47.21	0.00 [†]
Hemoglobin, g/L	14.6 (13.6–15.5)	14.6 (13.8–15.6)	14.5 (13.2–15.5)	0.68 ^{\$}
Hematocrit, %	44 (41-47.4)	44 (41.5–47.4)	44 (44-47.4)	0.98
Platelet count, x10 ³ /L	221 (160–274)	211 (156–266)	238.5 (167.5–316)	0.14
Neutrophil cell count, x10 ³ /L	6.3 (4-9.7)	4.7 (3.3-8.0)	9.3 (6.2–13.6)	0.00
Lymphocyte count, x10 ³ /L	0.9 (0.6–1.3)	1 (0.7–1.4)	0.8 (0.5-1.0)	0.00
Neutrophil-lymphocyte ratio	6.3 (3.6–12.5)	5.12 (2.8–9.38)	11.04 (7.75–21.41)	0.00
Sodium, mmol/L	135 (132.4–137)	135 (133–137)	134 (130.4-136.6)	0.13
Potassium, mmol/L	4.11 (3.78–4.58)	4 (3.6–4.4)	4.38 (3.97–4.87)	0.02
Calcium, mg/dL	8.3 (7.9–8.8)	8.37 (8.11–8.96)	8.2 (7.7–8.56)	0.01
Glucose, mg/dL	119 (105.8-174.8)	113 (103–148)	136.4 (115.4–226)	0.00
Creatinine, mg/dL	0.96 (0.75–1.3)	0.85 (0.72–1.1)	1.25 (0.8–1.9)	0.00
Blood urea nitrogen, mg/dL	17.8 (12.1–27.4)	16(11-20.6)	27 (19.2–46.7)	0.00
eGFR, ml/min/1.73m ²	82.3±38.5	86.7±38.21	57.37±35.93	0.00 [†]
C-reactive protein, mg/L	81 (27.5–192)	51.8 (17.2-118.6)	186 (99.5–278)	0.00 ^{\$}
D-dimer level, µg/mL	0.35 (0.22–0.75)	0.29 (0.2–0.75)	0.51 (0.27–0.82)	0.09
hsTnI, pg/mL	9.5 (5.1–32.9)	7.9 (4.9–15.4)	22.6 (10.7–114)	0.00
NT-proBNP, pg/mL	202 (87-1145)	175 (63–605)	737 (220–2103)	0.00
Creatine kinase, U/L	108 (47.6-196.4)	82 (44.4–194)	141.5 (80.4-217.7)	0.12
CK-MB fraction, U/L	1.59 (0.83–4.7)	1.5 (0.7–4.8)	2.1 (1.1–3.6)	0.77
Ferritin, ng/ml	481.7 (249-894.4)	457 (196.3–840)	629.7 (320.9–1290)	0.02
Fibrinogen, g/L	4.96 (3.87-6)	4.6 (3.7–5.5)	5.74 (5–7)	0.00
Alkaline phosphatase, U/L	81.5 (65–113)	79.7 (61.9-102.8)	97.35 (76.1-125.5)	0.02
LDH, U/L	310 (222–440)	274 (203.7–371)	394 (264-473.1)	0.00
AST, U/L	37.6 (20.9–49.9)	35.8 (21.7–54.7)	37.6 (25-56.8)	0.64
ALT, U/L	31.5 (21-49.9)	33.2 (20.9–53.9)	28.9 (21.6–44.8)	0.37
Direct bilirubin, mg/dL	0.16 (0.11–0.23)	0.14 (0.11–0.22)	0.19 (0.11–0.26)	0.12

Critical Illness				
Total bilirubin, mg/dL	0.66 (0.47–0.97)	0.67 (0.47–0.93)	0.65 (0.47–1.05)	0.89
Albumin, g/L	3.53±0.59	3.68±0.57	3.11±0.41	0.56 [†]
INR	1.11 (1.02–1.2)	1.1 (1-1.2)	1.16 (1.06–1.23)	0.12
<p>Values are expressed in number (percentage) and median (interquartile range).</p> <p>AST = aspartate aminotransferase, ALT = alanine aminotransferase, CK-MB = creatine kinase-MB, eGFR = estimated glomerular filtration rate, FiO2 = fraction of inspired oxygen, hsTnl = high sensitive Troponin-I, INR = international normalized ratio, LDH = lactate dehydrogenase, NT-proBNP = NT-pro-brain natriuretic peptide, PaO2 = partial pressure of oxygen</p> <p>* media (Standard deviation), [†]Student's <i>t</i>-test, [§]Mann–Whitney U test</p>				

Table 3 shows the tomography findings according to the severity of the patients. In general, GGO were present in 98 patients (89.9%), 54 patients (49.5%) had CORADS-5 upon admission, and in 55 (50.46%), there was a peripheral distribution of the interstitial infiltrate int the left lower lobe.

Table 3
Chest Computed Tomography findings on admission in patients with COVID-19

Critical Illness				
Chest CT findings, No. (%)	Total (n = 109)	No (n = 77)	Yes (n = 32)	p
GGO	98 (89.9)	67 (87)	31 (96.8)	0.10 [¶]
Consolidation	61 (55.9)	36 (46.7)	25 (78.12)	0.00 [‡]
Crazy paving pattern	6 (7.5)	3 (5.4)	3 (12)	0.27 [¶]
Linear pattern	41 (37.6)	27 (35)	14 (43.7)	0.39 [‡]
Lymphadenopathy	32 (29.36)	19 (24.6)	13 (40.62)	0.09
Pleural effusion	22 (20.18)	7 (9)	15 (46.8)	0.00
Pericardial effusion	17 (15.6)	5 (6.49)	12 (37.5)	0.00 [¶]
Pulmonary fibrosis	3 (2.78)	1 (1.32)	2 (6.25)	0.20
Pneumothorax	1 (0.92)	1 (1.3)	0	0.70
Steatosis	23 (21.3)	18 (23.6)	5 (15.62)	0.25 [‡]
Emphysema	2 (1.83)	0	2 (6.25)	0.08 [¶]
CO-RADS, No. (%)				
CO-RADS 0	0	0	0	
CO-RADS 1	7 (6.42)	6 (7.79)	1 (3.12)	0.33
CO-RADS 2	0	0	0	
CO-RADS 3	7 (6.42)	5 (6.49)	2 (6.25)	0.66
CO-RADS 4	18 (16.51)	14 (18.18)	4 (12.50)	0.46 [‡]
CO-RADS 5	54 (49.5)	36 (46.75)	18 (56.25)	0.36
CO-RADS 6	23 (21.10)	16 (20.78)	7 (21.88)	0.89
Distribution, No. (%)				
Peripheral distribution	55 (50.46)	43 (55.84)	12 (37.50)	0.08
Central distribution	22 (20.18)	11 (14.29)	11 (34.38)	0.01
Peripheral and central distribution	20 (18.35)	12 (15.58)	8 (25)	0.24
None	12 (11.01)	11 (14.29)	1 (3.12)	0.08 [¶]
CT score, mean (SD)				
Left upper lobe	2.33 (1.48)	1.96 (1.29)	3.25 (1.54)	0.00 [†]
Left lower lobe	3.12 (1.69)	2.78 (1.61)	3.93 (1.61)	0.00
Right upper lobe	2.36 (1.52)	1.97 (1.33)	3.32 (1.55)	0.00
Middle lobe	2.33 (1.55)	1.90 (1.37)	3.38 (1.47)	0.00
Right lower lobe	3.03 (1.57)	2.68 (1.56)	3.90 (1.22)	0.00

Critical Illness				
Total severity score	14 (8–19)*	11 (7–16)*	20 (16–23)*	0.00§
Values are expressed in number (percentage) and mean (standard deviation).				
CO-RADS = COVID-19 reporting and data system, CT = computed tomography, GGO = ground glass opacity, IQR = interquartile range.				
* median (IQR), [†] Student's <i>t</i> -test, [‡] Chi-squared test, [§] Mann–Whitney U test, [¶] Fisher's exact test				

Table 4
Risk factors for Critical Illness

Risk factors for critical illness				
	Univariate analysis		Multivariate analysis	
Variables	OR (95 % CI)	p	OR (95 % CI)	p
Ager, years	1.03	0.02		0.14
Laboratories findings				
PaO2, mmHg	0.96	0.00	0.96	0.05
FiO2, %	1.11	0.00	1.11	0.00
Neutrophil cell count, x10 ³ /L	1.23	0.00		0.33
Neutrophil-lymphocyte ratio	2.19	0.00	1.94	0.00
Potassium, mmol/L	2.02	0.01		0.86
Calcium, mg/dL	0.43	0.01		0.53
eGFR, ml/min/1.73m ²	0.98	0.01		0.17
Fibrinogen, g/L	1.10	0.01		0.18
Chest CT findings				
Consolidation	4.06	0.00		0.11
Pleural effusion	8.82	0.00		0.06
CT score ≥18	13.82	0.00	5.13	0.01
Risk Clinical Scores				
High risk COVID-GRAM	5.57	0.00		0.07
High risk qCSI	5.83	0.00		0.07
CI = confidence interval, COVID-GRAM = Critical Illness Risk Score, eGFR = estimated glomerular filtration rate, FiO2 = fraction of inspired oxygen, OR = odds ratio, PaO2 = partial pressure of oxygen, qCSI = quick COVID-19				

Results of the development of the Model

For each increase in FiO₂ (%), the Odds for critical illness increases by 10%, OR 1.10 (1.04–1.15), NLR 1.15 (1.05–1.26) and CT score 18 had an OR of 6.32 (1.89–21.05). Table 5 shows the Sensitivity (Se), Specificity (Sp), Positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (LR +), negative likelihood ratio (-) and the OR of each predictor in simple and combined form.

Table 5

Performance characteristics of COVID-19 severity risk scores and total severity score by CT in the prediction of Critical Illness

	AU-ROC	Sensitivity	Specificity	Positive LR	Negative LR	OR	PPV	NPV
NLR severe	0.64(0.55–0.73)	34.4(18.6–53.2)	94.8(87.2–98.6)	6.62(2.2–19.2)	0.69(0.53–0.89)	9.56(2.8–31.4)	73.9(49.4–89.2)	77.7(72.3–81.3)
CT score ≥ 18	0.78(0.69–0.87)	71.9(53.3–86.3)	84.4(74.4–91.7)	4.61(2.63–8.1)	0.33(0.19–0.58)	13.8(5.2–36.7)	66.4(53–77.6)	87.5(80–92.5)
High risk COVID-GRAM	0.68(0.58–0.77)	53.1(34.7–70.9)	83.1(72.9–90.7)	3.15(1.74–5.6)	0.56(0.38–0.82)	5.58(2.2–13.8)	57.4(42.7–70.9)	80.5(73.8–85.8)
High risk qCSI	0.68(0.59–0.76)	84.4(67.2–94.7)	51.9(40.3–63.5)	1.76(1.33–2.3)	0.30(0.13–0.69)	5.84(2–16.2)	42.9(36.3–49.8)	88.6(77.1–94.7)
Combination of clinical scores and TSS*								
NLR severe plus TSS	0.77(0.64–0.91)	57.1(28.9–82.3)	98.4(91.5–100)	36(4.89–263)	0.43(0.23–0.79)	82.7(10.8)	93.9(67.7–99.1)	84.3(74.5–90.8)
High risk COVID-GRAM plus CT score ≥ 18	0.83(0.72–0.94)	72.2(46.5–90.3)	94.8(85.6–98.9)	14(4.4–43.4)	0.29(0.13–0.61)	47.7(10.5–213)	85.7(65.7–94.9)	88.8(79–94.4)
High risk qCSI plus CT Score total	0.85(0.77–0.94)	90.9(70.8–98.9)	80.4(66.1–90.6)	4.65(2.55–8.4)	0.11(0.02–0.42)	41.1(8.75)	66.6(52.2–78.4)	95.4(84.5–98.7)
<p>* total severity score greater than 18</p> <p>AU-ROC = area under the ROC, CT = computed tomography, COVID-GRAM = Critical Illness Risk Score, LR = likelihood ratio, NLR = Neutrophil-lymphocyte ratio, NPV = negative predictive value, OR = odds ratio, PPV = positive predictive value, qCSI = quick COVID-19 severity index</p>								

The patients in critical condition were older, the respiratory rate, breaths / min higher and the tomography showed that consolidation and pericardial effusion were more frequent. In the univariate analysis, risk factors for developing severe disease were found, such as an increase in FIO₂% and an increase in the Neutrophil-Lymphocyte ratio. The COVID-GRAM and qCSI score was seven times higher in the critically ill patients.

Figure 1 shows tomography images of patients in different severity conditions.

Discussion

During the COVID-19 pandemic, the provision of optimal treatment for patients emerged as a priority which led to the implementation of measures with multiple therapies. At the same time, protecting health workers involved in the management and care of these patients also became a priority. (37) Additionally, several clinical indexes were proposed, aiming at the

evaluation and selection of the patients that might receive therapy at home, those that required hospitalization and those that were in need of ventilatory support.

An index that was already in use was the CURB-65 Score for Pneumonia Severity. It calculates mortality from community-acquired pneumonia and was proposed to define subjects that might be treated as outpatients and those that were in need of hospitalization. This score includes Respiratory Rate ≥ 30 , within its parameters (38).

A comparative analysis of the precision of the CURB-65 Score, the Pneumonia severity score (PSI) and COVID-GRAM A was performed in patients with COVID-19. These indexes were proposed to predict mortality and to determine the need for invasive mechanical ventilation. It was found that the COVID-GRAM index score was more accurate in identifying patients with higher mortality from SARS-CoV-2 pneumonia (39). Neither of these scores accurately predicted the need for invasive mechanical ventilation upon admission to an intensive care unit. (40). Among the parameters that COVID-GRAM the abnormality of the X-ray study, the presence of dyspnea and the NLR index are included.

On the other hand, other indexes directed to determine the need for anticoagulation in hospitalized patients due to the risk of venous thrombosis, VTE or bleeding were suggested. However they include heart and respiratory failure within their scoring parameters (41). In all of them, the authors found usefulness and suggested their employment during the classification and follow-up of patients with COVID-19. Some other indexes, such as the qSOFA (Quick SOFA) Score for Sepsis, were also proposed for the prediction of mortality; however, these are more frequently used for the diagnosis of sepsis, which occurs in critically ill COVID patients.

Among the indexes that evaluate respiratory compromise the NEWS is found. This score was analyzed in 35,585 medical admissions and includes respiratory rate, oxygen saturations, any supplemental oxygen, temperature and systolic blood pressure. Therefore, it could classify the degree of disease and the intervention required for intensive care. The authors suggested that prospective studies were needed to confirm the reliability of their scales. (42) Moreover, the Berlin study for the diagnosis of acute respiratory distress syndrome (ARDS) includes the deterioration of oxygenation, defined by the relationship between (PaO₂ / FiO₂) or by the relationship between peripheral O₂ saturation (pulse oximetry) and FiO₂ (SpO₂ / FiO₂). (REF)

Chest CT, an imaging parameter, is useful in the evaluation of patients with lung damage or serious complication of viral pneumonia, mainly when the finding on the chest radiograph is normal or inconclusive (43). In this study, we found that CT provides us with a quick evaluation and predicts critical severity in the short term (4,11). Through the use of the CT score, we could predicted which patient would require priority ventilatory support and hospitalization. The use of the indexes, alone or combined, even when evaluated retrospectively in this study, allowed us to recognize that these parameters make the difference between a health condition without seriousness and a condition that evolves to a serious condition. However, patients have an important respiratory compromise in which care must be defined in a timely manner both for ventilatory support and for the comprehensive initial therapy most useful in the intensive care unit.

We found that the use of CT alone as a diagnostic test has a good specificity and a moderate sensitivity; however, when combining its use with other indexes such as qCSI, both specificity and sensitivity are increased and the PPV and NPV increase. In a study by Liang and Cols (44), the authors sought the validation of a clinical score to predict the occurrence of critical illness and found that the associated factors were chest radiograph with abnormality, hemoptysis, dyspnea, unconscious state, number of comorbidities, previous cancer, NLR index, lactic dehydrogenase and direct bilirubin. The area under the curve was 0.88, and the authors concluded that the scale predicts which patients will develop critical disease. The findings in our study are very similar in all the medical parameters to those reported in that study, but we also show statistical robustness when comparing these parameters between critically ill and non-serious patients. In this study the tomographic status of the patient was analyzed together with the compromised ventilatory status.

These results make us consider that all laboratory parameters are essential to evaluate a patient with COVID-19 at the time of admission; however, it is relevant that the degree of respiratory compromise is of special importance since it is included in most of the indexes. In the study by Yuan et al. the utility of a clinical computed tomography-based receiver with operating

characteristic and a curve model for the diagnosis of COVID-19 was assessed (12). These authors demonstrated that mortality can be predicted with a sensitivity of 86% and specificity of 85%, and by means of a regression model of the ROC curve based on chest CT signs according to lung involvement. They showed a high diagnostic value of this method.

Furthermore, other indexes such as the Quick COVID-19 Severity Index (qCSI), include for their evaluation 3 variables among which the respiratory rate, pulse oximetry and nasal cannula flow rate are mentioned. Respiratory rate is also a parameter that is included in the scores of other indexes.

The qCSI index was widely used by some countries during the pandemic. Studies comments that its results surpassed other models, including the evaluation of rapid sequential organ failure related to sepsis and that of the CURB-65. Therefore, this index was proposed as a useful clinical tool to help make decisions about the level of care required in patients admitted to a hospital (13).

In the present study we found that the qCSI index showed good sensitivity and low specificity; however, its usefulness showed greater utility when combined with the CT evaluation, reaching a better specificity and a high percentage of NPV. This indicates that it predicts the probability for the individual to reach a severity condition when the score is not met.

One of the tools that is most often accessible when evaluating any condition in a patient are the laboratory determinations. In this pandemic, the NLR was proposed as a useful marker of an inflammatory state, which allows us to act in the comprehensive management of the patient. In this study of critically ill patients with COVID-19, we found an area under the curve (AUC) of 0.65 with a sensitivity and a specificity of 0.37 and 0.90 respectively. While the same analysis of this index was carried out in China it only reached an AUC 0.84 with sensitivity of 0.55 and specificity of 0.84. The explanations for these differences are several, and one of them could be the day on which the measurement of this index was made. The result would depend on whether the determination was made at the beginning of symptoms or when they were already in an advanced stage. Although it is a good parameter that may determine the clinical judgment, it only integrates part of a systemic problem that may be related to damage to different organs.

We evaluated the combined use of the LRN index with CT and found that sensitivity and specificity increased, and in relation to CT. The average CT Score in critically ill patients was 11.01.

Of all the indexes used in critically ill patients, the combination High risk qCSI plus CT score > 18 was the most useful. It should be noted that the High risk qCSI includes the respiratory parameters, breaths / min rate, pulse oximetry and O₂ flow rate, L / min, which emphasizes the importance of ventilatory care.

The multivariate analysis showed that the variables FiO₂, CT Score > 18 and the NRL index are the main risk factors. This shows biological coherence, since the respiratory rate, breaths / min was clearly increased and the Horowitz Index (P / F ratio) decreased in critically ill patients.

On the other hand, the correlation between the CT Score and the respiratory rate, breaths / min was moderate (40%) $p = 0.0001$, which indicates that the parameters observed in the increase in respiratory work correlate with the damage found at the lung level reported by the CT Score

Limitations

This was an observational, retrospective study. Being a third-level hospital, admitted patients do not represent the behavior of mild cases of COVID-19. There is loss of follow-up after their discharge and further evaluations are difficult. The FiO₂ (%) provided to the patient had fluctuations due to the administration method. It was dynamic and therefore, the calculation had limitations.

Interpretation

The use of clinical risk indexes (COVID-19 and qCSI) in combination with a CT score > 18 obtained by Chest CT could represent a good option in the risk stratification of critical disease development.

Implications

The importance of imaging methods and their appropriate clinical use is relevant. The studied indexes show predictive support with good sensitivity and specificity, which could be considered in the context of the initial evaluation for a SARS-CoV-2 infection. The data shown could also be considered in the current state of relapses. These indexes should be considered for the initial evaluation of patients infected with SARSCoV2 and may help in taking accurate clinical decisions that prevent the patient from progressing to seriousness. They may prove useful even asymptomatic subjects, who may have lung damage not detectable by symptoms or due to minor signs in the laboratory.

Conclusion

The combined use of indexes such as the CT Score, Neutrophil lymphocyte Rate, Quick COVID-19 Severity Index, classify and select with better precision the severity of the patient infected with SARSCoV2. This allows for a better classification of patients with COVID-19 at the moment of hospital admission and it guides to the optimal comprehensive therapeutic management in hospitalized patients at risk of evolution to critical condition. Respiratory rate, breaths / min, is a clinical parameter that suggests severity in the patients. A large majority of indexes include this parameter in their classification score, and it should be considered a clinical parameter of impact.

Abbreviations

CT= Computed Tomography.

ACS= Acute coronary ischemic syndrome

RT-PCR= Acronym for Reverse Transcriptase Polymerase Chain Reaction (Reverse Transcription)

COVID-19= Infectious disease caused by the coronavirus

CORADS= Acronym: Radiology developed a standardized evaluation scheme for the lung condition due to COVID-19

NLR= neutrophil-lymphocyte ratio

ICU= Critical care unit

COVID-GRAM= Critical Illness risk score in Hospitalized COVID 19 patients.

qCSI= Severity index that predicts the risk of critical respiratory disease in 24 hours,

Declarations

All evaluations were approved by the local Research and Ethics Committee of the local National Institute of Cardiology (research protocol number 17-1033). Informed consent was obtained in writing from all patients. The study was based on patients treated at the Institution during this pandemic and is registered at (ClinicalTrials.gov, Identifier: and registered at www.clinicaltrials.gov (NCT04557345).

Consent for publication. This was obtained within the ethical approval, the participants of the study gave their consent to publish the data collected during the study period.

Availability of data and materials. The basic data are part of the Mexican cohort of patients treated for SARS CoV2 infection with suspected lung disease. The head of the Computed Tomography area is Dr. Sergio Ciales who has data available if

someone requires it. order. The procedure would be through your email scriales@gmail.com. All the results to which the manuscript refers are duly documented in the text, figures and tables.

Conflict of interest statement

No party having a direct interest in the results of the research supporting this article has or

Will confer a benefit on the author(s) or on any organization with which the author(s) is/are

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References

1. Lieveld AWE, Azijli K, Teunissen BP, van Haaften RM, Kootte RS, van den Berk IAH, et al. Chest CT in COVID-19 at the ED: Validation of the COVID-19 Reporting and Data System (CO-RADS) and CT Severity Score: A Prospective, Multi-Center, Observational Study. *Chest*. 2020/12/04. 2020;
2. Chung M, Bernheim A, Mei X, Zhang N, Huang M, Zeng X, et al. CT Imaging Features of 2019 Novel Coronavirus (2019-nCoV). *Radiology* [Internet]. 2020;295(1):202–7. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/32017661>
3. Ding X, Xu J, Zhou J, Long Q. Chest CT findings of COVID-19 pneumonia by duration of symptoms. *Eur J Radiol* [Internet]. 2020 Jun;127:109009. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/32325282>
4. Pan F, Ye T, Sun P, Gui S, Liang B, Li L, et al. Time Course of Lung Changes at Chest CT during Recovery from Coronavirus Disease 2019 (COVID-19). *Radiology* [Internet]. 2020;295(3):715–21. Available from:

<http://www.ncbi.nlm.nih.gov/pubmed/32053470>

5. Ye Z, Zhang Y, Wang Y, Huang Z, Song B. Chest CT manifestations of new coronavirus disease 2019 (COVID-19): a pictorial review. *Eur Radiol* [Internet]. 2020 Aug;30(8):4381–9. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/32193638>
6. Hani C, Trieu NH, Saab I, Dangeard S, Bennani S, Chassagnon G, et al. COVID-19 pneumonia: A review of typical CT findings and differential diagnosis. *Diagn Interv Imaging* [Internet]. 2020 May;101(5):263–8. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/32291197>
7. Salehi S, Abedi A, Balakrishnan S, Gholamrezanezhad A. Coronavirus Disease 2019 (COVID-19): A Systematic Review of Imaging Findings in 919 Patients. *AJR Am J Roentgenol* [Internet]. 2020/03/17. 2020;215(1):87–93. Available from: [internal-pdf://241.243.36.81/Salehi-2020-Coronavirus Disease 2019 \(COVID-19\).pdf](internal-pdf://241.243.36.81/Salehi-2020-Coronavirus Disease 2019 (COVID-19).pdf)
8. Liang W, Liang H, Ou L, Chen B, Chen A, Li C, et al. Development and Validation of a Clinical Risk Score to Predict the Occurrence of Critical Illness in Hospitalized Patients With COVID-19. *JAMA Intern Med* [Internet]. 2020/05/13. 2020;180(8):1081–9. Available from: <internal-pdf://65.167.196.198/Liang-2020-Development and Validation of a Cli.pdf>
9. Prokop M, van Everdingen W, van Rees Vellinga T, Quarles van Ufford H, Stöger L, Beenen L, et al. CO-RADS: A Categorical CT Assessment Scheme for Patients Suspected of Having COVID-19-Definition and Evaluation. *Radiology* [Internet]. 2020/04/28. 2020;296(2):E97–e104. Available from: internal-pdf://186.149.248.113/Prokop-2020-CO-RADS_ A Categorical CT Assessme.pdf
10. Sánchez-Oro R, Torres Nuez J, Martínez-Sanz G. Radiological findings for diagnosis of SARS-CoV-2 pneumonia (COVID-19). *Med Clin* [Internet]. 2020/04/24. 2020;155(1):36–40. Available from: <internal-pdf://196.11.173.249/Sánchez-Oro-2020-Radiological findings for dia.pdf>
11. Franccone M, lafrate F, Masci GM, Coco S, Cilia F, Manganaro L, et al. Chest CT score in COVID-19 patients: correlation with disease severity and short-term prognosis. *Eur Radiol* [Internet]. 2020/07/06. 2020;30(12):6808–17. Available from: <internal-pdf://189.27.88.183/Franccone-2020-Chest CT score in COVID-19 patie.pdf>
12. Li X, Yuan F, Zhang Z, Yang J, Zhang J, Li Z, et al. Clinical utility of a computed tomography-based receiver operating characteristic curve model for the diagnosis of COVID-19. *Ann Palliat Med* [Internet]. 2021 Feb;10(2):2048–61. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/33725765>
13. Haimovich AD, Ravindra NG, Stoytchev S, Young HP, Wilson FP, van Dijk D, et al. Development and Validation of the Quick COVID-19 Severity Index: A Prognostic Tool for Early Clinical Decompensation. *Ann Emerg Med* [Internet]. 2020/10/06. 2020;76(4):442–53. Available from: <internal-pdf://145.144.205.228/Haimovich-2020-Development and Validation of t.pdf>
14. Yang A-P, Liu J-P, Tao W-Q, Li H-M. The diagnostic and predictive role of NLR, d-NLR and PLR in COVID-19 patients. *Int Immunopharmacol* [Internet]. 2020 Jul;84:106504. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/32304994>
15. Martins EC, Silveira LDF, Viegas K, Beck AD, Fioravanti Júnior G, Cremonese R V, et al. Neutrophil-lymphocyte ratio in the early diagnosis of sepsis in an intensive care unit: a case-control study. *Rev Bras Ter Intensiva* [Internet]. 2019/03/28. 2019;31(1):64–70. Available from: <internal-pdf://209.155.80.10/Martins-2019-Neutrophil-lymphocyte ratio in th.pdf>
16. Hong KH, Lee SW, Kim TS, Huh HJ, Lee J, Kim SY, et al. Guidelines for Laboratory Diagnosis of Coronavirus Disease 2019 (COVID-19) in Korea. *Ann Lab Med* [Internet]. 2020;40(5):351–60. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/32237288>
17. Sule WF, Oluwayelu DO. Real-time RT-PCR for COVID-19 diagnosis: challenges and prospects. *Pan Afr Med J* [Internet]. 2020/12/08. 2020;35(Suppl 2):121. Available from: <internal-pdf://243.123.141.217/Sule-2020-Real-time RT-PCR for COVID-19 diagno.pdf>
18. Younes N, Al-Sadeq DW, Al-Jighefee H, Younes S, Al-Jamal O, Daas HI, et al. Challenges in Laboratory Diagnosis of the Novel Coronavirus SARS-CoV-2. *Viruses* [Internet]. 2020/05/30. 2020;12(6). Available from: <internal-pdf://247.36.198.123/Younes-2020-Challenges in Laboratory Diagnosis.pdf>
19. Zitek T. The Appropriate Use of Testing for COVID-19. *West J Emerg Med* [Internet]. 2020/04/18. 2020;21(3):470–2. Available from: <internal-pdf://0945117273/Zitek-2020-The Appropriate Use of Testing for.pdf>

20. Bhimraj A, Shumaker AH, Laverigne V, Baden L, Cheng VC, Edwards KM, Gandhi R, Gallagher J, Muller WJ, O'Horo JC, Shoham S, Murad MH, Mustafa RA, Sultan S, Falck-Ytter Y. MRL. Infectious Diseases Society of America Guidelines on the Treatment and Management of Patients with COVID-19 [Internet]. Version 4. Infectious Diseases Society of America; 2021. Available from: <https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/>.
21. Panel C-19 TG. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. [Internet]. National Institutes of Health.; 2019. Available from: <https://www.covid19treatmentguidelines.nih.gov/>.
22. Metlay JP, Waterer GW, Long AC, Anzueto A, Brozek J, Crothers K, et al. Diagnosis and Treatment of Adults with Community-acquired Pneumonia. An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America. *Am J Respir Crit Care Med* [Internet]. 2019/10/02. 2019;200(7):e45–67. Available from: <internal-pdf://67.83.208.202/Metlay-2019-Diagnosis and Treatment of Adults.pdf>
23. Kumar N, Law A. Teaching Rounds: A Visual Aid to Teaching Internal Medicine Pearls on the Wards [Internet]. McGraw-Hill Education; 2016. Available from: <https://books.google.nl/books?id=OKyZDAAAQBAJ>
24. Roca O, Messika J, Caralt B, García-de-Acilu M, Sztrymf B, Ricard J-D, et al. Predicting success of high-flow nasal cannula in pneumonia patients with hypoxemic respiratory failure: The utility of the ROX index. *J Crit Care* [Internet]. 2016;35:200–5. Available from: <https://www.sciencedirect.com/science/article/pii/S0883944116300946>
25. World Health O. Clinical management of severe acute respiratory infection when Middle East respiratory syndrome coronavirus (MERS-CoV) infection is suspected: interim guidance [Internet]. Geneva: World Health Organization; 2019. Available from: <https://apps.who.int/iris/handle/10665/178529>
26. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med*. 2020;382(8):727–33.
27. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia. *N Engl J Med* [Internet]. 2020;382(13):1199–207. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/31995857>
28. Lu H, Stratton CW, Tang Y-W. Outbreak of pneumonia of unknown etiology in Wuhan, China: The mystery and the miracle. *J Med Virol* [Internet]. 2020;92(4):401–2. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/31950516>
29. Hui DS, I Azhar E, Madani TA, Ntoumi F, Kock R, Dar O, et al. The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health - The latest 2019 novel coronavirus outbreak in Wuhan, China. *Int J Infect Dis* [Internet]. 2020;91:264–6. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/31953166>
30. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet (London, England)* [Internet]. 2020;395(10223):497–506. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/31986264>
31. Unger T, Borghi C, Charchar F, Khan NA, Poulter NR, Prabhakaran D, et al. 2020 International Society of Hypertension Global Hypertension Practice Guidelines. *Hypertension* [Internet]. 2020/05/07. 2020;75(6):1334–57. Available from: <internal-pdf://176.6.200.59/Unger-2020-2020 International Society of Hyper.pdf>
32. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2021. *Diabetes Care* [Internet]. 2020/12/11. 2021;44(Suppl 1):S15–s33. Available from: <internal-pdf://121.226.169.224/2021-2. Classification and Diagnosis of Diabet.pdf>
33. Mach F, Baigent C, Catapano AL, Koskinas KC, Casula M, Badimon L, et al. 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. *Eur Hear J* [Internet]. 2019/09/11. 2020;41(1):111–88. Available from: internal-pdf://0628175008/Mach-2020-2019 ESC_EAS Guidelines for the mana.pdf
34. Inker LA, Astor BC, Fox CH, Isakova T, Lash JP, Peralta CA, et al. KDOQI US commentary on the 2012 KDIGO clinical practice guideline for the evaluation and management of CKD. *Am J Kidney Dis*. 2014/03/22. 2014;63(5):713–35.
35. WHO Guidelines Approved by the Guidelines Review Committee. In: WHO Guidelines on Drawing Blood: Best Practices in Phlebotomy. Geneva: World Health Organization Copyright © 2010, World Health Organization.; 2010.
36. Kleinbaum DG. Applied regression analysis and other multivariable methods: (AISE). Belmont, Calif.: Thomson; 2008.

37. Etkind SN, Bone AE, Lovell N, Cripps RL, Harding R, Higginson IJ, et al. The Role and Response of Palliative Care and Hospice Services in Epidemics and Pandemics: A Rapid Review to Inform Practice During the COVID-19 Pandemic. *J Pain Symptom Manage* [Internet]. 2020;60(1):e31–40. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/32278097>
38. Lim WS, van der Eerden MM, Laing R, Boersma WG, Karalus N, Town GI, et al. Defining community acquired pneumonia severity on presentation to hospital: an international derivation and validation study. *Thorax* [Internet]. 2003 May;58(5):377–82. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/12728155>
39. Fine MJ, Auble TE, Yealy DM, Hanusa BH, Weissfeld LA, Singer DE, et al. A prediction rule to identify low-risk patients with community-acquired pneumonia. *N Engl J Med* [Internet]. 1997 Jan 23;336(4):243–50. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/8995086>
40. Esteban Ronda V, Ruiz Alcaraz S, Ruiz Torregrosa P, Giménez Suau M, Nofuentes Pérez E, León Ramírez JM, et al. Application of validated severity scores for pneumonia caused by SARS-CoV-2. *Med Clin (English ed)* [Internet]. 2021 Jun 30; Available from: <http://www.ncbi.nlm.nih.gov/pubmed/34226877>
41. Barbar S, Noventa F, Rossetto V, Ferrari A, Brandolin B, Perlati M, et al. A risk assessment model for the identification of hospitalized medical patients at risk for venous thromboembolism: the Padua Prediction Score. *J Thromb Haemost* [Internet]. 2010 Nov;8(11):2450–7. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/20738765>
42. Smith GB, Redfern OC, Pimentel MA, Gerry S, Collins GS, Malycha J, et al. The National Early Warning Score 2 (NEWS2). *Clin Med* [Internet]. 2019;19(3):260. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/31092526>
43. Simpson S, Kay FU, Abbara S, Bhalla S, Chung JH, Chung M, et al. Radiological Society of North America Expert Consensus Document on Reporting Chest CT Findings Related to COVID-19: Endorsed by the Society of Thoracic Radiology, the American College of Radiology, and RSNA. *Radiol Cardiothorac Imaging*. 2021/03/30. 2020;2(2):e200152.
44. Liang W, Liang H, Ou L, Chen B, Chen A, Li C, et al. Development and Validation of a Clinical Risk Score to Predict the Occurrence of Critical Illness in Hospitalized Patients With COVID-19. *JAMA Intern Med* [Internet]. 2020;180(8):1081–9. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/323961>

Figures

Figure 1

A) Image of computed tomography in lung window, axial and coronal section as well as representation by artificial intelligence with quantitative analysis . Ground glass areas are demonstrated in the posterior and lateral segments of the right lower lobe. CT Score 3/40. B) Image of computed tomography in the lung window, axial and coronal section as well as representation by artificial intelligence with quantitative analysis showing areas of ground glass in the upper right lobe and other scattered areas in the left lung. CT Score 10/40. C) Image of computed tomography in lung window, axial and coronal section as well as representation by artificial intelligence with quantitative analysis showing areas of ground glass with diffuse distribution in both lungs. CT Score 24/40