

Radiographic findings that predict a poor clinical course or outcome in patients hospitalized with pneumonia due to SARS-CoV-2 infection

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OBJECTIVE. Radiographic findings that predict a poor clinical course or outcome in patients hospitalized with pneumonia due to SARS-CoV-2 infection.

METHODS. To study radiographic observational study of patients diagnosed with pneumonia and COVID-19 who were attended in a tertiary care hospital emergency department between March 1 and May 30, 2020. We gathered information on patient referral and clinical, radiographic, and laboratory findings. Distinct radiographic patterns were identified, and their usefulness for predicting a poor outcome was evaluated. A poor course/outcome was defined by the presence of one of the following events: need for high-flow oxygen administration, noninvasive mechanical ventilation, or intubation and invasive mechanical ventilation; intensive care unit admission; or death. Areas under the receiver operating characteristic curves for the radiographic patterns were calculated.

RESULTS. A total of 381 patients were hospitalized for SARS-CoV-2 pneumonia during the study period; 114 were included for analysis after applying exclusion criteria. Thirty-four of these patients (29.8%) experienced a poor outcome. Radiographic features that were independently associated with SARS-CoV-2 pneumonia were the presence of non-peripheral opacities and the involvement of at least 4 out of 6 possible lung zones. Multivariate analysis showed that the best predictive model included these radiographic findings along with a high respiratory rate.

CONCLUSIONS. Certain radiographic features can predict a poor clinical course/outcome in patients with SARS-CoV-2 pneumonia. Non-peripheral radiographic findings and the involvement of at least 4 out of 6 possible lung zones are independent factors related to a poor outcome.

Keywords: COVID-19. Chest radiograph. Pneumonia. SARS-CoV-2. Prognostic factors. Emergency Department. Respiratory rate.

Patrones radiológicos predictivos de mala evolución en pacientes hospitalizados por neumonía secundaria a infección por SARS-CoV-2

OBJETIVO. Estudiar la relación entre distintos patrones radiográficos y mala evolución de pacientes con diagnóstico de neumonía por COVID-19.

MATERIAL Y MÉTODO. Estudio observacional retrospectivo en pacientes con diagnóstico de neumonía secundaria a COVID-19 atendidos en el servicio de urgencias de un hospital de tercer nivel durante el periodo del 1 de marzo al 30 de mayo de 2020. Se recogieron datos de filiación, clínica, analítica y radiología. Se definieron distintos patrones radiológicos y se determinó el valor pronóstico de mala evolución del paciente. Se estableció como mala evolución la necesidad de oxígeno a alto flujo, ventilación mecánica no invasiva, intubación con ventilación mecánica invasiva, ingreso en unidad de cuidados intensivos o muerte. Se realizó un análisis de curva ROC para el modelo predictivo de mala evolución.

RESULTADOS. Se estudiaron 381 pacientes hospitalizados por neumonía por SARS-CoV-2. Tras aplicar los criterios de exclusión, 114 pacientes fueron incluidos. De estos, 34 (29,8%) presentaron mala evolución. Los patrones radiológicos asociados de forma independiente a mala evolución de neumonía por COVID-19 fueron: patrón no periférico y número de campos afectados igual o mayor a 4 de 6 posibles. El análisis multivariante mostró que el mejor modelo predictivo es la asociación de estos patrones junto a una frecuencia respiratoria elevada.

CONCLUSIONES. Existen patrones radiográficos que predicen mala evolución en pacientes con neumonía por SARS-CoV-2. El patrón no periférico y un número de campos afectados igual o mayor a 4 de 6 se asocian de forma independiente a mala evolución.

Palabras clave: COVID-19. Radiografía de tórax. Neumonía por SARS-CoV-2. Factores pronóstico. Urgencias. Frecuencia respiratoria.

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Introduction

At the end of 2019, a new variant of coronavirus, known as COVID-19, emerged in Wuhan (China). This coronavirus is the cause of severe acute respiratory syndrome (SARS-CoV-2), which rapidly spread throughout the world. Spain was one of the countries most affected during the initial phase, with more than 174,000 confirmed cases, 86,000 hospitalizations, and 18,975 deaths as of May 10th, 2020.¹ The national health care system had to make a huge effort to withstand the hospital overload, with emergency departments (EDs) being among the most affected areas. They were forced to reorganize their care model to handle the massive influx of cases caused by the pandemic.^{2,3}

The infection caused by SARS-CoV-2 shows wide clinical variability—ranging from asymptomatic patients to those with extremely severe illness requiring prolonged stays in intensive care units.^{4,5} This makes it necessary to identify predictive factors that help anticipate disease evolution in an individual patient. Among these, lymphopenia and elevated levels of D-dimer, interleukin-6, and C-reactive protein (CRP) have been associated with poor outcomes in COVID-19 infection.^{3,6,7} Even so, results from the existing studies are inconsistent,⁸⁻¹¹ and there are few investigations aimed at identifying risk factors for poor outcomes in patients who have already developed COVID-19-induced pneumonia.¹² In this regard, the use of chest radiography, an inexpensive and accessible tool, has been insufficiently studied.^{3,6,8,13} Computed tomography (CT), on the other hand, has also not shown results that justify its use as a predictor of poor outcomes.^{10,14,15}

The objective of this study is to identify radiographic patterns that predict poor outcomes in patients who have already developed COVID-19-induced pneumonia at the time of presentation to the ED.

Materials and methods

We conducted a retrospective observational study including all patients aged 18 years or older who presented to the emergency department with SARS-CoV-2 pneumonia between March 1st and May 30th, 2020 (the first wave of the pandemic) in a tertiary referral center.

All patients were required to have a positive nasopharyngeal swab for SARS-CoV-2, and have a primary diagnosis of pneumonia due to SARS-CoV-2 infection. SARS-CoV-2 infection was diagnosed via RT-PCR detection of viral RNA on a nasopharyngeal swab sample. Pneumonia was diagnosed based on the presence of new infiltrates on chest X-ray together with compatible clinical symptoms: dyspnea, cough, and/or fever.

Data were extracted from the hospital's electronic health records and entered into a database created for the study. We collected demographic, clinical, laboratory, and radiologic data; treatments administered; need for high-flow oxygen therapy (HFOT), non-invasive mechanical ventilation (NIV), or invasive mechanical ventilation (IMV); length of stay; and discharge disposition. All radiographs were reviewed independently by a pulmonologist and a

Table 1. Radiological classification

Distribution	Central	Peripheral	Diffuse
Pulmonary parenchyma	No opacities	With opacities	Interstitial pattern
Type of involvement	Single lobar	Unilateral	Bilateral
Number of affected fields	0–3 fields	4–6 fields	—

radiologist. Different radiological patterns were defined according to infiltrate type and distribution, unilateral vs. bilateral involvement, and the number of affected lung zones (Table 1). For counting affected zones, the X-ray was divided into six fields (Figure 1). Patients were categorized into 2 groups: ≤ 3 affected fields and > 3 affected fields. Patients with any documented limitation of therapeutic intensity were excluded.

Poor clinical outcome was defined as the need for HFOT, NIV, orotracheal intubation with IMV, admission to the intensive care unit (ICU), or death. These criteria have been used in previous studies predicting poor outcomes in patients with COVID-19.¹⁰

The study was approved by the Ethics Committee of our center and conducted according to the principles of the Declaration of Helsinki.

For statistical analysis, R for Windows was used. Student's t-test was applied to compare continuous variables, or the Mann–Whitney U test for non-normally distributed variables. For categorical variables and proportion comparisons, the chi-square test with Fisher's correction when necessary was used. A multivariate analysis was performed to identify independent risk factors for poor disease progression of COVID-19-induced pneumonia. A ROC curve was generated to evaluate the best predictive model. Statistical significance was set at $P < .05$, with a 95% confidence interval (95% CI).

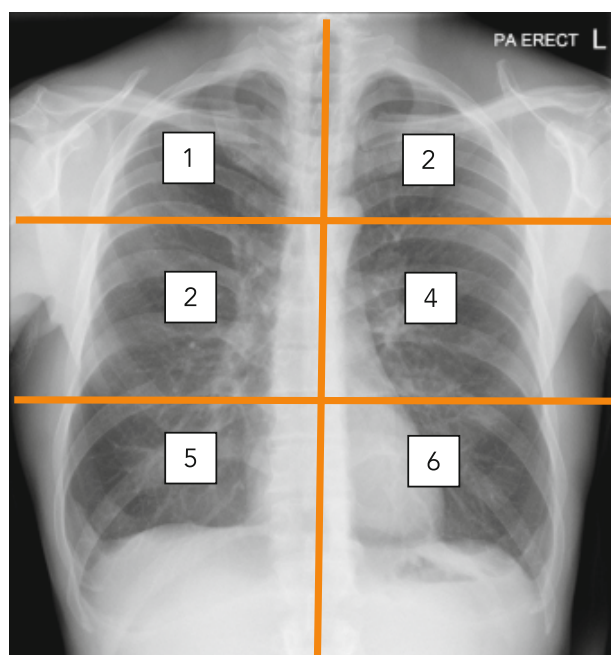


Figure 1. Division of the chest radiograph into 6 fields.

Results

During the study period, a total of 1,009 patients were evaluated with a diagnosis or suspicion of SARS-CoV-2 infection. Of these, 381 were diagnosed with COVID-19-induced pneumonia, and 188 met the inclusion criteria. Seventy-four patients were excluded due to missing data in the electronic medical records. Ultimately, 114 patients were included in the study. The mean age was 59.2 years (SD, 16), and 60.5% were men. The most frequent comorbidities were overweight or obesity in 50 patients (43.9%) and arterial hypertension in 34 (29.8%). Seventeen patients (14.9%) had diabetes, and 12 (10.5%) had cardiovascular disease. The most common clinical symptoms were subjective fever in 99 patients (86.8%), cough in 89 (78.1%), and dyspnea in 70 (61.4%). Regarding radiologic patterns: 102 patients (89.5%) presented bilateral involvement, 77 (67.5%) had diffuse lung involvement, and 42 (36.8%) had > 4 lung fields affected (out of 6 possible fields). Regarding oxygen requirements: 100 patients (87.7%) required nasal cannula oxygen, 48 (42.1%) required reservoir mask oxygen (Monaghan-type mask) for high-concentration oxygen delivery.

Of all included patients, 34 (29.9%) had at least one variable indicating poor course of the disease: 10 deaths (8.8%), 21 ICU admissions (18.4%), 19 requiring high-flow oxygen therapy (16.7%), 24 requiring non-invasive mechanical ventilation (21%), and 12 requiring intubation with IMV (10.5%). A comparison between groups is shown in [Table 2](#), and the distribution of radiologic patterns according to the patient's disease progression is shown in [Table 3](#).

Multivariate analysis demonstrated that independent risk factors for poor disease progression were peripheral distribution, having 4 to 6 lung fields affected, and respiratory rate ([Table 4](#)). The ROC curve for this predictive model is shown in [Figure 2](#), with an area under the curve (AUC) of 0.8718.

Discussion

Chest radiography is a universally available, cost-effective tool in emergency departments and carries minimal risk for patients. This study demonstrates its usefulness in predicting poor outcomes in patients with COVID-19-induced pneumonia. We found an association between certain radiographic patterns and poor course of the disease.

As in other studies, the patients analyzed were adults,^{9,10} with a mean age of 59 years. Most patients had cardiovascular risk factors, the most common being hypertension, diabetes, and overweight/obesity. The most frequent symptoms—subjective fever, cough, and dyspnea—are consistent with findings from other European^{3,8-10,16,17} and U.S. studies,¹⁸ with some differences compared to Chinese cohorts, which show lower rates of cardiovascular risk factors and lower percentages of cough and dyspnea.^{11,12,15,19,20} Overweight and obesity affected 43.9% of patients in our series, similar to values obtained in other studies when overweight and obesity

are combined.¹⁰ Neoplasms were present in nearly 13% of patients, also similar to other reports,³ whereas Chinese studies show only 1–4%.^{11,15,19} Differences were also observed in GI symptoms, such as vomiting and diarrhea, with European samples reporting around 30%^{3,8} vs only 7% in Chinese studies.^{11,15,19,20} As these studies were conducted during the first wave, these discrepancies cannot be attributed to different viral strains, but more likely to ethnic or genetic differences and possibly information bias.¹⁰ In contrast, vital signs on arrival were similar to those described in other studies.^{8,9}

The proportion of patients requiring intubation and mechanical ventilation was similar to previous reports,¹⁰ although the percentage requiring non-invasive ventilation was lower, likely reflecting an effort to avoid intubation by maximizing the use of NIV. Differences with *García et al.*⁹ must take into consideration that their study focused on ICU patients.

Variations in the use of nasal cannula oxygen and reservoir masks vs other studies³ may reflect differences in local oxygen therapy protocols rather than differences in disease severity.

Multiple laboratory variables predictive of poor disease progression were identified in this study. Variables such as LDH, CRP, total leukocytes, neutrophils, troponins, and AST showed associations consistent with findings from other publications.^{9,10,13,15} However, none reached significance in the multivariate analysis, limiting their independent prognostic value.

Other parameters—total lymphocytes, D-dimer, procalcitonin, and platelet count—did not reach significance, unlike in other studies.^{6,9,11,15} This may be due to sample size, but more likely to our inclusion of only patients with confirmed pneumonia, rather than both pneumonia and non-pneumonia cases. Regarding prognostic pneumonia scales, all were useful in predicting poor outcomes, consistent with the SIESTA study.¹²

Few data exist on the prognostic importance of radiographic patterns in hospitalized patients with COVID-19. Former studies reported no association between chest X-ray abnormalities and poor disease progression^{3,8,13}—likely because they compared the presence or absence of abnormalities, rather than evaluating specific radiographic patterns.

Our study is novel in that all patients had abnormal X-rays, allowing evaluation of which abnormalities predict poor disease progression.

On univariate analysis, peripheral distribution, diffuse distribution, bilateral involvement, number of affected fields, non-consolidated opacities, and consolidated opacities were associated with poor outcomes. Of these, peripheral distribution and damage to > 4 lung fields remained independently associated with poor disease progression. Respiratory rate—a simple, clinically relevant measure—showed a 12% increase in risk per additional breath per minute, and a 120% increase for a rise of 10 breaths/min.

Table 2. Comparison of the patients' characteristics based on the course of their disease

	Good disease progression N = 80 n (%)	Poor disease progression N = 34 n (%)	Total N = 114 n (%)	P
Age	57.6 (16.0)	63.0 (15.6)	59.2 (16.0)	.102
Sex				.552
Female	33 (41.3)	12 (35.3)	45 (39.5)	
Male	47 (58.7)	22 (64.7)	69 (60.5)	
Smoking status				.08
Non-smoker	58 (72.5)	18 (52.9)	76 (66.7)	
Smoker	1 (1.3)	2 (5.9)	3 (2.6)	
Former smoker	21 (26.2)	14 (41.2)	35 (30.7)	
Days with symptoms	8.5 (3.5)	6.6 (2.3)	8.0 (3.3)	.004
Length of stay (days)	9.6 (5.7)	25.1 (20.5)	14.1 (13.9)	< .001
Nursing home resident	2 (2.5)	2 (5.9)	4 (3.5)	.369
Comorbidities				
Diabetes	9 (11.3)	8 (23.5)	17 (14.9)	.092
Dementia	1 (1.3)	2 (5.9)	3 (2.6)	.157
Overweight/Obesity	30 (37.5)	20 (58.8)	50 (43.9)	.016
Hypertension	19 (23.8)	15 (44.1)	34 (29.8)	.03
Cardiovascular disease	5 (6.3)	7 (20.6)	12 (10.5)	.022
Stroke	1 (1.3)	2 (5.9)	3 (2.6)	.157
Liver disease	2 (2.5)	1 (2.9)	3 (2.6)	.893
Chronic kidney disease	3 (3.8)	5 (14.7)	8 (7.0)	.036
COPD	6 (7.5)	4 (11.8)	10 (8.8)	.461
Asthma	7 (8.8)	3 (8.8)	10 (8.8)	.99
OSA (Sleep apnea)	2 (2.5)	1 (2.9)	3 (2.6)	.893
Neoplasm	8 (10)	7 (20.6)	15 (13.2)	.126
Clinical presentation				
Feverish symptoms	73 (91.3)	26 (76.5)	99 (86.8)	.033
Cough	61 (76.3)	28 (82.4)	89 (78.1)	.471
Sputum production	8 (10.0)	3 (8.8)	11 (9.6)	.846
Dyspnea	44 (55.0)	26 (76.5)	70 (61.4)	.031
Anorexia	9 (11.3)	1 (2.9)	10 (8.8)	.151
Loss of taste	17 (21.3)	5 (14.7)	22 (19.3)	.418
Loss of smell	22 (27.5)	7 (20.6)	29 (25.4)	.438
Headache	13 (16.3)	4 (11.8)	17 (14.9)	.539
Myalgia	22 (27.5)	10 (29.4)	32 (28.1)	.835
Chest pain	6 (7.5)	4 (11.8)	10 (8.8)	.461
Vomiting/Diarrhea	27 (33.8)	11 (32.4)	38 (33.3)	.885
Vital signs				
Body temperature	36.8 (1.0)	37.0 (1.0)	36.9 (1.0)	.333
Heart rate	91.7 (14.9)	93 (18.3)	92.0 (15.9)	.683
Systolic BP	127 (18.2)	125.8 (16.5)	126.7 (17.7)	.721
Diastolic BP	78.7 (12.9)	73.9 (12.6)	77.3 (13.0)	.072
Respiratory rate	23.1 (5.2)	28.2 (7.4)	24.6 (6.4)	< .001
Oxygen saturation	95.4 (3.1)	92.9 (7.0)	94.6 (4.7)	.01
P/F ratio (PaO ₂ /FiO ₂)	363.8 (92.7)	237.3 (107.0)	318.5 (115.0)	< .001

(Continued)

Respiratory rate was included in the predictive model alongside the 2 radiologic criteria, producing an ROC AUC of 0.87.

The main limitation of this study is the sample size, which prevented the creation of a formal risk score. Its retrospective nature also risks missing some cases. Additionally, being a single-center study limits generalizability.

In conclusion, this study demonstrates the utility of chest radiography in predicting poor outcomes in patients with COVID-19-induced pneumonia. Non-peripheral distribution and involvement of > 4 lung fields are associated with poor disease progression.

	Good disease progression N = 80 n (%)	Poor disease progression N = 34 n (%)	Total N = 114 n (%)	P
Laboratory tests				
Glucose	115.1 (30.4)	136.8 (69.0)	121.6 (46.2)	.021
Urea	31.9 (18.7)	55.7 (60.9)	39.0 (38.0)	.002
Creatinine	0.9 (0.4)	1.3 (1.0)	1.0 (0.6)	.003
Glomerular filtration rate	88.0 (22.1)	73.9 (31.4)	83.8 (25.9)	.007
Sodium	137.3 (3.0)	136.6 (5.1)	137.1 (3.7)	.411
Potassium	4.2 (0.4)	4.2 (0.5)	4.2 (0.4)	.331
Chloride	97.0 (3.8)	96.7 (5.0)	96.9 (4.2)	.756
Lactate dehydrogenase (LDH)	286.1 (88.3)	408.9 (202.4)	321.9 (142.5)	< .001
Creatine kinase (CK)	120.7 (124.1)	250.1 (347.0)	157.5 (218.5)	.008
Total bilirubin	0.5 (0.2)	0.6 (0.3)	0.5 (0.2)	.073
Aspartate aminotransferase (AST)	36.8 (18.5)	56.7 (78.5)	42.7 (46.0)	.037
Alanine aminotransferase (ALT)	35.7 (22.5)	49.6 (101.3)	39.8 (58.2)	.25
Albumin	3.7 (0.4)	3.4 (0.5)	3.6 (0.4)	.02
Total cholesterol	136.3 (31.7)	143.6 (22.5)	138.0 (29.7)	.579
Procalcitonin	0.2 (0.3)	0.5 (1.4)	0.3 (0.8)	.064
Ferritin	904.5 (1336.9)	1321.4 (865.5)	1004.8 (1247.8)	.206
C-reactive protein (CRP)	8.9 (7.6)	15.3 (9.3)	10.8 (8.6)	< .001
Troponin T	16.1 (8.4)	22.8 (20.0)	18.1 (13.3)	.018
NT-proBNP	172.8 (209.5)	2,231.9 (4465.7)	781.8 (2573.8)	.002
Interleukin-6	35.0 (32.5)	83.0 (64.3)	50.4 (50.1)	< .001
Hemoglobin	13.7 (1.4)	13.4 (2.0)	13.7 (1.6)	.332
Total leukocytes (×1,000)	6.7 (2.7)	8.6 (3.6)	7.3 (3.1)	.002
Neutrophils (×1,000)	5.0 (2.5)	7.2 (3.6)	5.6 (3.0)	< .001
Lymphocytes (×1,000)	1.2 (0.6)	1.0 (0.6)	1.1 (0.6)	.057
Neutrophil-to-lymphocyte ratio	5.0 (3.3)	10.6 (10.0)	6.7 (6.6)	< .001
Platelets (×1,000)	225.6 (79.6)	204.2 (76.9)	219.2 (79.1)	.188
ESR	42.5 (25.5)	54.9 (25.6)	45.7 (25.9)	.078
Prothrombin time	1.0 (0.2)	3.6 (14.9)	1.8 (8.2)	.128
Fibrinogen	494.2 (49.1)	510.6 (65.7)	498.8 (54.4)	.185
D-dimer	1,080.0 (1,722.2)	1,307.9 (1,529.0)	1,148.6 (1,663.0)	.506
pH	7.5 (0.1)	7.4 (0.1)	7.5 (0.1)	.194
Arterial pO ₂	84.9 (41.2)	93.7 (43.0)	88.1 (41.8)	.331
Arterial pCO ₂	32.3 (5.8)	32.5 (5.1)	32.4 (5.6)	.885
Lactate	1.3 (0.4)	1.8 (1.0)	1.4 (0.7)	.002
Treatment				
Corticosteroids	32 (40.0)	34 (100.0)	66 (57.9)	< .001
Antivirals	15 (18.8)	4 (11.8)	19 (16.7)	.36
Anticoagulants	59 (73.8)	30 (88.2)	89 (78.1)	.087
Antibiotics	59 (73.8)	33 (97.1)	92 (80.7)	.004
Azithromycin	79 (98.8)	34 (100.0)	113 (99.1)	.513
Hydroxychloroquine	80 (100.0)	33 (97.1)	113 (99.1)	.123
Tocilizumab	16 (20.0)	21 (61.8)	37 (32.5)	< .001
Severity scores				
CURB-65	0.7 (0.9)	1.5 (1.1)	1.0 (1.0)	< .001
qSOFA	0.6 (0.5)	0.9 (0.5)	0.7 (0.5)	.004
PSI	64.2 (25.9)	96.5 (33.5)	73.8 (31.9)	< .001
MEWS	2.2 (1.3)	3.0 (1.3)	2.5 (1.3)	.003

Results express number (%) for categorical variables and mean (standard deviation) for quantitative variables.

COPD: chronic obstructive pulmonary disease; OSA: obstructive sleep apnea syndrome; P/F ratio: PaO₂/FiO₂; pO₂: arterial oxygen pressure; pCO₂: arterial CO₂ pressure; PSI: Pneumonia Severity Index; MEWS: Modified Early Warning Score.

Table 3. Radiological characteristics of patients with good and poor outcomes

	Good progress N = 80 n (%)	Poor performance N = 34 n (%)	Total N = 114 n (%)	P
Number of fields affected	4 (5.0)	0 (0.0)	4 (3.5)	.007
2	20 (25.0)	0 (0.0)	20 (17.5)	
3	11 (13.8)	2 (5.9)	13 (11.4)	
4	25 (31.3)	17 (50.0)	42 (36.8)	
5	7 (8.8)	3 (8.8)	10 (8.8)	
6	13 (16.3)	12 (35.3)	25 (21.9)	
Isolated opacity	5 (6.3)	0 (0.0)	5 (4.4)	.136
Opacity without consolidation	21 (26.3)	3 (8.8)	24 (21.2)	.037
Opacity with consolidation	51 (63.8)	31 (91.2)	82 (71.9)	.003
Interstitial pattern	58 (72.5)	24 (70.6)	82 (71.9)	.835
Central distribution	1 (1.3)	0 (0.0)	1 (0.9)	.513
Peripheral distribution	31 (38.8)	3 (8.8)	34 (29.8)	.001
Diffuse distribution	46 (57.5)	31 (91.2)	77 (67.5)	< .001
Single lobe involvement	4 (5.0)	0 (0.0)	4 (3.5)	.184
Right involvement	73 (91.3)	34 (100.0)	107 (93.9)	.075
Left involvement	74 (92.5)	34 (100.0)	108 (94.7)	.101
Afectación bilateral	68 (85.0)	34 (100.0)	102 (89.5)	.017

Table 4. Multivariate analysis of risk factors associated with poor outcomes in COVID-19 pneumonia

	Odds Ratio	95% CI	P
Radiological pattern with non-peripheral distribution	5.25	1.14-24.23	.033
More than 3 affected fields	7.92	1.56-40.24	.013
Respiratory rate	1.12	1.00-1.27	.053

The peripheral distribution has been inverted to assess a risk model.

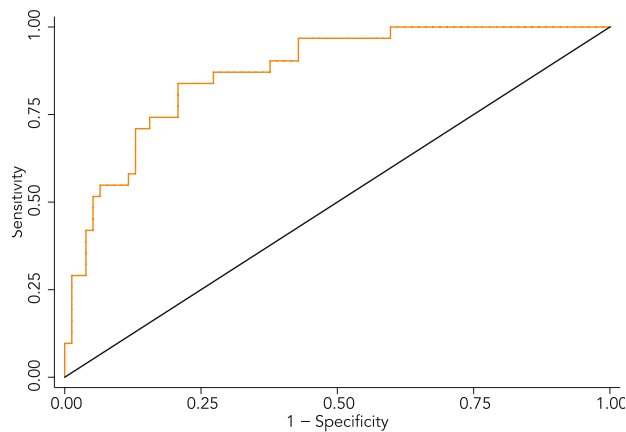


Figure 2. ROC curve based on non-peripheral pattern, > 3 affected lung fields, and respiratory rate.

Adding respiratory rate further strengthens predictive capacity of poor disease progression. Identifying specific risk patterns on chest radiography helps predict poor clinical progression in patients with COVID-19 pneumonia, allowing clinicians to recognize those at risk of deterioration early and to implement appropriate measures.

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