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Comparative analysis of chest radiography and lung ultrasound to predict intra-hospital prognosis of patients admitted for acute SARS-CoV-2 pneumonia (COVID-19)

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A B S T R A C T

Background: Point of care lung ultrasound (POCUS) has been recently used to assess prognosis in COVID-19 patients. However, there are no data comparing POCUS and chest-X ray, a technique widely used.

Patients and methods: Retrospective analysis in stable COVID-19 patients. Schalekamp radiological lung scale and LUZ-Score ultrasound scale were compared. Primary end-point was in-hospital death and/or need for Intensive Care Unit admission.

Results: A total of 138 patients were included. Median Schalekamp scale was 2 (2) and median LUZ-Score scale was 21 (10). No significant correlation was observed between both techniques. Patients with a LUZ-Score ≥ 21 points at admission had worse lung function and higher concentrations of LDH, CRP and Interleukine-6. Schalekamp scale failed to identify patients at a higher risk at admission for the primary end-point. Addition of POCUS to a previous clinical model, improved risk prediction (AUC 0.805 [95% CI: 0.662–0.948]; P=0.001).

Conclusions: Chest X-ray and POCUS showed no correlation at admission in this analysis. Only POCUS identified a group of patients with greater clinical and analytical involvement. POCUS improved, previous clinical model, while chest X-ray did not add relevant predictive information for the primary endpoint.

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Análisis comparativo de la radiografía de tórax y la ecografía pulmonar para predecir el pronóstico intrahospitalario de pacientes ingresados por neumonía secundaria a SARS-CoV-2 (COVID-19)

R E S U M E N

Antecedentes: La ecografía torácica es una técnica novedosa para estratificar el riesgo de los pacientes COVID-19. Sin embargo, no existen datos que comparen dicha técnica con la radiografía de tórax, una técnica ampliamente utilizada en esta enfermedad.

 Pacientes y métodos: Análisis retrospectivo en pacientes estables COVID-19. Se compararon la escala de daño pulmonar radiológica de Schalekamp y ecográfica de LUZ-Score. El objetivo primario fue la muerte intrahospitalaria o la necesidad de ingreso en la UCI para tratamiento con ventilación mecánica.

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Resultados: Se reclutaron 138 pacientes. La mediana de la escala de Schalekamp fue de 2 (2) y la del LUZ-Score de 21 (10). No se objetivó una correlación significativa entre ambas escalas. Los pacientes con un LUZ-Score ≥ 21 puntos al ingreso presentaron peor función pulmonar y mayores concentraciones de LDH, PCR e interleucina-6. La escala radiológica de Schalekamp no logró identificar a una población de mayor riesgo. Únicamente la adición de la ecografía pulmonar a un modelo de valoración clínica mejoró de manera significativa el área bajo la curva para el objetivo primario (ABC 0.805 [IC 95%: 0.662–0.948]; \( p < 0.001 \)).

Conclusiones: No se objetivó una correlación entre la afectación radiológica y la ecográfica. Únicamente la ecografía pulmonar identificó un subgrupo de pacientes con una mayor afectación clínico-analítica. La ecografía pulmonar mejoró el modelo de predicción clínico, mientras que la radiografía de tórax no añadió información relevante.

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Introduction

Severe adult respiratory distress virus type 2 (SARS-CoV-2) infection, known as COVID-19, has led to high morbidity and mortality worldwide\(^1\). The disease has a significant respiratory involvement, capable of producing adult respiratory distress syndrome (ARDS) regardless of age, even in vulnerable patients\(^2\)-\(^4\). Given that this is an infectious disease capable of producing severe disease in young patients with no medical history\(^2\)-\(^5\), objective tools for early identification of patients at higher risk are vital to improve the prognosis of the disease.

Plain chest X-ray is a simple, safe and widely used technique in the initial assessment of COVID-19\(^9\). Bilateral radiological involvement has been identified in critically ill patients as an independent risk factor\(^7\). However, despite its usefulness, it is an operator-dependent technique and has been found to be most cost-effective when using complex computer models analysing radiological images\(^7\), a resource that is not always available in hospitals.

In contrast, lung ultrasound has represented a major breakthrough in the management of this disease\(^9\). It is an easy-to-apply, reproducible, harmless technique with results similar to those obtained by computed tomography (CT)\(^10\). Grading of COVID-19 lesions using ultrasound scoring systems has been correlated with short-term prognosis\(^1\)-\(^13\), and research related to this technique in COVID-19 is becoming increasingly common\(^14\)-\(^16\).

The hypothesis of this study is that the predictive ability of lung ultrasound is superior to that of X-ray. The objectives of this study are: 1) To analyse the baseline characteristics of a cohort of hospitalised patients according to lung lesions generated by SARS-CoV-2 and identified by X-ray or lung ultrasound. 2) Analyse the correlation between X-ray and lung ultrasound findings. 3) To analyse the predictive capacity of X-ray versus lung ultrasound on admission to identify patients with worse outcome during hospitalisation.

Patients and methods

Study design

A retrospective study conducted in the Infectious Diseases and Internal Medicine departments of a university hospital between July and October 2020. Inclusion criteria for the study have been previously published\(^11\). In summary, these were patients aged ≥ 18 years admitted with a diagnosis of symptomatic SARS-CoV-2 infection confirmed by PCR or serology (IgM and/or IgG) and who agreed to the study terms. The most important exclusion criteria were previous admission to the intensive care unit (ICU), refusal of the patient or the presence of advanced chronic diseases such as COPD, advanced cognitive impairment or significant functional dependence\(^11\). The patient’s biological and clinical variables were recorded during the first 72 h of admission for COVID-19. An approximate calculation of the PaO\(_2\)/FiO\(_2\) was made, defined as the quotient between the saturation of O\(_2\) and FiO\(_2\) administered (estimated PaO\(_2\)/FiO\(_2\)) and the patient’s degree of dyspnoea was quantified using the subjective Borg scale (between 0 and 10)\(^11\).

Chest X-ray

The images were obtained from chest X-ray in posteroanterior and/or anteroposterior projection, when performed by portable equipment, during the first 24 h of admission and were independently analysed by an expert radiologist, blinded to other clinical and laboratory parameters or clinical events that occurred during follow-up. The quantification of radiological lung lesions was performed according to the validated scale of Schalekamp et al.\(^1\)-\(^7\). This scale is based on the analysis of four lung quadrants (two in each lung), each one rated from 0 to 2 according to the degree of lung involvement caused by COVID-19, with a final score between 0 and 8 points\(^7\)-\(^18\). The maximum time accepted between the performance of both techniques (chest X-ray and chest ultrasound) was 24 h, starting from the first care provided in the emergency department, in order to avoid differences in the identification of lesions depending on the test used.

Lung ultrasound

The protocol used was the LUZ-Score\(^11\). It is a quantitative scale that analyses the degree of ultrasound involvement based on the findings in each of the twelve thoracic quadrants analysed, with a final score between 0 and 48 points. This technique focuses primarily on the analysis of the different lung patterns, paying particular attention to the presence of pulmonary b-lines and/or subpleural consolidations\(^1\).

Objectives

The primary endpoint of the study was defined as the combined event of in-hospital death and/or need for ICU admission to initiate mechanical ventilation. Several secondary endpoints were also considered: 1) the need for increased flow (FiO\(_2\)) of oxygen during the first 72 h; 2) the need to change or increase previously prescribed drug therapy during the first 72 h after admission; and 3) the need to increase oxygen flow and/or drug therapy during the first 72 h after admission.

Statistical analysis

Categorical variables were expressed as percentages. Continuous variables were expressed as mean ± standard deviation or
The comparative analysis of quantitative variables was carried out using Student’s t-test or Mann-Whitney U test, in the case of non-continuous variables. Categorical variables were analysed using the chi square test ($\chi^2$). The correlation between the two scales was analysed using Spearman’s test.

An initial univariate analysis was carried out to create the different prediction models for the primary endpoint, including those variables that were significant or with a $p < 0.100$ in the hypothesis test. The multivariate model was designed taking into account those variables that were significant in the univariate analysis, including also those parameters that have been shown in previous work to have a poor prognostic in COVID-19 patients and whose $p$-value in the univariate analysis was less than 0.100 (age, lactate dehydrogenase [LDH], body mass index [BMI] and previous history of diabetes). Once the clinical model was designed, its power was calculated by analysing the areas under the curve (AUC) and the corresponding ROC curves. Based on this clinical model, alternative models were designed, including the parameters of this study (lung ultrasound and/or chest X-ray) in case they were significant in the univariate analysis. Lastly, survival curves were analysed using Kaplan-Meier curves and the Log-Rank test.

Confidence intervals were 95%, with statistical significance established at a $p$-value of less than 0.05. Statistical analysis was conducted using the SPSS statistical package in its version 24.0 for Windows.

## Results

### Baseline sample characteristics (Tables 1 and 2)

#### Chest X-ray versus lung ultrasound

The median Schalekamp score (X-ray) was 2 points (IR: 2) and the median LUZ-score (lung ultrasound) was 21 points (IR: 10), with no significant degree of correlation between both techniques (Spearman’s Rho = 0.146; $p = 0.086$).

The baseline characteristics of the sample according to the radiological score (median) can be assessed in Table 1. With the exception of the prevalence of hypertension (53.5% vs. 30.5%; $p = 0.010$), no differences were found in the baseline characteristics of the sample of those patients with the highest Schalekamp score (3 or more points) (Table 1).

The baseline characteristics of the sample according to the ultrasound score are shown in Table 2. Patients with higher LUZ-Score (≥21 points) had a higher heart rate on admission, a lower estimated PaO2/FIO2, as well as a greater subjective feeling of dyspnoea (Borg scale). Laboratory tests showed a significant elevation of inflammatory markers, such as CRP and interleukin-6 (IL-6). Creatinine and LDH concentrations were also higher in those patients with greater lung involvement determined by ultrasound (≥21 points) (Table 2).

### Endpoint analysis and clinical prediction models

A total of 15 patients (10.9%) reached the primary endpoint of in-hospital death and/or need of ICU admission for mechanical ven-
tillation. A total of 45 patients (34.1%) needed to increase oxygen flow during the first 72 h, 53 patients (39.6%) saw their drug therapy increased during the first 72 h and 64 patients (49.2%) required either an increase in oxygen flow or an increase in drug therapy (Appendix B Supplementary Table 1).

When comparing the Schalekamp and LUZ-Score scales, statistically significant differences were only found for primary and secondary endpoints when using lung ultrasound (Appendix B Supplementary Table 1). The analysis of the survival curves did not show statistically significant differences neither for the chest X-ray (Log-Rank test = 0.155) nor for pulmonary ultrasound (Log-Rank test = 0.077) (Fig. 1A and B).

Only the clinical model (AUC: 0.790 [0.652–0.928]; p < 0.001) and lung ultrasound (AUC 0.747 [0.595–0.899]; p = 0.002) showed statistically significant results (Fig. 2 and Table 3). When combining the baseline clinical model with pulmonary ultrasound on admission, an increase in predictive capacity was observed (AUC 0.805 [CI95%: 0.662–0.948]; p ≤ 0.001). In contrast, the X-ray (Schalekamp et al.17) did not show statistically significant results (AUC: 0.561 [CI 95%: 0.369–0.754]; p = 0.440) (Fig. 2 and Table 3).

**Discussion**

In the present study we performed a comparative analysis between X-ray (Schalekamp et al.17) and lung ultrasound (LUZ-Score11) to identify COVID-19 patients with a worse outcome during their hospital stay. Our results show that the quantitative assessment of lung damage by lung ultrasound is superior to that by X-ray, without a good correlation between the two techniques. In fact, only the addition of lung ultrasound to a clinical prediction model improved its predictive capacity, demonstrating its potential usefulness in identifying patients with a worse prognosis on admission. These results are unprecedented, and no similar studies have been found comparing both techniques using quantitative scales in the medical literature.

Early selection and identification of patients with COVID-19 whose clinical characteristics make them high-risk patients is a key objective in order to improve prognosis during admission. Since the start of the pandemic, many prognostic tools have been developed, some based on purely clinical data15 or predictive models including laboratory25 or imaging test11,16,17,21 parameters.
Schalekamp et al.\textsuperscript{17} researched whether quantification of lung damage, using a quantitative radiological scale, was able to identify COVID-19 patients with worse outcomes. Their results showed that this scale was an independent predictor of poor in-hospital prognosis\textsuperscript{17}. However, this study included approximately 47% of critical patients and data such as oxygen saturation or BMI were not included, factors that could have overestimated the usefulness of this scale as a predictor of risk\textsuperscript{17}.

Compared to X-ray, lung ultrasound has been a breakthrough in COVID-19 patients\textsuperscript{11,16,21,22}. Its accuracy has been compared to lung CT in a small series of cases\textsuperscript{15,22,23}, and its intrinsic characteristics (reproducibility, absence of irradiation, etc.) make it an attractive technique\textsuperscript{9}.

\textbf{Fig. 1.} Survival curves for the primary endpoint (in-hospital death and/or admission to the intensive care unit for mechanical ventilation) according to lung involvement determined by: A) Chest X-ray (greater or less than the median of the Schalekamp scale [2 points]), and B) Lung ultrasound (higher or lower than the median of the LUZ-Score [21 points]).
In our analysis, population stratification using a quantitative ultrasound scale (LUZ-Score ≥ 21 points) identified a subgroup of patients with worse lung function (estimated PaO2/FiO2 and LDH) and higher concentrations of acute phase reactants (CRP, fibrinogen and IL-6), suggesting that the LUZ-Score can identify the most severely affected patients. In contrast, the Schalekamp\textsuperscript{17} scale did not find differences among the population, and there was no significant correlation with the ultrasound scale either, which could be due to several causes. Our sample had an average BMI of 28.9 kg/m\textsuperscript{2}, so the high degree of overweight could have hindered radiological interpretation, especially if we take into account that, given that this is a highly transmissible disease, most X-rays were taken with portable equipment in an anteroposterior projection, reducing the test’s diagnostic yield\textsuperscript{18,24,25}. Furthermore, it is essential to point out the clinical-radiological dissociation that many COVID-19 patients have on admission due to the distinctive pathophysiological chronology of this disease, a situation that may cause the chest X-ray to underestimate the existing lung damage\textsuperscript{1,2,26–28}. Our results suggest this, and indeed, the Schalekamp scale\textsuperscript{17} was not significant in the univariate logistic regression analysis. Lung ultrasound, however, showed a good area under the curve on its own, only slightly lower than that of the clinical model designed from our population, and the combination of both parameters (ultrasound and clinical model) allowed the generation of a clinical prediction model with an area under the curve of 0.805 (95% CI 0.662–0.948), although no significant differences were observed in the survival curves, probably due to the low number of events (10.9%).

As for the limitations of our study, we have to take into account that it is a retrospective analysis conducted on a cohort of patients from a single hospital centre, so our results have not been validated and cannot be applied to another population. In addition, it would have been useful to have chest CT images (gold standard) with which to compare the radiological and ultrasound images; however, not all patients with COVID-19 included in this analysis had this technique available, as the request was left to the physician responsible for the patient on the basis of clinical criteria. Finally, the sample size used may have reduced the final power of the study, which is a characteristic of this type of analysis.

In conclusion, we did not find a correlation between the Schalekamp scale and the LUZ-Score to quantify lung involvement on admission in patients with COVID-19. Patients with greater ultrasound involvement (higher LUZ-Score) had worse lung function as measured by clinical and/or laboratory parameters, a situation that was not observed in patients with greater radiological involvement (Schalekamp). The addition of a first lung ultrasound assessment on admission improved the predictive ability of a clinical model, so we suggest its use to identify higher-risk COVID-19 patients on admission.

Ethical considerations

The study complied with the general guidelines of the Declaration of Helsinki and was approved by the corresponding ethics committee on 13 May 2020 (CEICA, Ref. CP-CI PI20/248).

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Conflict of interests

The authors declare that they have no conflict of interest in the conduct of this article.
Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.medcle.2022.01.024.

References

1. Guan W, Ni Z, Hu Y, Liang W, Ou C, He J, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. 2020;382:1708–20.

2. Grasselli G, Zangrillo A, Zanella A, Antonelli M, Cabrini L, Castelli A, et al. Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy Region, Italy. JAMA. 2020;323:1574–81.

3. Signes-Costa J, Núñez-Gil IJ, Soriano JB, Arroyo-Espiguero R, Eid CM, Romero R, et al. Prevalence and 30-day mortality in hospitalized patients with Covid-19 and prior lung diseases. Arch Bronconeumol. 2021;57:13–20.

4. Ramos-Rincon JM, Buñauito V, Ricci M, Martín-Carmona J, Paredes-Ruiz D, Calderón-Moreno M, et al. Clinical characteristics and risk factors for mortality in very old patients hospitalized with covid-19 in spain. J Gerontol A Biol Sci Med. 2021;76:E28–37.

5. Blumenthal D, Fowler EJ, Abrams M, Collins SR. Covid-19 — implications for the health care system. N Engl J Med. 2020;383:1483–8.

6. Sadiq Z, Rana S, Mahfoud Z, Raoof A. Systematic review and meta-analysis of chest radiograph (CXR) findings in COVID-19. Clin Imaging. 2021;80:229–38.

7. Cocconcelli E, Biondini D, Giraudo C, Locofo S, Bernardinello N, Fichera G, et al. Clinical features and chest imaging as predictors of intensity of care in patients with COVID-19. J Clin Med. 2020;9:2990.

8. Dilshad S, Singh N, Atif M, Hanif A, Yuqub N, Faruq WA, et al. Automated image classification of chest X-rays of COVID-19 using deep transfer learning. Results Phys. 2021;28:104529.

9. Gargani L, Soliman-Aboumarie H, Volpicelli G, Corradi F, Pastore MC, Cameli M. Why, when, and how to use lung ultrasound during the COVID-19 pandemic: Enthusiasm and caution. Eur Heart J Cardiovasc Imaging. 2020;21:941–8.

10. Lopes AJ, Mafort TT, da Costa CH, Rufino R, de Cásia Firmida M, Kirk KM, et al. Comparison between lung ultrasound and computed tomographic findings in patients with COVID-19 pneumonia. J Ultrasound Med. 2020;2:1–9.

11. Rubio-Gracia J, Giménez-López I, Garcés-Horna V, López-Delgado D, Sierra-Monzón J, Martínez-Lostao L, et al. Point-of-care lung ultrasound assessment for risk stratification and therapy guiding in COVID-19 patients. A prospective non-interventional study. Eur Respir J. 2021;25, 2004283.

12. Volpicelli G, Elbarbary M, Blayvas M, Lichtenstein DA, Mathis G, Kirkpatrick AW, et al. International evidence-based recommendations for point-of-care lung ultrasound. Intensive Care Med. 2012;38:577–91.

13. Castelao J, Graziani D, Soriano JB, Izquierdo JL. Findings and prognostic value of lung ultrasound in COVID-19 pneumonia. J Ultrasound Med. 2020;46:1873–83.

14. Lichter Y, Topilsky Y, Taieb P, Banai A, Hochstadt A, Merridar I, et al. Lung ultrasound predicts clinical course and outcomes in COVID-19 patients. Intensive Care Med. 2020;46:1873–83.

15. Tung-Chen Y, Martí de Gracia M, Diez-Tascón A, Alonso-González R, Agudó-Fernández S, Parra-Gordo ML, et al. Correlation between chest computed tomography and lung ultrasonography in patients with coronavirus disease 2019 (COVID-19). Ultrasound Med Biol. 2020;46:2918–26.

16. Lerchbaumer MH, Lauryn JH, Bachmann U, Enghard P, Fischer T, Grune J, et al. Point-of-care lung ultrasound in COVID-19 patients: inter- and intra-observer agreement in a prospective observational study. Sci Rep. 2021;11, 10678.

17. Schalekamp S, Huisman M, van Dijk RA, Boomsma MF, Freire Jorge PJ, de Boer WS, et al. Model-based prediction of critical illness in hospitalized patients with COVID-19. Radiology. 2020;298:E64–54.

18. Martínez Chamarro E, Diez Tascón A, Ibáñez Sanz I, Ossaba Vélez S, Bor- ruei Nacenta S, Diagnóstico radiológico del paciente con COVID-19. Radiología. 2021;63:56–73.

19. Torres-Macho J, Ryan P, Valencia J, Pérez-Butragueño M, Jiménez E, Fontán-Vela M, et al. The PANDEMYC Score. An easily applicable and interpretable model for predicting mortality associated With COVID-19. J Clin Med. 2020;9:3066.

20. Sánchez-Martínez M, Rubio-Gracia J, Peña-Fresnedo N, Garcés-Horna V, Gracia-Tello B, Martínez-Lostao L, et al. Early measurement of blood sST2 is a good predictor of death and poor outcomes in patients admitted for COVID-19 infec-

21. J Clin Med. 2021;10:3534.

22. Iodice V, Pisaturo M, Fusco FM, Tambaro O, Parrella G, Di Flumeri G, et al. Use of lung ultrasound in covid-19: comparison with ultra-high-resolution computed tomography among 29 patients at “di cotugno” hospital, Naples, Italy. Infez Med. 2020;28:346–50.

23. Colombi D, Petrini M, MaFi G, Villani GD, Bodini FC, Morelli N, et al. Comparison of admission chest computed tomography and lung ultrasound performance for diagnosis of COVID-19 pneumonia in populations with different disease prevalence. Eur J Radiol. 2020;133:109344.

24. Machnicki S, Pat D, Singh A, Talwar A, Mina B, Oks M, et al. The usefulness of chest CT imaging in patients with suspected or diagnosed COVID-19. Chest. 2021;160:652–70.

25. Chao WY, Hamid MTR, Gowdh NMF, Rahmat K, Yaakup NA, Chai CS. Chest radiograph (CXR) manifestations of the novel coronavirus disease 2019 (COVID-19): A mini-review. Curr Med Imaging. 2021:17:677–85.

26. Liu J, Chen T, Yang H, Cai Y, Yu Q, Chen J, et al. Clinical and radiological changes of hospitalised patients with COVID-19 pneumonia from disease onset to acute exacerbation: a multicentre paired cohort study. Eur Radiol. 2020;30:5702–8.

27. Gtiman MR, Shaban MV, Paniz-Mondolfi AE, Sordillo EM. Laboratory diagnosis of SARS-CoV-2 pneumonia. Diagnostics. 2021;11:1270.

28. Stenmark KR, Frid MC, Gerasimovskaya E, Zhang H, McCarthy MK, Thurman JM, et al. Mechanisms of SARS-CoV-2-induced lung vascular disease: potential role of complement. Pulm Circ. 2021;11:2044589021110157.

29. Mehra MR, Desai SS, Kuy S, Henry TD, Patel AN. Cardiovascular disease, drug therapy, and mortality in Covid-19. N Engl J Med. 2020;382:e102.