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Original

Impact of systemic corticosteroids on hospital length of stay among patients with COVID-19

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ABSTRACT

Background and objective: The COVID-19 pandemic has posed a threat to hospital capacity due to the high number of admissions, which has led to the development of various strategies to release and create new hospital beds. Due to the importance of systemic corticosteroids in this disease, we assessed their efficacy in reducing the length of stay (LOS) in hospitals and compared the effect of 3 different corticosteroids on this outcome.
Methods: We conducted a real-world, controlled, retrospective cohort study that analysed data from a hospital database that included 3934 hospitalised patients diagnosed with COVID-19 in a tertiary hospital from April to May 2020. Hospitalised patients who received systemic corticosteroids (CG) were compared with a propensity score control group matched by age, sex and severity of disease who did not receive systemic corticosteroids (NCG). The decision to prescribe CG was at the discretion of the primary medical team.
Results: A total of 199 hospitalized patients in the CG were compared with 199 in the NCG. The LOS was shorter for the CG than for the NCG (median = 3 [interquartile range = 0–10] vs. 5 [2–8.5]; p = 0.005, respectively), showing a 43% greater probability of being hospitalised ≤ 4 days than > 4 days when corticosteroids were used. Moreover, this difference was only noticed in those treated with dexamethasone (76.3% hospitalised ≤ 4 days vs. 23.7% hospitalised > 4 days [p < 0.001]). Serum ferritin levels, white blood cells and platelet counts were higher in the CG. No differences in mortality or intensive care unit admission were observed.
Conclusions: Treatment with systemic corticosteroids is associated with reduced LOS in hospitalised patients diagnosed with COVID-19. This association is significant in those treated with dexamethasone, but no for methylprednisolone and prednisone.

Impacto de los corticoides sistémicos en el tiempo de hospitalización en pacientes con COVID-19

Palabras clave:
COVID-19
corticoides
dexametasona
hospitalización

RESUMEN

Objetivo: El COVID-19 supuso una amenaza para la capacidad hospitalaria por el elevado número de ingresos, lo que llevó al desarrollo de diversas estrategias para liberar y crear nuevas camas hospitalarias. Dada la importancia de los corticoides sistémicos en esta enfermedad, se evaluó la eficacia de estos en la reducción de la duración de la estancia hospitalaria (LOS) y se comparó el efecto de tres corticosteroides diferentes sobre este resultado.
Método: Se realizó un estudio en vida real de cohorte retrospectivo, controlado que analizó una base de datos hospitalaria que incluyó 3.934 pacientes hospitalizados diagnosticados con COVID-19 en un hospital terciario de abril a mayo de 2020. Se comparó un grupo de enfermos que recibieron corticosteroides sistémicos (CG) frente

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a un grupo de control que no recibió corticosteroides sistémicos (NCG) emparejado por edad, sexo y gravedad de la enfermedad mediante una puntuación de propensión. La decisión de prescribir CG dependía principalmente del criterio del médico responsable.

Resultados: Se compararon un total de 199 pacientes hospitalizados en el GC con 199 en el GNC. La LOS fue más corta para el GC que para el NCG (mediana = 3 [rango intercuartílico = 0-10] vs. 5 [2-8,5]; p = 0,005, respectivamente), mostrando un 43% más de probabilidad de ser hospitalizado ≤ 4 días que > 4 días cuando se usaron corticosteroides. Además, esta diferencia solo la mostraron aquellos tratados con dexametasona (76,3% hospitalizados ≤ 4 días vs. 23,7% hospitalizados > 4 días [p < 0,001]). Los niveles de ferritina sérica, glóbulos blancos y plaquetas fueron más elevados en el GC. No se observaron diferencias en la mortalidad ni en el ingreso a la unidad de cuidados intensivos.

Conclusiones: El tratamiento con corticosteroides sistémicos se asocia con una disminución de la estancia hospitalaria en pacientes hospitalizados con diagnóstico de COVID-19. Esta asociación es significativa en aquellos tratados con dexametasona, no así en metilprednisolona o prednisona.

Introduction

The coronavirus disease 2019 (COVID-19) continues to be responsible for a high number of hospitalizations. 12%–20% of patients with COVID-19 need hospitalisation due to a severe illness causing acute respiratory failure that can develop even just a few hours after the beginning of the dyspnoea[1,2]. Mortality is extremely high in this subgroup of patients, with a reported rate of 20%–52%[3,4].

These alarming statistics have posed an enormous threat to the capacity of hospitals, which have had to reduce the use of hospital beds for non-COVID-19 illnesses and expand the number and availability of ICU hospital beds as well as providing other resources and amenities. In fact, the demand for available beds was so high in Madrid during the first pandemic surge that it was necessary to convert hotels to hospital-hotels[5] and to adapt an exhibition space into a provisional hospital. In fact, a new pandemic hospital has been constructed specifically for this difficult situation, and throughout the Spanish territory numerous field hospitals have been built.

To improve the data on treatments and outcomes, several therapies for hospitalised patients have been evaluated. Thus far, corticosteroids[3], together with anticoagulation, the antiviral remdesivir, or immunomodulators such as tocilizumab or the Janus kinase inhibitor baricitinib have shown some efficacy in randomised clinical trials, but many others are under investigation[6].

Regarding systemic corticosteroids, experience in other viral acute respiratory distress syndromes (ARDS), such as Middle East respiratory syndrome, severe acute respiratory syndrome and influenza, had shown delayed viral clearance, no benefit and even potential injury[7–9]. Therefore, although corticosteroids were not recommended for COVID-19 treatment in the early phases of the pandemic[10], we now know that in the inflammatory phase of severe COVID-19 they can reduce proinflammatory and augment anti-inflammatory cytokines, as well as improve lung barrier integrity and microcirculation[11–13]. Fortunately, the evidence is growing, and in the RECOVERY randomised trial, dexamethasone demonstrated a reduction in mortality in patients with respiratory failure[3]. In addition, in several observational studies, the benefits of corticosteroids in regard to delaying intensive care unit (ICU) admission, shortening mechanical ventilator support[14], and even reduced mortality have been observed[14,15].

Dexamethasone is a well-known drug with more than 60 years of clinical use. Its therapeutic potential comes from several actions. First, it binds to glucocorticoid receptors present in the cell cytoplasm, which are responsible for the initiation of immune cells responses that lead to proinflammatory suppression of several cytokines, some of which are related to COVID-19 progression. It also increases the gene expression of interleukin (IL)-10, which is an anti-inflammatory cytokine mediator. Second, it inhibits neutrophil adhesion to endothelial cells, preventing the release of lysosomal enzymes and chemotaxis at the site of inflammation, as well as inhibiting macrophage activation, one of the main authors of cytokine storms in COVID-19, which in turn is the landmark of severe COVID-19. Additionally, dexamethasone has other important benefits, such as its low-cost, easy availability and its long-lasting effect that allows a once-a-day regimen[11,16].

Given the positive results of previously mentioned studies on corticosteroids, we suspected that corticosteroids also could shorten the hospital length of stay (LOS), thus reducing the consumption of resources and increasing available beds for other patients who need them. However, no study has focused on this outcome. Furthermore, while the evidence has been accumulating on dexamethasone, other groups of corticosteroids have not yet been evaluated.

Thus, we focused on the first wave of the pandemic, when corticosteroids were beginning to be used, and we compared patients who received corticosteroids with patients who did not. We conducted a real-world study in which we aimed to determine the efficacy of corticosteroids in shortening the LOS in patients with COVID-19 compared with patients who did not receive corticosteroids. In addition, we evaluated which group of corticosteroids was the most effective in reducing the LOS.

Methods

Study design and objectives

This was a real-world, controlled, retrospective cohort study. Our main objective was to determine the impact of systemic corticosteroids on the LOS in hospitalised patients with COVID-19. We also evaluated whether the use of corticosteroids was associated with the occurrence of severe complications of COVID-19, such as death and admission to the ICU. Finally, we aimed to assess which specific subgroup of corticosteroids acts most effectively on theses outcomes.

Patient population and COVID-19 database

We included all individuals, 18 years or older, who were hospitalised in a 1286-bed hospital in Madrid (La Paz University Hospital) with a diagnosis of COVID-19 from April to May 2020, who received systemic corticosteroids (corticosteroid therapy group [CG]). Due to the limited evidence on the use of systemic corticosteroids in this disease until this time, their prescription mainly depended on the physicians' previous experience in their use.

Patients not hospitalised or discharged from the emergency department after a stay of less than 24 h were not included. A control group of patients who did not require systemic corticosteroid treatment (non-corticosteroid therapy group [NCG]) was recruited from a hospital database that comprised all patients hospitalised with a COVID-19 diagnosis during the same period. The characteristics of this database have been

previously published[17] and included 3934 patients consecutively treated in the Emergency Department of an University Hospital between February 25, 2021 and June 16, 2021, and who were later hospitalised. The database (called COVID@HULP) includes 372 variables, grouped into demographics, medical history, infection exposure history, symptoms, complications, treatments (excluding clinical trials) and disease progression during hospitalisation. For this study, we extracted age, sex, smoking status, transmission, comorbidities, symptoms on admission, severity of disease, complications, ICU admission and death during hospitalisation. The severity of disease was evaluated according to the Spanish Official Document on the management of COVID-19. It considered mild pneumonia as oxygen saturation higher than 90%, with no signs of severity and a CURB-65 pneumonia severity score lower than 2; and severe COVID-19 pneumonia as organ failure, oxygen saturation lower than 90% or respiratory rate higher than 30[18].

Patients (with or without systemic corticosteroid treatment) were matched 1:1 by age, sex and severity of disease. Matching was performed by statisticians of the Central Clinical Research Unit who were blinded to completion of the data.

Laboratory results (haematology, biochemistry, microbiology) were extracted from various hospital data management systems, and information regarding the drugs used during hospitalisation was extracted from the electronic prescription system.

Patients with corticosteroids were identified using the computerised physician order entry (CPOE) program to make prescriptions. The task of identifying patients treated with corticosteroids was performed by a pharmacist with high experience using the CPOE program.

The study was approved by the Research Ethics Committee of La Paz University Hospital (PI-4455).

Outcomes

The main outcomes were LOS in hospital, death and admission to the ICU. We also evaluated differences between the CG and NCG as well as the development of complications during hospitalisation.

Statistical analysis

In the first part of the analysis, baseline characteristic data on both groups (CG and NCG) were evaluated. In the second part, analyses were focused on the subgroups of corticosteroids used. Patients in both groups were propensity score matched 1:1, accounting for age, sex and severity of disease. Quantitative variables were expressed as medians with interquartile range (IQR). For categorical variables, frequencies and proportions were used. Prior to the analyses, a normality analysis was performed with the Shapiro–Wilk test. For the parametric analysis, Student's t-test was used, and the Mann–Whitney U test was used for non-parametric analyses. For correlations between quantitative variables, Spearman's correlation was employed. For the associations between qualitative variables, the chi-squared test (or Fisher's test when necessary) was used. Finally, to investigate the association between corticosteroids and the LOS, we employed a logistic regression analysis. For this purpose, the hospital LOS was dichotomised into ≤ 4 and > 4 days, given it corresponded to the median of the included population. Statistical significance was set at a p-value ≤ 0.05. Statistical analyses were performed using R version 4.0.4.

Results

Baseline characteristics of the included patients

A total of 288 hospitalised patients diagnosed with COVID-19 were identified as treated with corticosteroids during the study period. Of these, 89 were not included because of the inability to find a control participant in the hospital's database after applying the propensity score matching. Ultimately, 199 patients allocated to the CG and 199 patients in the NCG were included in the analysis (Fig. 1).

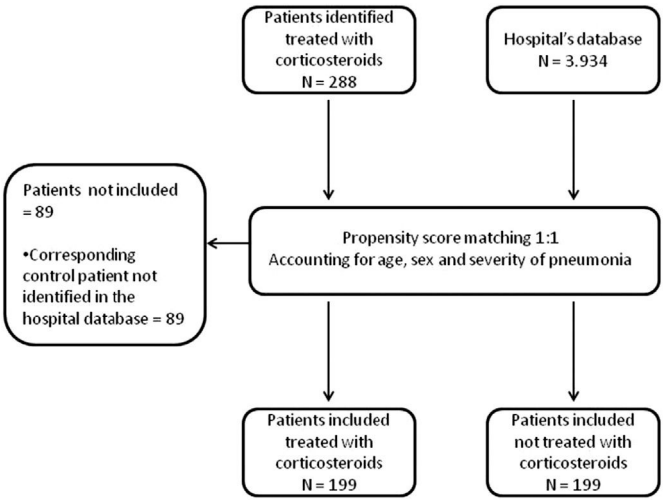

Fig. 1. Flowchart of the study.

The distributions of comorbidities were not different when comparing the CG with the NCG. Regarding the systemic inflammatory response to COVID-19, only serum ferritin levels (620.5 [IQR 216.5–1191.8] vs 312.5 [IQR 105.5–594.5]; $p < 0.001$), white blood cell count (6.5 [IQR 5–9.4] vs 5.9 [IQR 4.4–8.5]; $p = 0.041$) and platelets (256 [IQR 192–342] vs 225.5 [IQR 179–301.5]; $p = 0.016$) were significantly higher in the CG compared with the NCG. Comparisons between both groups are detailed in Table 1.

In the group treated with corticosteroids, the median age was 68 (IQR 56–78) and 57.8% were men. The total systemic corticosteroid dose classified according to the group of corticosteroids were 60 mg (IQR 22–98) for dexamethasone, 492.5 mg (IQR 145–1000) for methylprednisolone and 60 mg (IQR 28.8–152.5) for prednisone (Table 1). The amounts of corticosteroids employed were converted to an equivalent dose of dexamethasone, resulting in a total median dexamethasone dose of 12 mg (IQR 22–98) (Table 1).

Outcomes associated with the prescription of corticosteroids

The hospital LOS was statistically shorter in the CG than in the NCG (3 [IQR 0–10] vs. 5 [IQR 2.0–8.5] days; $p = 0.005$). This difference might not be associated with higher mortality, given the mortality rate was not different between the groups (31% vs. 29.6%; $p = 0.861$); or with a higher severity of the disease at the time of hospital admission, because severity was considered in the matching process of the NCG with the CG. In fact, the CG had a higher rate of ARDS complications during hospitalisation than the NCG ($p = 0.006$). No differences were observed in the rate of admission to the ICU or in the development of other complications during hospitalisation (Table 2). In addition, when converting the doses of the different types of corticosteroids into equivalent doses of dexamethasone, this dose was well correlated with LOS. ($r = 0.31$; $p = 0.058$).

The LOS was dichotomised into ≤ 4 and > 4 days, which corresponded to the median of the included population. The logistic regression model revealed that the prescription of corticosteroids was associated with a 43% greater probability of being hospitalised ≤ 4 days compared with the NCG (OR 0.57 [0.37-0.87; $p = 0.009$]).

Analysis of the impact of the type of corticosteroid on the length of hospital stay

For this purpose, we only included patients treated with a single group of corticosteroids throughout their hospitalisation. Differences were only noticed in those treated with dexamethasone, in which 76.3% were hospitalised ≤ 4 days and 23.7% stayed > 4 days ($p < 0.001$). In the other groups, no differences in LOS were observed (Fig. 2).

Table 1
Baseline characteristics of hospitalised patients diagnosed with COVID-19 treated or not with systemic corticosteroids.

	CG (n = 199)	NCG (n = 199)	p
Men, n (%)	115 (57.8)	115 (57.8)	1
Age, years	68 [56–78]	68 [56–78]	1
Current smoker, n (%)	16 (8.4)	13 (6.8)	0.688
Comorbidities			
Obesity, n (%)	33 (16.8)	27 (13.8)	0.510
Cardiac disease, n (%)	49 (24.6)	46 (23.1)	0.814
Hypertension, n (%)	97 (49)	101 (50.8)	0.802
COPD, n (%)	17 (8.6)	20 (10.1)	0.730
Asthma, n (%)	15 (7.6)	8 (4.0)	0.197
Diabetes mellitus, n (%)	46 (23.2)	52 (26.1)	0.580
Dyslipidaemia, n (%)	84 (42.9)	84 (42.2)	0.978
Liver disease, n (%)	11 (5.5)	9 (4.5)	0.243
Neurological disease, n (%)	37 (18.9)	24 (12.1)	0.086
Neoplastic disease, n (%)	36 (18.4)	29 (14.6)	0.390
Kidney disease, n (%)	28 (14.1)	18 (9.0)	0.153
Patient's functional status			
Totally dependent	16 (8.5)	10 (5.3)	0.454
Partially dependent	12 (6.4)	11 (5.9)	
Independent	160 (85.1)	167 (88.8)	
Long-term oxygen therapy	2 (1)	1 (0.5)	0.868
Pregnancy	1 (0.5)	4 (2.0)	0.374
Cohabitation/familial infection	33 (18.2)	30 (16.2)	0.710
Severe COVID-19	105 (52.8)	105 (52.8)	1
Laboratory results			
RCP, mg/L	48.3 [10.9–126.5]	64.40 [17.9–147.6]	0.120
Fibrinogen, mg/dL	562.5 [357.3–808.5]	625 [445–777]	0.078
Ferritin, ng/mL	620.5 [216.5–1191.8]	312.5 [105.5–594.5]	< 0.001
WBC count, $x10^3/\mu L$	6.5 [5–9.4]	5.9 [4.4–8.5]	0.041
AL count, $x10^3/\mu L$	0.9 [0.6–1.3]	1 [0.7–1.5]	0.214
Platelet count, $x10^3/\mu L$	256 [192–342]	225.5 [179–301.5]	0.016
Total systemic corticosteroid dose			
Dexamethasone, mg	60 [22–98]	-	
Methylprednisolone, mg			
(Median dose [CI 95%])	492.5 [145–1000]	-	
(Median of equivalent dose of dexamethasone [CI 95%])	98.5 [29–200]		
Prednisone, mg			
(Median dose [CI 95%])	60 [28.8–152.5]	-	
(Median of equivalent dose of dexamethasone [CI 95%])	9.6 [4.61–24.4]		

Data expressed as median [interquartile range] or number (percentage).
Comparisons between groups by unpaired samples using Student's t-test, Mann–Whitney U test and chi-squared test. Abbreviations: AL = absolute lymphocyte; CG = corticosteroid group; COPD = chronic obstructive pulmonary disease; NCG = non-corticosteroid group; RCP = C-reactive protein; WBC = white blood cell.

Discussion

The COVID-19 pandemic has meant, especially during the first wave, the near paralysis of hospitalisations for non-COVID-19 health problems as well as for non-urgent surgeries, in order to deal with all the patients with serious COVID-19 who required hospital admission. In addition, although the number of ICU beds has been significantly increased, in some time periods it was still insufficient[19]. Therefore, reducing the hospital LOS was (and still is) profoundly beneficial in helping cope with new patients who need hospitalisation.

In the first wave of the COVID-19 pandemic, we had a period in which corticosteroids were not routinely recommended and were even contraindicated, after which the first evidence supporting their use was

Table 2
Outcomes among hospitalised patients diagnosed with COVID-19 treated or not with systemic corticosteroids.

	CG (n = 199)	NCG (n = 199)	p
Length of stay in hospital	3 [0–10]	5 [2.0–8.5]	0.005
Admission to the ICU, n (%)	21 (10.7)	16 (8.1)	0.470
Death, n (%)	61 (31.0)	59 (29.6)	0.861
Invasive mechanical ventilation, n(%)	11 (6.6)	15 (9.2)	0.508
Concomitant infections during hospitalisation, n (%)	31 (15.8)	19 (9.5)	0.085
ARDS, n (%)	31 (15.8)	13 (6.5)	0.006
Concomitant bacterial pneumonia, n (%)	20 (10.3)	11 (5.5)	0.120
Heart failure, n (%)	10 (5.1)	7 (3.5)	0.598
Cardiac arrest, n (%)	5 (2.6)	5 (2.5)	1.000
Renal insufficiency, n (%)	23 (11.8)	22 (11.1)	0.942
Acute confusional syndrome, n (%)	26 (13.3)	26 (13.1)	1.000
Psychiatric complications	7 (3.6)	6 (3.0)	0.985

Data expressed as median [interquartile range] or number (percentage). Comparisons between groups by unpaired samples Student's t-test, Mann–Whitney U test and chi-squared test. Abbreviations: ARDS = acute respiratory distress syndrome; GC = corticosteroid group; ICU = intensive care unit; NCG = non-corticosteroid group.

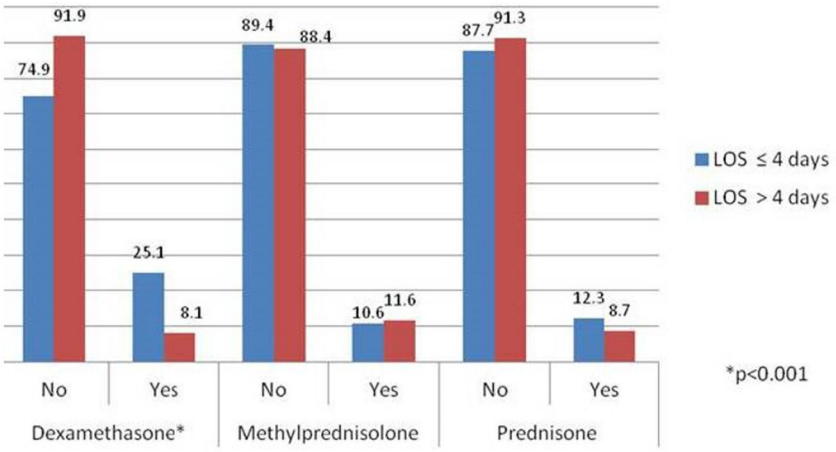

Fig. 2. Distribution of length of stay in hospital according to the group of corticosteroids used.

reported[18]. This real-world controlled retrospective cohort study suggests that corticosteroids, specifically dexamethasone, reduced the LOS in patients with higher inflammation markers compared with the control group. As we have seen, patients in the CG expressed higher levels of platelets and white blood cells, and they had two times higher ferritin levels than those in the NCG. Severe COVID-19 is caused by an excessive systemic increase of cytokines and chemokines in the patient, also called a "cytokine storm", which leads to immunopathological lung damage and diffuse alveolar injury, with the development of ARDS and death[20]. In this subgroup of patients, a hyperinflammatory phenotype has been described in which the serum concentrations of inflammatory and coagulation markers (including ferritin, D-dimer, and C-reactive protein), as well as pro-inflammatory cytokines (such as IL-2R, IL-6, IL-10 and tumour necrosis factor-α) are increased, accompanied by reduced lymphocytes and neutrophils with immunometabolic reprogramming[13,21,22]. Given corticosteroids are potent immunomodulatory drugs that can break the inflammatory feedforward loop in some individuals [11], as we have seen in the CG group, those with higher inflammation might obtain a greater benefit in terms of LOS[11–13,21].

This investigation occurred during a time period in which the first evidence on the benefit of corticosteroids in COVID-19 was being published. At the time of this study, given the data were heterogeneous and we did not know which corticosteroid type was the most appropriate, our hospital protocol allowed us to choose between the 3 corticosteroids described based on the criteria of the attending physicians. We have shown that, while dexamethasone reduces the LOS, methylprednisolone and prednisone did not achieve this outcome.

Most of the evidence accumulated to date on COVID-19 is on dexamethasone. Indeed, the largest randomised study with corticosteroids in severe COVID-19 was the RECOVERY trial, in which it was observed that dexamethasone administration led to a reduction in mortality in patients with respiratory failure[3]. This outcome has been further supported in 2 meta-analyses that included a high number of critically ill patients with heterogeneous data[23,24]. Methylprednisolone has also been shown better clinical outcomes, to increase ventilator-free days, and a lower mortality rate in moderate to severe COVID-19[14,25,26]. In fact, there have been published two randomized trials with hospitalized COVID-19 patients in which methylprednisolone demonstrated a lower ventilator use and shorter length of hospital stay compared to dexamethasone[27,28].

It is important to note that, when assessed both clinical trials, the applied dose of methylprednisolone was much higher than that of dexamethasone, which makes difficult to draw conclusions regarding whether methylprednisolone is better option than methylprednisolone, or if the higher dose of corticosteroid is the reason for the improvement in this group of patients. In the other hand, when comparing the results of our study with other series, we have several observations. First, although this cohort exhibited a higher mortality rate than that of the RECOVERY trial[3], it is within the range reported in other series[2–4]. We must consider the selection bias of randomised clinical trials, in which the most severe patients could be excluded. Fortunately, mortality might be decreasing as the pandemic progresses. Second, there was also a lower proportion of patients who were admitted to the ICU compared with other cohorts[3,4,29]. This difference is probably due to the participation of the Intermediate Respiratory Care Units within the Pulmonary Department in our hospital during the pandemic[19,30]. Noninvasive ventilation and other noninvasive respiratory support, such as high-flow nasal cannula oxygen therapy, have played an important role here[1,29,31]. These therapies could be applied together with close cardiorespiratory monitoring in these units to try to reduce or delay ICU admissions among patients who require noninvasive respiratory support in a crisis situation, as well as to manage early discharges from the ICU and for those patients who were ineligible for admission to the ICU due to comorbidities.

The main strength of our study is that it is a real-world cohort at a time when corticosteroid treatment had started; therefore, corticosteroid treatment groups could be compared in the same clinical setting (one hospital's treatment protocols, during the same COVID-19 surge). Additionally, we included a control group, matched for sex, age and severity of disease, and representative of a large proportion of hospitalised patients with COVID-19 in Spain.

This study has several potential concerns and limitations. First, it is a single-centre study with a limited sample size, which reduces the external validity of our results and is insufficient to analyse the effect on mortality. However, it is larger than most of the observational studies evaluating corticoid effects[14,26,27]. Second, although we have explored several baseline characteristics of the patients, due to the design of the study and its retrospective nature, it is possible that confounders have not been evaluated. Nevertheless, the data have been extracted from a complex database that includes a multitude of possible confounders as described previously. Third, the cross-sectional design only permits assessing potential associations or relationships. To evaluate causality, it would be necessary to conduct a longitudinal study with long-term patient follow-up. Additionally, we have no information about the need for oxygen supplementation or noninvasive mechanical ventilation. A final limitation is that, at the time of the compilation of these results, we did not have data on long-term outcomes and mortality, which would further enrich the results. However, these patients are in a post-COVID follow-up consultation, which could resolve this limitation in the future.

In conclusion, corticosteroids, especially dexamethasone, might reduce the length of stay in hospitalised patients, which would have a positive impact on hospital capacity during the COVID-19 pandemic.

Author contributions

- Ester Zamarrón: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Project administration; Resources; Software; Supervision; Validation; Visualization; Roles/Writing - original draft; Writing - review & editing.
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- Antonio Buño: Data curation; Formal analysis; Supervision; Validation; Visualization; Roles/Writing Writing - review & editing
- Concepción Prados: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Project administration; Resources; Software; Supervision; Validation; Visualization; Roles/Writing - original draft; Writing - review & editing

Declaration of Competing Interest

The authors declare that they do not have conflict of interest.

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Appendix A

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Corcuera-Pindado	Maria Teresa
Rico-Nieto	Alicia
Department:	**Pharmacy**
Herrero	Alicia
Medicine	**Laboratory**
Prieto Arribas	Daniel
Oliver-Saez	Paloma
Mora Corcovado	Roberto
Fernández-Calle	Pilar
Alcaide Martín	Mª José
Díaz-Garzón Marco	Jorge
Fernández-Puntero	Belén
Nuñez Cabetas	Rocío
Crespo Sánchez	Gema
Rodriguez Fraga	Olaia
Mendez del Sol	Helena
Duque Alcorta	Marta
Gomez Rioja	Rubén
Sanz de Pedro	María
Pascual García	Lydia
Segovia Amaro	Marta
Iturzaeta Sánchez	Jose Manuel
Rodriguez Gutiérrez	Mercedes
Perez Garcia Morillon	Amparo
Martinez Gallego	Miguel Angel
Fabre Estremera	Blanca
Martinez	Estefaní
Moreno Parra	Isabel
Rodriguez Roca	Neila
Ortiz Sánchez	Daniel
Simon Velasco	Manuela
Gabriela Tomoiu	Ileana
Pizarro Sanchez	Cristina
Montero San Martín	Blanca
Qasem Moreno	Ana Laila
Gómez López	Marta
Casares Guerrero	Ismael
Buño Soto	Antonio
Department:	**Radiology**
Martí de Gracia	Milagros
Parra Gordo	Luz
Diez Tascón	Aurea
Ossaba Vélez	Silvia
Pinilla	Inmaculada
Cuesta	Emilio
Fernández-Velilla	María
Torres	Maria Isabel
Garzón.	Gonzalo
Medicine	**Preventive**
Pérez-Blanco	Verónica
Quintás-Viqueira	Almudena
San Juan	Isabel
Cantero-Escribano	José Miguel
Pérez-Romero	César
Castro-Martínez	Mercedes
Hernández-Rivas	Lucia
Pedraz	Teresa
Fernández-Bretón	Eva

García-Vaz	Claudia
Robustillo-Rodela	Ana
Medicine	**Emergency**
Torres Santos-Olmo	Rosario María
Rivera Núñez	Angélica
Fernández Fernández	Ignacio
Noguerol Gutiérrez	Marina
Martínez Virto	Ana María
González Viñolis	Manuel
Cabrera Gamero	Regina
Mayayo Alvira	Rosa
Marín Baselga	Raquel
Lo-Iacono García	Victoria
Lerín Baratas	Macarena
Romero Gallego-Acho	Paloma
Reche Martínez	Begoña
Tejada Sorados	Renzo
Rico Briñas	Mikel
Deza Palacios	Ricardo
Fabra Cadenas	Sara
Arroyo Rico	Isabel
Dani Ben-Abdellah	Lubna
Labajo Montero	Laura
Soriano Arroyo	Rubén
López Corcuera	Lorena
Calvin García	Elena
Martínez Álvarez	Susana
López-Tappero Irazábal	Laura
Pilares Barco	Martín
González Peña	Olga
Bejarano Redondo	Guillermina
Iglesias Sigüenza	Alberto
Tung Chen	Yale
Maroun Eid	Charbel
Bravo Lizcano	Ruth
Silvestre Niño	Miguel
Perdomo García	Frank
Alonso González	Berta
Antón Huguet	Berta
Arenas Berenguer	Isabel
Cabré-Verdiell Surribas	Clara
Marqués González	Francisco
Muñoz Del Val	Elena
Molina	María Ángeles
Cancelliere Fernández	Nataly
Pastor Yvorra	Sivia
Frade Pardo	Laura
López Arévalo	Paloma
García	Isabel
Medicine	**Internal**
Fernández Capitán	Carmen
González Garcia	Juan José
Herrero	Juan
Quesada Simón	María Angustias
Robles Marhuenda	Angel
Soto Abanedes	Clara
Noblejas Mozo	Ana María
Ramos	Juan Carlos
Jaras Hernandez	Maria Jesús
Martinez Robles	Elena
Moreno Fernandez	Alberto
Sanchez Purificación	Aquilino
Martin Gutiérrez	Juan Carlos
Martinez Hernández	Pedro Luis
Sancho Bueso	Teresa
Lorenzo Hernández	Alicia
Gutierrez Sancerni	Belén
Salgueiro	Giorgina
Martin Carbonero	Luz
Mostaza	Jose mAría
Martinez-López	María Angeles
Hontañon	Victor
Menéndez	Araceli
Alvarez Troncoso	Jorge
Castellano	Arancha
Marcelo Calvo	Cristina
Vives Beltrán	Ivo
Ramos Ruperto	Luis

Daroca Bengoa	German
Arcos Rueda	María
Vasquez Manau	Julia
Fernández Cidón	Pelayo
Herrero Gil	Carmen Rosario
Palmier Peláez	Esmeralda
Untoria Tabares	Yeray
Lahoz	Carlos
Estirado	Eva
Hernández	Clara
Garcia-Iglesias	Francisca
Monteoliva	Enrique
Martínez	Mónica
Varas	Marta
González Alegre	Teresa
Valencia	Maria Eulalia
Moreno	Victoria
Montes.	Maria Luisa
Department:	**Neumology**
Alcolea Batres	Sergio
Cabanillas Martín	Juan José
Carpio Segura	Carlos
Casitas Mateo	Raquel
Fernández-Bujarrabal Villoslada	Jaime
Fernández Navarro	Isabel
Fernández Lahera	Juan
García Quero	Cristina
Hidalgo Sánchez	María
Galera Martínez	Raúl
García Río	Francisco
Gómez Carrera	Luis
Gómez Mendieta	María Antonia
Mangas Moro	Alberto
Martínez Cerón	Elisabet
Martínez Redondo	María
Martínez Abad	Yolanda
Martínez-Verdasco	Antonio
Plaza Moreno	Cristina
Quirós Fernández	Sarai
Romera Cano	Delia
Romero Ribate	David
Sánchez Sánchez	Begoña
Santiago Recuerda	Ana
Villasante Fernández-Montes	Carlos
Zamarrón De Lucas	Ester
Arnalich Montiel	Victoria
Mariscal Aguilar	Pablo
Falcone	Adalgisa
Laorden Escudero	Daniel
Prados Sánchez	María Concepción
Álvarez-Sala Walther	Rodolfo
Care	**Intensive**
García	Andony
Arévalo	Cristina
Gutiérrez	Carola
Yus	Santiago
Asensio	Maria José
Sánchez	Manolo
Manuel Añón	Jose
Manzanares	Jesús
García De Lorenzo	Abelardo
Perales	Eva
Civantos	Belén
Cachafeiro	Lucía
Agrifoglio	Alexander
Estébanez	Belén
Flores	Eva
Hernández	Mónica
Millán	Pablo
Rodríguez	Montserrat
Nanwani	Kapil
Intensive	**Pediatric**
Arizcun	Beatriz
Pérez-Costa	Elena
Rodríguez-Álvarez	Diego
Sánchez-Martín	María

(continued on next page)

Quesada	Úrsula
Román-Hernández	Carmen
Dorao	Paloma
Álvarez-Rojas	Elena
Menéndez	Juan José
Verdú	Cristina
Gómez-Zamora	Ana
Schüffelmann	Cristina
Calderón-Llopis	Belén
Laplaza-González	María
Río-García	Miguel
Amores-Hernández	Irene
Rodríguez-Rubio	Miguel
de la Oliva	Pedro
Department:	**Cardiology**
Ruiz	Jose
Rosillo	Sandra
González	Oscar
Iniesta	Angel
Ponz.	Ines
Department:	**Anesthesiology**
Muñoz Ramón	José María
Hernández Gancedo	María Carmen
Uña Orejón	Rafael
Sanabria Carretero	Pascual
Moreno Gómez-Limón	Isidro
Seiz-Martinez	Alverio
Guasch-Arévalo	Emilia
Martín-Carrasco	Cristina
Alvar	Elena
Serrá	Lucía
Iannuccelli	Fabricio
Latorre	Julieta
Casares	Sandra
Valbuena	Isabel
Díaz Díez Picazo	Luis
Rodríguez Roca	Cristina
Cervera	Omar
García de las Heras	Esteban
Durán	Pilar
Castro	Carmen
Manrique de Lara	Carlos
Veganzones	Javier
López-Tofiño	Araceli
Fernandez-Cerezo	Estefanía
Zurita	Sergio
López-Martinez	Mercedes
Prim	Teresa
Alvárez Del Vayo	Julía
Alcaraz	Gabriela
Castro	Luis
Yagüe	Julio
Díaz-Carrasco	Sofía
González-Pizarro	Patricio
Montero	Ana
Sagra	Francisco Javier
Suárez.	Alejandro
Care	**Palliative**
Díez Porres	Leyre
Varela Cerdeira	María
Alonso Babarro	Alberto
Entry	**Data**
Abellán Martínez	Francisco
Alonso Eiras	Jorge Ignacio
Álvarez Brandt	Alejandra
Archinà	Martina
Arribas Terradillos	Silvia
Baselga Puente	Trinidad
Barco Núñez	Pilar
Barrera López	Natalia Guadalupe
Barrera López	Lorena
Bartrina Tarrio	Andres
Bassani	Gemma
Betancort De la Torre	Paula
Blanco Bartolomé	Irene
Blasco Andres	Celia
Brieba Plata	Lucia
Cadenas Gota	Fernando
Carrera Vázquez	Paloma
Cascajares Sanz	Carlota
Catino	Arianna
Cavallé Pulla	Raquel
Ceniza Pena	Daniel
Conde Alonso	Ylenia María
Currás Sánchez	Laura
Daltro Lage	Marcelo
Esteban Romero	Ana
Fernández Vidal	María Luisa
Ferrer Ortiz	Inés
de la Fuente Regaño	Lydia
Galindo Ballesteros	Pablo
Garcia-Bellido Ruiz	Sara
García-Mochales Fortún	Carlos
Gómez Ballesteros	Teresa
Gómez Domínguez	Cecilia
González Aguado	Nelsa
González García	Sofía
Guisández Martín	Jorge
Hernández Liebo	Paula Alejandra
Hernando Nieto	Raquel
Llorente Cortijo	Irene María
Marín García	Antonio
López Pirez	Pilar
Mejuto Illade	Lucía
Palma	Marco
Peña Hidalgo	Adrian
Platero Dueñas	Lucía
Pujol Pocull	David
Ramírez Verdyguer	Miguel
Redondo Gutierrez	Marta
Reinoso Lozano	Francisco
Rodríguez Revillas	Ana
Rodríguez Saenz de Urturi	Alejandro
Romero Imaz	Lucía
Sánchez Rico	Susana
Sánchez Santiuste	Mónica
Serrano de la Fuente	Patricia
Serrano Martín	Henar
Silva Freire	Thamires
Soria Alcaide	Eva
Suárez Plaza	Andrés Enrique
Tejero Soriano	Beatriz
Torrecillas Mainez	Andrea
Torres Cortés	Javier
Valentín-Pastrana Aguilar	María de Las Mercedes
Villanueva Freije	Angélica
Virgós Varela	Marta
Yagüe Barrado	Marta
Yustas Benitez.	Natalia
Prevention	**Risk**
Núñez	Mª Concepción
Pharmacology	**Clinical**
Montserrat	Jaime
Queiruga	Javier
Rodriguez Mariblanca	Amelia
Martínez de Soto	Lucía
Urroz	Mikel
Seco	Enrique
Zubimendi	Mónica
Stuart	Stephan
Díaz	Lucía
García	Irene
Management:	**Data**
García Morales	María Teresa
Martín-Vega	Alberto
Revision	**Data**
Caro	Abel
Martínez-Alés	Gonzalo

Appendix B

POSTCOVID HULP GROUP

Department	Surname	Name
Medicine	Arnalich Fernández	Francisco
	Fernández Capitán	Carmen
	Salgueiro Origlia	Giorgina
	Moreno Fernández	Alberto
Laboratory	Buño Soto	Antonio
	Qasem Moreno	Ana Laila
	Prieto Arribas	Daniel
Respiratory Medicine	ÁlvarezSala Walther	Rodolfo
	Gómez Carrera	Luis
	Carpio Segura	Carlos
	Mariscal Aguilar	Pablo
	Laorden Escudero	Daniel
	Plaza Moreno	Cristina
	Arnalich Montiel	Victoria
Central Clinical Research Unit	Borobia Pérez	Alberto
	Jiménez González	María
Nursing	Alegre Segura	Carmen
	Cuesta Luzzy	Tania
	Martínez Gómez	Alejandra
	Moreno Juan	Ana María
	Rey Iborra	Cristina
	Sanz Jiménez	Andrea

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