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ORIGINAL ARTICLE

Utility of a Pulmonary Oedema Score for Predicting the Need for Mechanical Ventilation in COVID-19 Patients in a General Hospital

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Background. The Radiographic Assessment of Lung Edema (RALE) score has been used to estimate the extent of pulmonary damage in patients with acute respiratory distress syndrome and might be useful in patients with COVID-19.

Aim of the study. To examine factors associated with the need for mechanical ventilation in hospitalized patients with a clinical diagnosis of COVID-19, and to estimate the predictive value of the RALE score.

Methods. In a series of patients admitted between April 14 and August 28, 2020, with a clinical diagnosis of COVID-19, we assessed lung involvement on the chest radiograph using the RALE score. We examined factors associated with the need for mechanical ventilation in bivariate and multivariate analysis. The area under the receiver operating curve (AUC) indicated the predictive value of the RALE score for need for mechanical ventilation.

Results. Among 189 patients, 90 (48%) were judged to need mechanical ventilation, although only 60 were placed on a ventilator. The factors associated with the need for mechanical ventilation were a RALE score >6 points, age >50 years, and presence of chronic kidney disease. The AUC for the RALE score was 60.9% (95% CI 52.9–68.9), indicating it was an acceptable predictor of needing mechanical ventilation.

Conclusions. A score for extent of pulmonary oedema on the plain chest radiograph was a useful predictor of the need for mechanical ventilation of hospitalized patients with COVID-19. © 2022 Instituto Mexicano del Seguro Social (IMSS). Published by Elsevier Inc. All rights reserved.

Key Words: COVID-19, SARS-CoV-2, RALE, Mechanical ventilation, ROC curves, Chest radiograph.

Introduction

The COVID-19 pandemic began in 2020 and rapidly spread globally. From the declaration of a pandemic to August 13th, 2021, there have been 204.6 million of COVID-

19 confirmed cases of COVID-19 and 4.1 million deaths, with a global fatality rate of 2.1% (1).

Factors associated with greater severity of COVID-19 infection include older age (2-4), male sex (3,5), and presence of comorbidities (5,6). Severe COVID-19 clinically presents as pneumonia, with acute respiratory distress syndrome and blood oxygen saturation of less than 90%. Comorbidities associated with COVID-19 complications include high blood pressure (4,7), diabetes mellitus type 2 (7), obesity (8), cardiovascular diseases (7), chronic kidney

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disease (7,9), liver failure, chronic obstructive pulmonary disease, and asthma (7). Between 68% and 93% of patients with severe COVID-19 have at least one comorbidity (5,10). Patients with severe COVID-19 develop acute respiratory distress syndrome (ARDS) and may require mechanical ventilation (2).

The COVID-19 diagnosis is confirmed by the reverse transcription polymerase chain reaction (RT-PCR), in the acute disease between 3–7 d of disease onset, and by ELISA immunochromatography for the detection of IgM and IgG antibodies against SARS-CoV-2 virus, after 7 d of infection. The RT-PCR test is positive in about 80% in the first three days of the disease (11,12). Computed tomography (CT) is useful for assessing lung damage in ARDS, with or without PCR evidence of COVID-19 (13–15). However, few hospitals in low-income countries have access to a CT scanner.

Symptoms, blood test results, oxygen saturation and chest radiography are important in deciding the treatment of patients with COVID-19 (16,17). Chest radiography is useful to assess the severity of the disease and predicts the use of mechanical ventilation (5). The chest radiograph commonly shows changes of a viral pneumonia. Wong adapted and simplified the Radiographic Assessment of Lung Edema (RALE) score proposed by Warren (18,19), to assess the severity of lung involvement in serial chest radiographs of 255 patients with COVID-19. He assessed areas of consolidation, ground glass opacities, and pleural effusion.

The RALE score could be useful to relate radiographic findings to clinical status of patients with COVID-19, and potentially could help to guide their clinical management. Unlike computed tomography, chest radiography is widely accessible even in low resource settings. The objective of this study was to estimate the predictive value of the RALE score for the need for mechanical ventilation in patients with a clinical diagnosis of COVID-19 in an acute hospital setting in Acapulco, Mexico, and to examine other factors associated with the need for ventilation.

Materials and Methods

The study was a case series of patients admitted by the emergency service at the "Vicente Guerrero" Hospital, of the Mexican Social Security Institute, from April 14th–July 28th, 2020. Eligible patients were those with a clinical diagnosis of COVID-19, having had a chest radiograph and a RT-PCR test for COVID-19, and with complete records available. Of 388 patients admitted to the hospital, 189 met the study eligibility criteria.

Three of the authors designed a data collection instrument for the study and validated it by roundtable discussion (20) including a specialist in medical-surgical emergencies, an imaging specialist and two epidemiologists. The instrument collected information from the patients'

hospital records only, including sociodemographic information, clinical status and laboratory results, and chest radiographic findings.

The first section included the patient's name, membership number, sex, and age. Clinical information included comorbidities (diabetes mellitus type 2, high blood pressure, obesity, chronic obstructive pulmonary disease, heart failure, asthma, systemic lupus erythematosus, HIV infection, chronic kidney disease, and liver failure), peripheral oxygen saturation, measured by pulse oximetry on admission, need for mechanical ventilation and number of days on ventilation, number of days of hospitalization, disease duration from the onset of symptoms to hospital discharge and reason for hospital discharge, such as reference to another hospital or voluntary discharge. Laboratory results included the levels of haemoglobin, glucose and lymphocytes count, and the result of RT-PCR for COVID-19.

The radiographs were taken in the patient's bed, with anteroposterior projection and digital portable radiodiagnosis equipment (Technix, model TMB 400 DR). Interpretation of the chest radiograph followed the Wong adaptation of the Radiographic Assessment of Lung Edema (RALE) (18,19). A radiologist scored the chest radiograph blind to whether the patient had required mechanical ventilation or not. The radiologist scored severity from 0–8 points with increasing extent of the lung disease. To calculate the score, each lung is divided into four parts horizontally, each quadrant is scored as 0 or 1 point, depending on whether consolidation or ground glass opacities are present. The scores for the two lungs are summed to produce the final score. The lung involvement was categorized as: 0 points, normal chest radiograph; 1–2 points, mild involvement; 3–6 points, moderate involvement; 7 and 8 points, severe involvement (Figure 1).

The outcome variable was the need for mechanical ventilation, as recorded in the patient's record, whether the patient was actually intubated and ventilated.

Data entry relied on the EpiData program version 3.1 (21), and data analysis relied on CIETmap (22). Using the Mantel-Haenszel procedure, we estimated associations between the outcome and potentially associated variables, in bivariate and then multivariate analysis. We report the odds ratio and 95% confidence intervals (23) to indicate statistical significance. Multivariate analysis began with a saturated model including all variables significantly associated with the outcome in bivariate analysis and stepped down to a final model where all the remaining variables were associated with the outcome at the 5% significance level.

We tested the evolution of the RALE score over time from the onset of symptoms by X^2 for trend. Considering the RALE score as a diagnostic test for the need for ventilation as the condition, we estimated the utility of the RALE score for predicting the need for mechanical ventila-

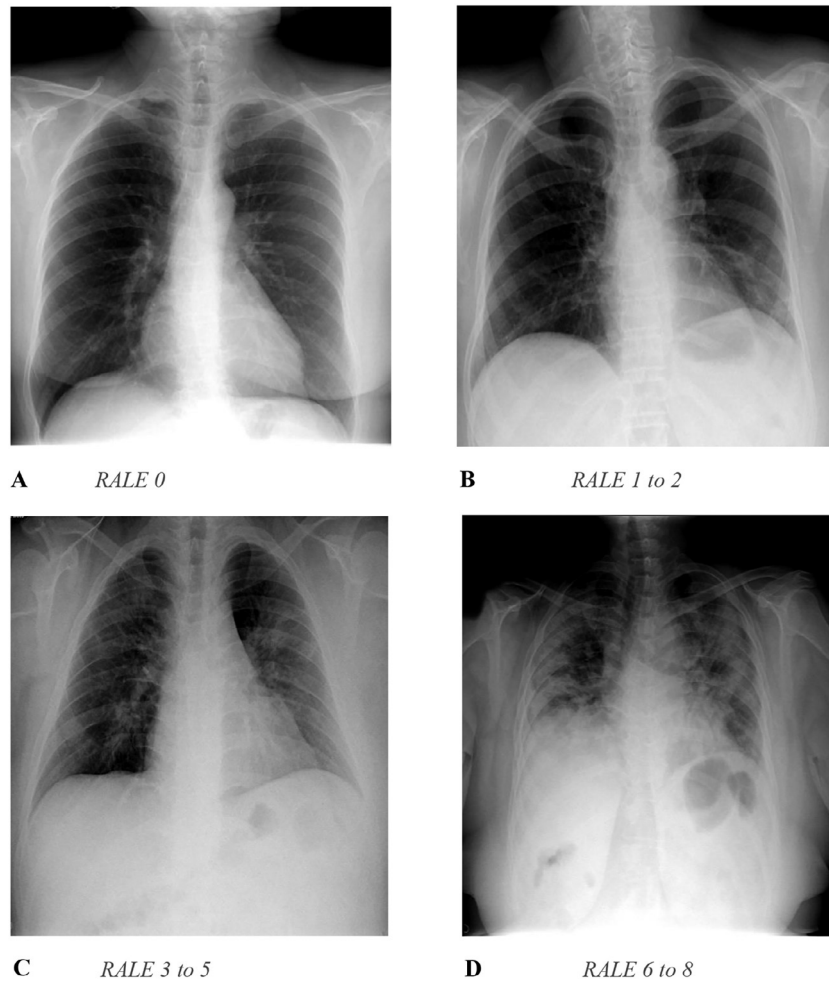


Figure 1. Examples of RALE evaluation of chest X-rays. A. Normal chest X-ray. RALE evaluation 0 points B. Highly suspicious lesions of Covid-19, basal pulmonary opacity with a reticular or linear interstitial pattern and halo sign. Mild RALE evaluation (1–2 points). C. Common pattern of Covid-19, predominance of ground glass image with slight interstitial linear thickening. Moderate RALE evaluation (3–5 points). D. Typical findings of Covid-19, extensive bilateral involvement, mixed ground glass pattern, nodular reticulum, and areas of consolidation. Severe RALE evaluation (≥ 6 points).

tion. We created Receiver Operating Characteristic (ROC) curves (24,25) using the R “pROC” package, treating the RALE score as an ordinal variable (26) and calculated the area under the curve (AUC) as an indicator of diagnostic accuracy of the RALE score.

Patient information was confidential but not anonymous. The full name and social security number of each patient was recorded on a separate list for monitoring the results of laboratory studies and their follow-up until discharge. Patients or relatives did not sign a consent form for inclusion of their data in the study. In the emergency, the local research committee gave approval to collect the data for research purposes. Only the field research team, two medical residents and the main researcher, had access to patients’ personal information. All data are in the keeping of the main researcher. The Local Research Committee of the Mexican Social Security Institute authorized the study, with folio number R-2020-1102-050.

Results

Of 388 patients admitted to the hospital with a clinical diagnosis of atypical pneumonia and suspected COVID-19, 189 (49%) met the study eligibility criteria. 199 patients (51%) were excluded because their clinical record was incomplete, or they did not have a chest radiograph.

Three patients were children, aged twelve months, six years, and twelve years. The average age of the adult patients was 56.6 years (SD 14.5, range 22 and 89 years). 36.5% (69/189) of the patients were female.

The most common comorbidities were high blood pressure and type 2 diabetes mellitus. Diabetes was more common among the women (52%, 36/69) than among the men (36%, 43/120). Table 1 shows the distribution of comorbidities and the sex of the patients. Most of the patients (96%, 182/189) had acute respiratory distress syndrome (ARDS) and 13% (25/189) had multiple organ failure.

Table 1. Comorbidities distribution in patients with a clinical diagnosis of COVID-19

Comorbidities	Female <i>n</i> = 69	Male <i>n</i> = 120	<i>p</i>
High blood pressure (HBP)	46% (32/69)	46% (55/120)	0.99
Type 2 diabetes mellitus (DM2)	52% (36/69)	36% (43/120)	0.04
Obesity	15% (10/69)	13% (16/120)	0.99
Chronic kidney disease (CKD)	13% (9/69)	11% (13/120)	0.82
Chronic obstructive pulmonary disease (COPD)	4% (3/69)	7% (8/120)	0.74
Heart failure (HF)	7% (5/69)	3% (3/120)	0.24
Asthma	3% (2/69)	0.8% (1/120)	0.60
Liver failure	1% (1/69)	0.8% (1/120)	0.99

Table 2. Period between onset of COVID-19 symptoms and RALE evaluation among adult patients only

Punctuation RALE	First week	Second week	Third week	Fourth week
1–2 points	5.4% (6/112)	11.7% (7/60)	18.2% (2/11)	0% (0/3)
3–6 points	41.1% (46/112)	50.0% (30/60)	27.3% (3/11)	0% (0/3)
7–8 points	53.6% (60/112)	38.3% (23/60)	54.5% (6/11)	100% (3/3)

χ^2 Trend test = 40.36, 6 fd, $p < 0.00001$.

Length of hospital stay ranged from 1 to 48 d, with an average of 10 d. Patient follow-up was an average of 17 d (range <24 h to 60 d), from the onset of symptoms to hospital discharge. The average time from onset of symptoms to hospital admission was 7 d (range 1–41 d). Nearly half (47%) of the patients (88/189) died in hospital: 29 women (42%, 29/69) and 59 men (48%, 59/120). Half (50%) of the patients (95/189) were discharged after clinical improvement, 3% (5/189) requested voluntary discharge, and one patient (0.5%) was referred to another medical unit and died.

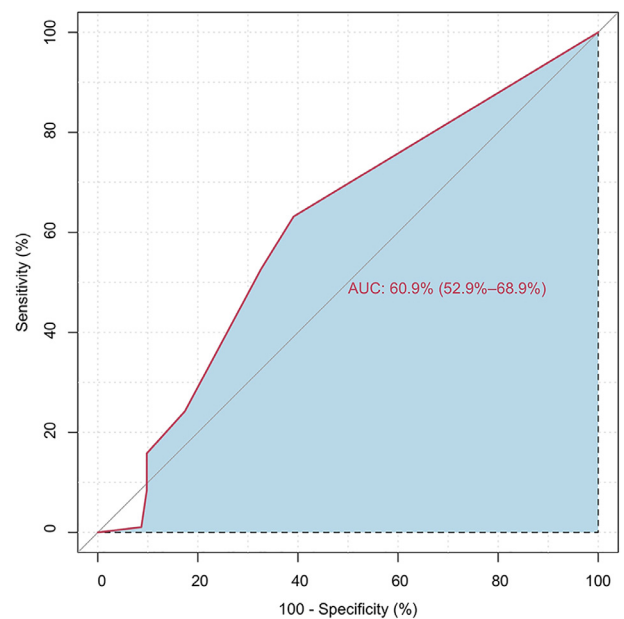
The great majority of the patients (80%, 152/189) had a positive RT-PCR test. Oxygen saturation by peripheral oximetry was recorded in 156 patients, 2% (3/156) had a saturation less than 40, and 6% (9/156) between 41 and 60, 43% (67/156) between 61 and 89, and 49% (77/156) 90% or greater.

Almost half of the patients (48%, 90/189) were judged to need mechanical ventilation, 42% (29/69) of the women and 51% (61/120) of the men. However, only 32% (60/189) received this support. Those who were placed on mechanical ventilation remained on the ventilator for six days on average (range <24 h to 27 d).

Chest radiography was performed in 60% (112/186) of adult patients in the first week after the onset of symptoms; in 32% (60/186) it was done in the second week; 6% (11/186) in the third week and 2% (3/186) in the fourth week.

The results of the classification of pulmonary involvement by RALE were mild 9% (17/189); moderate, 42% (80/189) and severe 49% (92/189). RALE scores were significantly higher when the radiograph was taken longer after the onset of symptoms. (Table 2).

The area under the curve (AUC) from the Receiver Operating Characteristic (ROC) curves indicated that the RALE score was an adequate estimator of the prediction of

**Figure 2.** Receiver Operating Characteristic (ROC) curve on sensitivity and specificity of RALE evaluation for predicting requirement of mechanical ventilation among patients with clinical diagnosis of COVID-19.

patients' requirement of mechanical ventilation, at 60.9% (95% CI 52.9–68.9) (Figure 2). The AUC can have any value between 0 and 1. A perfect diagnostic test has an AUC of 1. An excellent test has AUC values between 0.9–1.0, a very good test values of 0.8–0.9, good 0.7–0.8, adequate 0.6–0.7, bad 0.5–0.6. A test is not useful when the AUC value is ≤ 0.5 .

Table 3 shows the bivariate analysis of factors associated with requiring mechanical ventilation. The potentially associated factors were age, chronic kidney disease (CKD), chronic obstructive pulmonary disease (COPD), the RALE score, and multiple organ failure. The final multivariate

Table 3. Bivariate analysis of factors associated with the requirement for mechanical ventilation

Factor	Patients requiring mechanical ventilation	ORna ^a	95% CI ^b
Sex			
Female	42.0% (29/69)	0.68	0.37–1.23
Male	51.7% (61/118)		
Age			
≥50 years old	57.4% (74/129)	3.53	1.83–6.82
<50 years old	27.6% (16/58)		
Type 2 diabetes mellitus (DM2)			
With DM2	49.4% (39/79)	1.09	0.61 - 1.95
Without DM2	47.2% (51/108)		
High blood pressure (HBP)			
With HBP	55.2% (48/87)	1.70	0.95–3.03
Without HBP	42.0% (42/100)		
Obesity			
With obesity	46.2% (12/26)	0.91	0.40–2.10
Without obesity	48.4% (78/161)		
Chronic kidney disease (CKD)			
With CKD	77.3% (17/22)	4.28	1.61–11.44
Without CKD	44.2% (73/165)		
Chronic obstructive pulmonary disease (COPD)			
With COPD	63.6% (7/11)	1.96	0.56–6.82
Without COPD	47.4% (83/176)		
Asthma			
With asthma	66.7% (2/3)	2.18	0.20–23.26
Without asthma	47.8% (88/184)		
Liver failure (LF)			
With LF	50.0% (1/2)	1.08	0.07–17.63
Without LF	48.1% (89/185)		
Heart failure (HF)			
With HF	50.0% (4/8)	1.08	0.26–4.47
Without HF	48.0% (86/179)		
Classification of Radiographic Assessment Lung Edema (RALE)			
≥6 points	60.4% (55/ 91)	2.66	1.48–4.79
<6 points	36.5% (35/96)		
C-reactive protein			
Positive	50.0% (75/150)	1.47	0.71–3.04
Negative	40.5% (15/37)		
Days of hospitalization			
≥9 d	51.6% (48/93)	1.32	0.74–2.35
<9 d	44.7% (42/94)		
Days elapsed from onset illness to admission			
≥15 d	54.0% (47/87)	1.56	0.87–2.78
<15 d	43.0% (43/100)		

^aUnadjusted Odds Ratio^b95% Confidence Intervals.

included age over 50 years, suffering from chronic kidney disease and the RALE score (Table 4). The strongest association was with the presence of chronic kidney disease.

Discussion

The study included patients admitted between April and July 2020, during the peak of the first wave of the pandemic in the area. In this study, the severity of lung involvement assessed by the RALE score was significantly associated with the need for mechanical ventilation and the RALE score was an adequate predictor for this need.

In a previous study, severity of lung involvement, as detected in the chest radiograph, was predictive of intubation in patients with COVID-19 pneumonia (8). Acute respiratory distress syndrome (ARDS) is associated with the need for mechanical ventilation in COVID-19 patients (2). To our knowledge, our study is the first to use the RALE scale as a predictor of the need for mechanical ventilation. Chest X-ray evaluation by RALE, upon admission of patients with symptoms compatible with COVID-19, with a high score indicating the need for urgent mechanical ventilation, may be useful in hospitals in low- and middle-income countries that lack more specialised equipment. The RALE score could also guide the decision to

Table 4. Final model of the multivariate analysis of factors associated with requiring mechanical ventilation

Factors	ORna ^a	ORa ^b	95% CI ^c	X ² het ^d	p ^e
Chronic kidney disease	4.28	4.76	1.77 - 12.82	9.53	0.76
≥50 years old	3.53	3.51	1.73 - 7.13	12.08	0.83
RALE evaluation ≥6 points	2.66	2.27	1.22 - 4.22	6.63	0.99

^aNon-adjusted Odds Ratio^bAdjusted Odds Ratio^c95% Confidence Interval^dX² heterogeneity test^ep value

refer the patient to a facility with the resources to provide mechanical ventilation.

We did not find any other published articles that studied the predictive value of the RALE score for the requirement for mechanical ventilation to compare with our findings. The RALE score has been used as a predictor of mortality from COVID-19 (27-31), to assess the severity of COVID-19 (32,33) or to guide the discharge of patients from a service or hospital (27,32). One study compared the usefulness of different scoring methods for radiological images, including RALE, and their association with ARDS (34) during the SARS-CoV-2 epidemic. Different studies have reported different cut-off levels of the RALE score associated with different outcomes. Some studies used the original version of the score, with a maximum value of 48 (28,30,32,33) while others (27,29,31,34), like us, used the Wong version of the score, with a maximum value of 8.

The RALE severity score was higher if the radiograph was taken longer after the onset of symptoms. As in other studies, the most frequently described radiological features were consolidations and ground glass opacities (13,17,18).

Other factors associated with the need for ventilation in our study were the presence of chronic kidney disease, and age over 50 years. Several other studies have reported that older age is a predictor of intubation (3,6,8). An association between chronic kidney disease and the need for mechanical ventilation has been reported in other studies of patients with COVID-19 (9,35). Some authors have documented that the renal parenchyma is particularly sensitive to invasion by SARS-CoV-2 and severe inflammation and renal tubular damage occur (36,37). Patients with previous kidney damage are more likely to need mechanical ventilation for multiorgan failure. Previous chronic kidney disease exacerbates inflammation and kidney damage in COVID-19 patients (38). Other reported factors that predict mechanical ventilation in patients with COVID-19 such as sex (3,6) and obesity (3,8) did not have a significant effect in our study, perhaps because of the small sample size.

Nearly half (48%) of the patients were judged to require mechanical ventilation, but only 32% received this support. The main reason for not ventilating patients judged to need it was shortage of ventilators. A few patients or their families refused ventilation, and some patients died in the emergency room. The reported proportion of patients

with severe COVID-19 who require ventilation who receive it varies enormously, from 2.3 to 33% (39,40). Studies performed in intensive care units not surprisingly report high proportions of patients receiving mechanical ventilation (41,42).

Half of the patients in our study were discharged from hospital after clinical improvement, and the rest died, with no significant difference in terms of sex. This mortality is compatible with that reported in other studies, with hospital mortality ranging from 30.1–49.6% (5,43).

Strengths and Limitations

Half the patients admitted with a clinical diagnosis of COVID-19 during the study period were excluded from the study because of incomplete records or no chest radiograph. It is unlikely that the excluded patients would be systematically different from those included in terms of the relationship between the RALE score and the need for mechanical ventilation. The large number of hospitalized patients with COVID-19 during the first wave of the pandemic in Mexico presented a severe challenge; our study indicated a feasible, rapid way to identify patients who would require mechanical ventilation. The RALE score can be readily calculated in any hospital with basic X-ray equipment and a radiologist. This is a major contribution of our research.

Conclusion

The RALE score for extent of pulmonary oedema on the plain chest radiograph was a useful predictor of the need for mechanical ventilation of hospitalized patients with COVID-19. This could be a useful and accessible part of rapid evaluation of patients with COVID-19.

Conflict of Interest

The authors declare that they have no competing interests.

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