Ecografía pulmonar en el pronóstico de la COVID-19: Una experiencia única en pacientes ancianos

Lung Ultrasound for COVID-19 prognosis: A unique experience on elderly patients

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ABSTRACT

RESUMEN

Introduction: COVID-19 has been a challenging disease to manage at long term care facilities (LTCFs) and nursing homes (NHs). We present a unique experience in a medicalized-NH with elderly patients where we analyzed lung ultrasound (LUS) as a tool to predict the severity of the disease and death.

Methods: All patients admitted to the center were included, recording their background and the clinical features of the disease. We made a descriptive analysis and a multivariate analysis to identify variables linked to a severe disease and to mortality, specially focusing on the ability of LUS to predict clinical outcomes.

Results: We included 288 patients with a median age of 80 years old, 98 (34%) had a severe disease at admission, 38 (13.2%) died and 7 (2.4%) were transferred to the hospital. LUS was performed in 143 (49.7%) patients. We found a significant association between the presence of B lines or focal alteration and a severe disease (P<0.001 and P=0.006 respectively) or death (P=0.005 and P=0.001 respectively). The clinical variables linked to severity in the multivariable analysis were the elevation of RCP (OR=9.53; P=0.046; IC95% 1.03-87.51), the presence of crackles at lung auscultation (OR=10.63; P=0.018; IC95% 1.51-75.02) and focal alterations in LUS (OR=10.65; P=0.046; IC95% 1.04-108.99). If we focus on mortality we found, through the construction of the Cox regression model, that the main variables linked to it were a higher degree of dependence (OR=3.86; P=0.002; IC 95% 1.65 – 9.01) and the presence of B lines at day 1 in LUS (OR=6.06; P=0.019; IC 95% 1.12 – 32.81).

Conclusions: LUS is a useful, unharmful, reproducible and cheap tool that can be used in an outpatient environment in order to predict severity and death in COVID-19 patients and, surely, in other respiratory infections. We also propose an innovative way to manage a vulnerable population in a pandemic context.

Keywords: COVID-19, SARS-CoV-2, Elderly, Nursing Homes, Long-Term Care Facilities, Lung Ultrasound.

Introducción: La COVID-19 ha sido un desafío a la hora de su manejo en residencias de media-larga estancia. Presentamos una experiencia única en una residencia medicalizada con pacientes ancianos y analizamos la ecografía pulmonar como una herramienta útil para predecir la gravedad de la enfermedad y la mortalidad.

Métodos: Todos los pacientes del centro fueron incluidos en el estudio. Sus antecedentes personales y la presentación clínica de la enfermedad fueron recogidos y analizados. Realizamos un análisis descriptivo y un análisis multivariable para identificar variables relacionadas con la gravedad de la enfermedad y con la mortalidad, centrándonos especialmente en la capacidad de predicción de la ecografía pulmonar.

Resultados: Se incluyeron 288 pacientes con una edad media de 80 años, 98 (34%) tenían una enfermedad grave al ingreso, 38 (13.2%) fallecieron y 7 (2.4%) se trasladaron al hospital. En 143 (49.7%) pacientes se realizó al menos una ecografía pulmonar. Encontramos una asociación significativa entre la presencia de líneas B o alteraciones focales v una enfermedad severa (P<0.001 v P=0.006 respectivamente) o la muerte (P=0.005 y P=0.001 respectivamente). Las variables clínicas relacionadas con la gravedad en el análisis multivariable fueron la elevación de la PCR (OR=9.53; P=0.046; IC95% 1.03-87.51), la presencia de crepitantes en la auscultación pulmonar (OR=10.63; P=0.018; IC95% 1.51-75.02) y la presencia de alteraciones focales en la ecografía pulmonar (OR=10.65; P=0.046; IC95% 1.04-108.99). Mediante un modelo de regresión de Cox, encontramos que las variables relacionadas con la muerte fueron un alto grado de dependencia funcional (OR=3.86; P=0.002; IC 95% 1.65 - 9.01) y la presencia de líneas B en la ecografía al ingreso (OR=6.06; P=0.019; IC 95% 1.12 - 32.81).

Conclusiones: La ecografía pulmonar es una herramienta útil, inocua, reproducible y barata que se puede utilizar en un ambiente extrahospitalario para predecir la gravedad y la probabilidad de morir en los pacientes con COVID-19, y probablemente en otras infecciones respiratorias. Además, proponemos un manejo innovador de una población vulnerable en el contexto de una pandemia.

Palabras clave: COVID-19; SARS-CoV-2; Ancianos; Centro socio-sanitario; Ecografía pulmonar.

INTRODUCTION

COVID-19 pandemic has been one of the most challenging events for global healthcare in recent history. It has caused to date 800 million infections and nearly 7 million deaths around the world, pushing the

administrations to develop new healthcare strategies, especially in prevention, that have been never seen before¹. Plenty of tools have been tried to assess the severity of the disease and to identify bad

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prognosis factors. Among them, lung ultrasound (LUS) has emerged as a fast, non-invasive test that can be crucial at the initial evaluation and monitoring of patients with COVID-19.^{2–4}

It is well known that SARS-COV2 is more aggressive among certain clusters of population, being nursing homes (NHs) or long-term care facilities (LTCFs) residents the most vulnerable of them all⁵. Risk factors, usually present among these patients, such as advanced age, comorbidities, cognitive impairment, and functional limitations play a capital role in the higher rates of mortality⁶. Besides this, therapeutic management is difficult in this group of patients, since they suffer from more side effects and drug interactions, and studies including this population are still scarce.⁷

Considering this situation, each country has developed its own approach when managing COVID-19 outbreaks in these facilities. Some of them are based on collaborative models between hospitals and these centers, being the intervention of the specific NH or LTCF with hospital resources the most frequent type of approach.^{8–10}

In Galicia (north-western of Spain), with 762301 infections and 4155 deaths to date¹¹, a specific and innovative protocol was used to ensure medical care for NHs and LTCFs residents. Two centers were adapted during the epidemic period to admit infected patients during the disease.¹²

In the present work, we analyze the data of one of these centers, called CEGADI (Centro Galego de Desenvolvemento Integral). It was provided with medical material, drug provision, an installation of an oxygen circuit to dispense high flow oxygen therapy and staff with hospital training. It counted with access to electronic clinical history and hospital prescription system but had no access to imaging tests. Thus, the aim of this study was to sequentially evaluate patients with COVID-19 through LUS, to get to know how to identify those at higher risk of complications or death in an outpatient setting.

PATIENTS AND METHODS

Study design and population

The CEGADI admitted residents of NHs or LTCFs that tested positive by Polymerase Chain Reaction (PCR) for SARS-CoV-2 between October 2020 and March 2021, before the massive population vaccination. The only exclusion criterium to proceed to admission was a high grade of physical disability, evaluated through a Barthel index less than 30 points.

We collected data through electronic medical histories, including in our database the main demographic aspects of our patients, comorbidities, chronic treatments (considering polypharmacy in cases with 5 or more chronic treatments) and the degree of disability according to Barthel ´s index.¹³

The chronology of the disease was registered through the dates on which they tested positive on PCR tests, the date of admission and discharge. The end of their isolation period was determined by a negative PCR or a positive serological test for gamma globulin G (IgG) at least 10 days after the diagnosis and only in case the patient had remained asymptomatic, following the instructions given by public health authorities during the study period.

Clinical data, such as symptoms, signs, treatments, and laboratory tests, were included. The analyzed symptoms were cough, dyspnea, myalgias, diarrhea, anosmia and negative symptoms, which included mutism, somnolence and low level of consciousness. We classified the severity of the disease as mild, moderate and severe following our own specific protocol, taking in account the unavailability of imaging techniques at the time of admission and developed with the aim of properly classify patients and optimize the available resources.

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- Mild case: absence of respiratory failure with presence of no more than 2 signs/symptoms.
- Moderate case: absence of respiratory failure with presence of more than 2 signs/symptoms or hypoxemia with no more than 2 signs/symptoms.
- Severe case: presence of respiratory failure with high supplementary oxygen requirements, hypoxemia with more than 2 signs/symptoms or fever and abnormal respiratory sounds.

The main specific treatments authorized during this period were antibiotics and dexamethasone (considering dose-escalation), since Tocilizumab or Remdesivir were not authorized for outpatient settings.

If we focus on laboratory findings, we picked those related to infectious diseases and COVID-19 in particular. Following local laboratory criteria, we considered a normal range of leukocytes between 4090 and 10800/ μ L, of neutrophils between 1700 and 7300/ μ L, and of lymphocytes between 1700 and 4670/ μ L. The upper limit of normality of D Dimer was 500 ng/mL, of creatinine was 1,3 mg/dL, of Reactive C-Protein (RCP) was 0,5mg/dL, of procalcitonin was 0.05 and of Interleukin 6 was 5.

Regarding LUS, two evaluations were recorded, one at the date of admission and one 5 days after admission, assessing the presence of B lines, pleural effusion or a focal alteration. We considered a focal alteration the presence of an image compatible with pneumonia or atelectasis in at least two quadrants. We used a V-Scan Extend (General Electrics Health Care) device.

The main outcomes were complete recovery (defined as the absence of organic sequels, like chronic lung damage, neurological persistent alterations or permanent kidney injury), need to hospital transfer and death. Also, long-term outcomes (re-admission and death) were assessed by a telephonic follow-up three and six months after the discharge.

Statistical analysis

A descriptive analysis was performed by calculating qualitative variables rates plus mean and standard deviation (SD). We used X2 test or Fisher's exact test, as appropriate (expected frequency value <5), to compare qualitative variables, and the ANOVA test for quantitative variables. Kaplan-Meier tables were constructed to evaluate the relationship between variables and the need of hospital transference or death.

A logistic regression model was conducted to analyze the relationship between clinical and LUS variables and severity. The Cox regression model was used to evaluate variables linked to death, including only patients who had undergone LUS. A two-sided P value <0.05 was regarded as significant. All analyses were performed using the SPSS v25.0 software package.

	Men (n=101)	Women (n=187)	Р	Total (n=288)
Obesity	44 (45.8%)	71 (40.8%)	0.424	115 (42.6%)
Cachexia	21 (21.9%)	19 (10.9%)	0.015	40 (14.8%)
Alcohol	38 (39.6%)	6 (3.3%)	< 0.001	44 (15.9%)
Tobacco	45 (47.9%)	5 (2.8%)	< 0.001	50 (18.2%)
Hypertension	59 (58.4%)	122 (65.2%)	0.253	181 (62.8%)
Diabetes mellitus	33 (32.7%)	38 (20.3%)	0.020	71 (24.7%)
Dyslipidemia	57 (56.4%)	107 (57.2%)	0.898	164 (56.9%)
Atrial fibrillation	23 (22.8%)	29 (15.5%)	0.126	52 (18.1%)
Ischemic heart disease	11 (10.9%)	20 (10.7%)	0.959	31 (10.8%)
Heart failure	34 (33.7%)	50 (26.7%)	0.217	84 (29.2%)
COPD	17 (16.8%)	23 (12.3%)	0.289	40 (13.9%)
Peripheral artery disease	19 (18.8%)	4 (2.1%)	< 0.001	23 (8%)
Chronic kidney disease	27 (26.7%)	61 (32.6%)	0.301	88 (30.6%)
Brain stroke	19 (18.8%)	22 (11.8%)	0.106	41 (14.3%)
Parkinson disease	7 (6.9%)	8 (4.3%)	0.339	15 (5.2%)
Dementia	46 (45.5%)	115 (62,2%)	0.007	161 (56.3%)
Psychiatric illness	44 (44%)	69 (36.9%)	0.241	113 (29.4%)
Polypharmacy	80 (79.2%)	151 (80.7%)	0.754	231 (80.2%)

Table 1. Baseline characteristics and comparison regarding gender.

COPD: Chronic obstructive pulmonary disease.

	Men (n=101)	Women (n=187)	Р	Total (n=288)
Cough	34 (34.7%)	58 (31.7%)	0.610	92 (32.7%)
Dyspnea	31 (32%)	48 (26.2%)	0.311	79 (28.2%)
Myalgias	46 (46.9%)	64 (34.6%)	0.043	110 (38.9%)
Diarrhea	7 (7.9%)	13 (7.7%)	0.971	20 (7.8%)
Anosmia	9 (10.2%)	17 (10.3%)	0.985	26 (10.3%)
Negative symptoms	41 (43.2%)	87 (47.3%)	0.512	128 (45.9%)
Dysthermia	20 (29.4%)	20 (18.5%)	0.093	40 (22.7%)
Respiratory failure	24 (24%)	33 (17.7%)	0.103	57 (19.9%)
Hypoxemia	8 (8%)	30 (16.1%)	0.103	38 (13.3%)
Asymptomatic	37 (37.4%)	77 (41.2%)	0.532	114 (39.9%)
Fever	32 (32%)	39 (20.9%)	0.037	71 (24.7%)
Tachypnea	21 (21%)	36 (19.3%)	0.723	57 (19.9%)
Decreased breath sounds	38 (38%)	56 (29.9%)	0.166	94 (32.8%)
Crackling sounds	25 (25%)	42 (22,5%)	0.628	67 (23.3%)
Other respiratory sounds	14 (14%)	22 (11.8%)	0.586	36 (12.5%)
No signs	46 (46%)	110 (58.8%)	0.038	156 (54.4%)

Table 2. Symptoms and signs. Comparison regarding gender.

Respiratory failure: oxygen saturation \leq 90% with FiO2 0.21. Hypoxemia: oxygen saturation > 90% and \leq 94%.

Table 5. Wall valuables linked to mortality and severity.						
	Severe disease (n=98)	Non-severe disease (n=190)	Ρ	Dead (n=38)	Survivors (n=250)	Р
Leukocytosis	41 (61.2)	40 (45.5)	0.052	13 (76.5)	68 (49.3)	0.034
Neutrophilia	23 (34.3)	7 (8.0)	< 0.001	10 (58.8)	20 (14.5)	<0.001
Lymphopenia	22 (32.8)	7 (8.0)	< 0.001	6 (35.3)	23 (16.7)	0.069
D-dimer	42 (30.7)	52 (38.0)	0.411	16 (94.1)	78 (65.0)	0.015
RCP	56 (86.2)	50 (57.5)	<0.001	14 (82.4)	92 (68.1)	0.230
Procalcitonin	46 (70.8)	50 (57.5)	0.093	15 (88.2)	81 (60.0)	0.023
Obesity	41 (44.6)	74 (41.6)	0.637	11 (31.4)	104 (44.3)	0.152
Cachexia	22 (23.9)	18 (10.1)	0.002	11 (31.4)	29 (12.3)	0.003
Hypertension	69 (70.4)	112 (58.9)	0.057	31 (81.6)	150 (60.0)	0.010
Atrial fibrillation	27 (27.6)	25 (13.2)	0.003	9 (23.7)	43 (17.2)	0.333
Heart failure	42 (42.9)	42 (22.1)	< 0.001	15 (39.5)	69 (27.6)	0.134
COPD	20 (20.4)	20 (10.5)	0.022	6 (15.8)	34 (13.6)	0.716
CKD	37 (37.8)	51 (26.8)	0.057	18 (47.4)	70 (28.0)	0.016
Dementia	54 (55.1)	107 (56.9)	0.769	26 (68.4)	135 (54.4)	0.106
Barthel <20	30 (36.6)	47 (29.4)	0.205	19 (59.4)	58 (27.6)	0.001
Cough	65 (68.4)	27 (14.5)	< 0.001	14 (40.0)	78 (31.7)	0.328
Dyspnea	68 (70.8)	11 (6.0)	<0.001	26 (70.3)	53 (21.8)	<0.001
Flu-like	74 (78.7)	36 (19.0)	< 0.001	19 (55.9)	91 (36.5)	0.030
Anosmia	15 (20.0)	11 (6.2)	0.001	4 (14.8)	22 (9.7)	0.295
Negative symptoms	72 (77.4)	56 (30.1)	< 0.001	24 (72.7)	104 (42.3)	0.001
Fever	57 (58.8)	14 (7.4)	<0.001	17 (45.9)	54 (21.6)	0.001
Decreased sounds	73 (75.3)	21 (11.1)	<0.001	21 (56.8)	73 (29.2)	0.001
Crackles	56 (57.7)	11 (5.8)	<0.001	21 (56.8)	46 (18.4)	<0.001

Table 3. Main variables linked to mortality and severity.

RCP: reactive C-Protein; COPD: Chronic Obstructive Pulmonary Disease; CKD: Chronic Kidney Disease.

RESULTS

A total of 288 patients were included, 187 (64.9%) were women and the median age was 80 years old (IQR 16). A great percentage of them were over 85 years old (42%) and focusing their personal background, a significative difference was found regarding diabetes mellitus and dementia, both more frequent in women. Cachexia, alcohol and tobacco consumption and peripheral artery disease were more frequent in men. Baseline characteristics and differences by gender are shown in Table 1.

Regarding clinical presentation, the most frequent were negative symptoms (45.9%), followed by cough (32.7%) and myalgias (38.9%). It is remarkable that 114 (39.9%) patients were asymptomatic at diagnosis, but when they had objective signs, the most frequent were the presence of decreased breath sounds in pulmonary auscultation (32.8%) and fever (24.7%). The detailed characteristics of signs and symptoms are shown in Table 2.

If we focus on clinical classification by severity, 151 patients (52.4%) had a mild disease, 39 (13.5%) had a moderate disease and 98 (34%) had a severe disease at admission, following the previously described

criteria. A severe presentation was found in 39 (38,6%) men and in 59 (31,6%) women with no significant difference between them. The main factors linked to severity were the clinical presentation with fever, flu-like symptoms, cough and negative symptoms and also the presence of neutrophilia, lymphopenia and an elevated RCP.

Regarding treatment regimen, 160 patients (55.6%) were treated with corticosteroids, and 35 of them needed dose escalation. 60 (20.8%) were treated with Azithromycin and 105 (36.5%) with other antibiotics. Only 78 (27.1%) needed oxygen administration.

As main outcomes, it is remarkable that 38 (13.2%) patients died during their stay and 7 (2.4%) were transferred to the hospital. Mortality rate among mild cases was 4%, among moderate cases 10.3% and 28.6% in the group with a severe disease. We should highlight the higher percentage of patients with cachexia or hypertension among those who died and also the frequent clinical presentation with fever, dyspnea and negative symptoms in this group. The auscultatory findings of decreased breath sounds and crackles were both linked to severity and mortality. The complete analysis of variables potentially linked to mortality and severity is shown in Table 3.

	Severe disease	Non-severe disease	Р	Dead	Survivors	Р
B lines (Day 1)	31 (51.7)	17 (20.5)	< 0.001	14 (58.3)	34 (28.6)	0.005
Focal alteration (Day 1)	26 (43.3)	18 (21.7)	0.006	14 (58.3)	30 (25.2)	0.001
Pleural effusion (Day 1)	0 (0)	1 (1.2)	0.580	0 (0)	1 (0.8)	0.832

Table 4. Main findings in LUS and their correlation with severe disease and death.

LUS was performed in 143 (49.7%) patients at the time of admission since the ultrasound device was not available when the center was opened for the first time. The second LUS exploration was performed only in 84 (29.2%) of them. Taking both explorations into account, B lines were found in 61 (21,2%), a focal alteration in 62 (21,5%) and pleural effusion in 1 (0,3%) patient.

A significant association was found between the presence of B lines or focal alteration and a severe disease and/or death. Also, it is remarkable that a normal LUS had a significant relationship with a non-severe disease and survival (Table 4).

Regarding severity, the variables linked to it in the multivariable analysis were the elevation of RCP (OR=9.53; P=0.046; IC95% 1.03-87.51), the presence of crackles at lung auscultation (OR=10.63; P=0.018; IC95% 1.51-75.02) and focal alterations in LUS (OR=10.65; P=0.046; IC95% 1.04-108.99).

After the construction of the Cox regression model, we found that the main variables linked to mortality in our series were a higher degree of dependence (OR=3.86; P=0.002; IC 95% 1.65 - 9.01) and the presence of B lines at day 1 in LUS (OR=6.06; P=0.019; IC 95% 1.12 - 32.81).

Within the first three months since discharge 20 (6.9%) patients needed follow-up through medical consultation, 21 (7.3%) needed hospital readmission and 10 (3.5%) died. From this moment until the end of the sixth month since discharge 6 (2.1%) had a follow-up consultation, 9 (3.1%) needed hospital readmission and 6 (2.1%) died. Only 12 (4.2%) suffered from pulmonary sequels and 1 of them had a primary immune thrombocytopenia related to the infection, who required readmission.

DISCUSION

We present the results from a unique cohort of patients: elderly, residents of NHs and LTCFs and managed in an environment which was halfway between a residential home and a hospital. The closest experience we found was in Andorra, were they turned a reference nursing home into an intermediate healthcare facility, but unfortunately, there are no available data regarding medical resources¹⁴. Other similar experiences we were based on collaborative models between these facilities and hospitals, most of them centered on staff education, preventive actions and clinical assistance through telemedicine.^{9,10}

The baseline characteristics of the patients in our study had some differences with the previous reports. It is important to note the elder age of our patients, with 42% of them being over 85 years old, a cluster of population that is usually underrepresented in medical studies⁷. Regarding comorbidities, although hypertension and dementia were very prevalent as previously described, we also found obesity or dyslipidemia between the most frequent ones, which reflects the differences between the populations living in NHs and LTCFs in different areas or countries.^{5,6}

The clinical presentation showed more differences, with a higher rate of negative symptoms and a lower number of patients with the typical presentation, consisting of fever and shortness of breath¹⁵. The high mean age and the prevalence of dementia and functional impairment may be an explanation for these differences, since this group of patients have usually a different clinical presentation in most infectious diseases. We also must highlight that the main variables linked to death and the severity of the disease were congruent with previous series, such as cachexia and hypertension or having symptomatic disease^{6,8,14,16}. If we focus on analytical findings, lymphopenia, neutrophilia and an elevation of inflammatory biomarkers were also relevant in our analysis, probably due to their relationship with the activation of the immune response.^{6,14}

The most remarkable data regarding outcomes is the low global mortality, as we have found in previous framework mortality rates up to 40% in NHs a LTCFs^{8,17}. Moreover, the need to transfer patients to the hospital from our center was minimal. The explanation to this may be an early diagnosis and implementation of therapeutic measures and the disposition of hospital tools at our center without the risk of iatrogenic events since many of the studies we found were with no hospital intervention. This intervention was possible due to a proactive screening protocol implemented in all NHs and LTCFs in Galicia during the whole pandemic period.

Last, but not least, we found LUS to be a great technique to predict the severity of the disease and death in an outpatient environment. The presence of B lines and focal alterations at day one, sometimes even before the onset of symptoms, helped us when making decisions, so as a normal LUS did, and predicted the development of severe forms of disease and death even better than biochemical or clinical classical tools. Other studies have showed before the ability of LUS on predicting clinical outcomes, with typical findings of a COVID-19 ill lung or secondary complications. This can make of LUS a key tool at triage when deciding the need of hospitalization or even ICU admission in patients from NHs and LTCFs and also could be a helpful tool when monitoring the evolution of the disease during treatment in these facilities, not only in COVID-19 patients, but also in other infectious and non-infectious diseases.^{18,19}

The limitations of our study were the absence of data regarding LUS in the whole cohort, which reduced the sample. It is also remarkable the fact that this is an observational study in a single center. On the other hand, its strengths are the kind of population included, elderly and usually underrepresented in scientific literature, the report of a

unique approach with a specific protocol to these patients, less invasive but with hospital tools and a low mortality rate.

CONCLUSIONS

According to our findings, we conclude that LUS is a useful, unharmful, reproducible and cheap tool that can be used in an outpatient environment in order to predict severity and death in COVID-19 patients and, surely, in other respiratory infections. This study could be also useful by showing a different way to manage a vulnerable population in a global pandemic context.

FUNDING

This research has not received specific aid from public sector agencies, the commercial sector or non-profit entities.

CONFLIC OF INTEREST

There are no conflicts of interest.

ETHICAL ASPECTS

All participants submitted a consent form to be included in this study.

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