


RESEARCH ARTICLE

Corticosteroids for COVID-19 symptoms and quality of life at 1 year from admission

Ignacio Pérez Catalán¹  | Celia Roig Martí¹ | Daniela Palomo de la Sota¹ | Alejandro Cardenal Álvarez¹ | María José Esteve Gimeno¹ | Sergio Fabra Juana¹ | Germán Herrero Rodríguez¹ | Elena Domínguez Bajo¹ | Nuria Tornador Gaya¹ | Jorge Usó Blasco¹ | Jose Manuel Ramos Rincón²

¹Internal Medicine Service, University General Hospital of Castellon, Castellon, Spain

²Internal Medicine Service, University General Hospital of Alicante, Alicante, Spain

Correspondence

Ignacio Pérez Catalán, Internal Medicine Service, University General Hospital of Castellon (Spain), C/Gobernador, nº 10, 3º piso, puerta 1, Castellón de la Plana (España), Código, Castellon 12003, Spain.
Email: nachocs13@gmail.com

Abstract

The long-term evolution of COVID-19 is unknown, making it necessary to study the persistence of symptoms over time and their impact on quality of life in people who have had the disease. We analyzed these aspects 1 year after admission for COVID-19 and explored the influence of treatment with systemic corticosteroids during the acute phase of the illness. This observational cohort study took place in a tertiary hospital in March and April 2021 and included people admitted due to infection with SARS-CoV-2 in March, April, or May 2020. We excluded patients who had died, were unreachable or had substantial cognitive impairment. A telephone survey was undertaken to assess the presence of symptoms related to COVID-19 and to administer the SF-36 quality of life questionnaire. Other variables collected were demographic and clinical data along with the treatment received and the evolution over time. We analyzed 76 patients, including 44 who did not receive corticosteroids and 32 who did. Most symptoms were less frequent in the group that received corticosteroids, with statistically significant differences for headache, dysphagia, chest pain, and depression. These patients also showed significantly better outcomes in the SF-36 domains for “bodily pain” and “mental health.” Corticosteroids administered in the acute phase of COVID-19 could attenuate the presence of long-term symptoms and improve patients’ quality of life.

KEYWORDS

corticosteroids, COVID-19, long COVID, post-acute COVID-19 syndrome, quality of life, SARS-CoV-2

1 | INTRODUCTION

COVID-19 is a disease produced by the SARS-CoV-2 virus (severe acute respiratory syndrome coronavirus 2), which is responsible for the current pandemic^{1,2} and associated with a wide array of symptoms. About 80% of cases produce mild symptoms like anosmia and ageusia (loss of smell and taste), headache, muscle pain, fever, cough, and diarrhea, among others.^{3,4} In other cases, the virus triggers a

dysregulation of the immune system, which produces an acute respiratory distress syndrome (ARDS) that leads to admission to the intensive care unit (ICU).^{4–6} In this context of systemic hyperinflammation, corticosteroids have been used as nonselective anti-inflammatory agents, demonstrating significant reductions in mortality.⁷

The evolution and long-term sequelae of this emerging disease are still unknown, heightening the need to follow patients over time.

Recent contributions to the medical literature have described diverse clinical scenarios during follow-up, including the persistence of symptoms from the acute phase of illness, the onset of new symptoms in the postinfection period, exacerbation of symptoms that were present before the viral infection, and a wide range of post-COVID-19 sequelae.^{8,9} These situations should be detected to ensure treatment and improve patients' quality of life, which may be impaired following the acute episode. However, the best therapeutic approach and pharmacological management are currently unknown.⁸ In this context, the health professionals participating in this study had the impression, from anecdotal observation, that patients who received corticosteroids during their admission had a better long-term evolution, with fewer symptoms related to the COVID-19 infection.

This study aims to test that hypothesis, analyzing the impact of corticosteroid treatment on the presence of symptoms and quality of life 1 year after initial admission with COVID-19.

2 | MATERIALS AND METHODS

2.1 | Study design and participants

This observational cohort study took place in a tertiary hospital in March and April 2021 and included adults (≥ 18 years) admitted to the infectious diseases ward due to COVID-19 in March, April, or May 2020. Infection with SARS-CoV-2 was confirmed by real-time polymerase chain reaction (RT-PCR) or serology. We excluded patients who had died, were unreachable or had substantial cognitive impairment.

2.2 | Variables

A telephone survey was undertaken to assess the presence of symptoms related to COVID-19 (Annex 1). The questionnaire included items on the most frequently reported symptoms according to patient management guidelines in COVID-19.^{8,9} In their response to questions about whether they had specific symptoms, participants could answer yes or no, and if the symptom was present, specify whether it had appeared after the acute phase. There was also an open question about any other symptoms they had experienced, apart from those mentioned in the interview.

The survey on symptomology was followed by the SF-36 quality of life questionnaire.¹⁰ The SF-36 is a general questionnaire that is quick and straightforward to administer, generating a numerical score that enables assessment and comparison of key health domains (physical functioning, physical role limitations, bodily pain, social functioning, mental health, emotional role limitations, energy/vitality, and general health perceptions) in different populations. For each domain, the SF-36 generates a percentage value that is directly and proportionally related to a better quality of life in that domain. Before the administration of both surveys, the patient gave verbal consent, which is reflected in the data collection file.

In addition, the electronic health record (Orion Clinic program) was reviewed to extract demographic variables (age, sex); length of hospital stay; clinical data (relevant medical history, body mass index [BMI], age-adjusted Charlson comorbidity index, development of mild/moderate/severe acute respiratory distress syndrome); treatment received during admission (lopinavir/ritonavir, hydroxy-chloroquine, tocilizumab, anakinra, systemic corticosteroids); need for noninvasive or invasive mechanical ventilation), and admission to the ICU.

2.3 | Statistical analysis

We used SPSS statistical software (v.23; IBM) for analyses. In the initial descriptive study, quantitative variables were expressed as the mean (95% confidence interval, CI) or median (interquartile range, IQR), depending on the normality of the distribution. Categorical variables were described as absolute and relative frequencies. Statistical comparisons were undertaken, using the χ^2 test for categorical variables and the Student *t*-test or Mann-Whitney *U* test, as appropriate, to compare categorical with quantitative variables.

Our center's clinical research ethics committee approved the study. Patient confidentiality was preserved, and the performance of the study complied with the principles of the Declaration of Helsinki (2013) and good clinical practice rules.

3 | RESULTS

A total of 124 patients were admitted for COVID-19 during the study period. We excluded 48 of these from the study (24 died, 13 presented significant cognitive impairment, and 11 were unreachable), for a final sample of 76 people, 32 of whom received corticosteroids and 44 of whom did not. Table 1 details their clinical-epidemiological characteristics, comorbidities, treatment, and evolution, according to whether they received corticosteroids. The groups were largely similar across different variables, although the steroids group presented a larger proportion of men (75.0% vs. 52.3%, $p = 0.004$) and people with hypertension (71.9% vs. 40.9%, $p = 0.007$).

Regarding the complications experienced over the first year of follow-up, two patients—neither of whom received corticosteroids—were readmitted, one for stroke and the other for a urinary tract infection. The most frequently reported symptoms at 1 year of infection were forgetfulness (45.5% in patients that did not receive corticosteroid treatment vs. 43.8% in those who did), followed by asthenia (43.2% and 34.4% in the respective groups) and arthromyalgia (38.6% and 37.5%).

Patients who had received steroids presented significantly less headache, dysphagia, chest pain, and depression at 1 year. The rest of the symptoms also tended to appear less frequently in this group, with the exception of the loss of taste/smell, odynophagia, diarrhea, and alopecia. The steroids group also presented a lower number of symptoms (median 2, IQR 1–4) compared to the non-steroids group

TABLE 1 Participant characteristics at 1 year from admission for COVID-19, according to the administration of corticosteroids

Variables	No steroids (N = 44)	Steroids (N = 32)	p
Men, n (%)	33 (52.3%)	24 (75.0%)	0.004
Age, median (IQR), years	61.5 (52.7–72.5)	68.5 (60.2–75.7)	0.53
Charlson comorbidity index, median (IQR)	2 (1–3)	3 (2–4)	0.70
BMI, median (IQR), (kg/m ²)	29.5 (25.8–31.8)	28 (26.3–30.2)	0.59
Length of hospital stay, median (IQR), days	12 (8.2–20.7)	21 (16–25)	0.86
Comorbidities, n (%)			
Tobacco use			
Ex-smoker	7 (15.9%)	5 (15.6)	0.21
Current smoker	4 (9.1%)	0	
Hypertension	18 (40.9%)	23 (71.9%)	0.007
Dyslipidaemia	18 (40.9%)	12 (37.5%)	0.76
Atrial fibrillation	2 (84.5%)	1 (3.1%)	0.75
COPD	1 (2.3%)	0	0.39
Chronic bronchitis	1 (2.3%)	0	0.39
Asthma	2 (4.5%)	0	0.22
Diabetes mellitus without target organ damage	4 (9.1%)	4 (12.5%)	0.63
Diabetes mellitus with target organ damage	2 (4.5%)	2 (6.3%)	0.74
Obesity	17 (38.6%)	11 (34.4%)	0.70
Anxiety	3 (6.8%)	1 (3.1%)	0.48
Depression	2 (4.5%)	1 (3.1%)	0.75
Development of acute respiratory distress syndrome, n (%)			
Mild	1 (2.3%)	2 (6.3%)	
Moderate	1 (2.3%)	2 (6.3%)	0.10
Severe	8 (18.2%)	12 (37.5%)	
Treatment received, n (%)			
Lopinavir/ritonavir	31 (70.5%)	25 (78.1%)	0.45
Hydroxychloroquine	39 (88.6%)	30 (93.8%)	0.45
Tocilizumab	1 (2.3%)	1 (3.1%)	0.82
Anakinra	0	0	-
Need for ventilation and admission to ICU, n (%)			
Noninvasive mechanical ventilation	4 (9.1%)	7 (21.9%)	0.12
Invasive mechanical ventilation	7 (15.9%)	5 (15.6%)	0.97
ICU admission	7 (15.9%)	6 (18.8%)	0.95

Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; ICU, intensive care unit; IQR, interquartile range.

(median 3, IQR 1–6), although this difference was not significant ($p = 0.25$). These results are presented in full in Table 2 and Figure 1. Symptoms were seldom described as new in either group (Table 2), and just eight people (10.5%) reported having no symptoms at the time of the interview.

Regarding the quality of life, Table 3 presents the median scores (IQR) for each domain of the SF-36 in the steroids and non-steroid group. The steroids group had better median scores than the non-steroids group in four of the eight domains: bodily pain (100%, IQR 72.5%–100% vs. 75%, IQR 57%–100%; $p = 0.017$); general health perceptions (72.5%, IQR 55%–80%) versus 67.5%, IQR 40%–78.7%; $p = 0.265$); energy/vitality (80%, IQR 56.2%–85% vs. 62.5%, IQR 40%–85%; $p = 0.120$); and mental health (86%, IQR 69%–92% vs. 76%, IQR 54%–88%; $p = 0.027$). The median score was the same in both groups for the domains of physical role limitations, social functioning, and emotional role limitations (100%), although the IQRs were slightly better in the steroids group. In the remaining domain, physical functioning, median scores were comparable in people who received steroids (92.5%, IQR 75%–92.5%) and those who did not (95%, IQR 46.2%–100%; $p = 0.81$).

4 | DISCUSSION

Our results suggest that patients who receive corticosteroids during their admission for COVID-19 are less likely to experience persistent symptoms and more likely to have a better quality of life at 1 year of admission.

The long-term persistence of COVID-19 symptoms is currently among the topics attracting the most scientific interest. However, our exhaustive literature search yielded few publications analyzing this aspect in patients who were admitted for this disease, and the studies that do exist are heterogeneous, have a limited follow-up, and do not examine the association with corticosteroids—the only treatment that has been proven to increase survival in the short term and whose use has been widely adopted globally.⁷

Chopra et al. performed telephone interviews in 488 patients in Michigan (USA) 60 days after their admission due to COVID-19, and 32.6% reported persistent symptoms, including 18.9% who described new and sometimes worsening symptoms.¹¹ The most common were dyspnea, cough, and the persisting loss of smell and taste. In Wuhan (China), Wang et al. assessed 131 patients (52.6% with severe pneumonia) weekly for 1 month after discharge. On returning home, 40.4% had symptoms (especially cough, dyspnea, and expectoration), but at four weeks these persisted in just 9.1%, with no relation to the severity of the acute illness.¹²

As for European studies, Halpin et al. (UK) analyzed 100 patients (nearly a third of whom had been admitted to the ICU) at 48 days from discharge; 72% reported fatigue; 65.6%, dyspnea; and 46.9%, anxiety.¹³ In Italy, Carfi et al. reported similar results in 143 patients admitted for COVID-19 and interviewed at 60 days from symptoms onset. Fatigue (53.1%), dyspnea (43.4%), arthralgia (37.3%), and chest pain (21.7%) were the most frequently reported symptoms.¹⁴

Symptoms	Presence of symptoms, n (%)		p	Onset of symptoms following acute phase, n (%)		
	No steroids (N = 44)	Steroids (N = 32)		No steroids	Steroids	p
Forgetfulness	20 (45.5%)	14 (43.8%)	0.88	8 (18.2%)	8 (25%)	0.47
Asthenia	19 (43.2%)	11 (34.4%)	0.44	4 (9.1%)	1 (3.1%)	0.30
Arthromyalgia	17 (38.6%)	12 (37.5%)	0.92	2 (4.5%)	2 (6.3%)	0.74
Dyspnea	13 (29.5%)	6 (18.8%)	0.28	4 (9.1%)	0	0.080
Anxiety	12 (27.3%)	5 (15.6%)	0.23	2 (4.5%)	3 (9.4%)	0.40
Headache	11 (25%)	2 (6.3%)	0.032	4 (9.1%)	1 (3.1%)	0.30
Depression	10 (22.7%)	1 (3.1%)	0.016	3 (6.8%)	1 (3.1%)	0.48
Arthritis	10 (22.7%)	2 (6.3%)	0.052	4 (9.1%)	1 (3.1%)	0.30
Cough	10 (22.7%)	5 (15.6%)	0.44	0	1 (3.1%)	0.24
Rhinorrhoea	9 (20.5%)	6 (18.8%)	0.85	5 (11.4%)	5 (15.6%)	0.59
Hypoacusis	9 (20.5%)	3 (9.4%)	0.19	4 (9.1%)	1 (3.1%)	0.30
Alopecia	8 (18.2%)	6 (18.8%)	0.95	1 (2.3%)	2 (6.3%)	0.38
Dysphagia	5 (11.4%)	0	0.049	2 (4.5%)	0	0.22
Chest pain	5 (11.4%)	0	0.049	2 (4.5%)	0	0.22
Anosmia	5 (11.4%)	6 (18.8%)	0.37	0	1 (3.6%)	0.24
Ageusia	5 (11.4%)	4 (12.5%)	0.88	1 (2.3%)	0	0.39
Odynophagia	1 (2.3%)	1 (3.1%)	0.82	0	0	-
Diarrhea	1 (2.3%)	3 (9.4%)	0.17	0	0	-
Fever	0	0	-	0	0	-
N symptoms, median (IQR)	3 (1-6)	2 (1-4)	0.25			

Abbreviation: IQR, interquartile range.

Moreover, 55% reported having at least three symptoms, and 44.1% saw their quality of life decline, according to the EuroQoL visual analog scale.

In our country, Moreno-Pérez et al. (Alicante) assessed symptoms persistence face-to-face at 2-3 months of infection in 277 people, not all of whom required hospitalization; their median age was 56 years, and 8.7% were admitted to the ICU.¹⁵ In line with the literature, the most frequently reported symptoms were fatigue (34.8%), dyspnoea (34.4%), loss of taste/smell (21.4%), and cough (21.3%).

All of these studies have a quite limited follow-up compared to our study, which could explain the predominance of respiratory symptoms, as the SARS-CoV-2 pneumonia was still quite recent. The most prominent symptoms in our patients had a different nature and included forgetfulness, asthenia, and arthromyalgia.

Treatment with corticosteroids during admission for COVID-19 seemed to have a positive influence in practically all aspects of both symptoms and quality of life at 1 year. This tendency is clear, and the fact that statistically significant differences were not observed may be due in part to the small sample size. Furthermore, regarding the

TABLE 2 Presence of symptoms at one year, according to administration of corticosteroids during admission for COVID-19

SF-36 quality of life survey, if we analyze the distribution of the data and the IQRs in addition to the median scores, better scores can be inferred in the steroids group for all eight domains.

One possible explanation for these results could be that the symptoms or sequelae following the viral infection are consequences of the organ and tissue damage caused by the intense inflammation during the acute phase of the illness. By lessening that inflammation, its consequences would also be attenuated.

The strengths of this study reside in the direct form of collecting data on symptoms at 1 year, via a personal interview that specifically asked about each symptom and allowed participants to volunteer others. Moreover, our exhaustive literature search did not show any studies with such a long follow-up in patients who had been admitted for COVID-19 or studies that assessed the long-term impact of treatment with corticosteroids.

In contrast, limitations include its small sample size, the performance of non-parametric statistical analyses due to the non-normal distribution of the variables (as also occurs in the cited literature), and the lack of a control group.

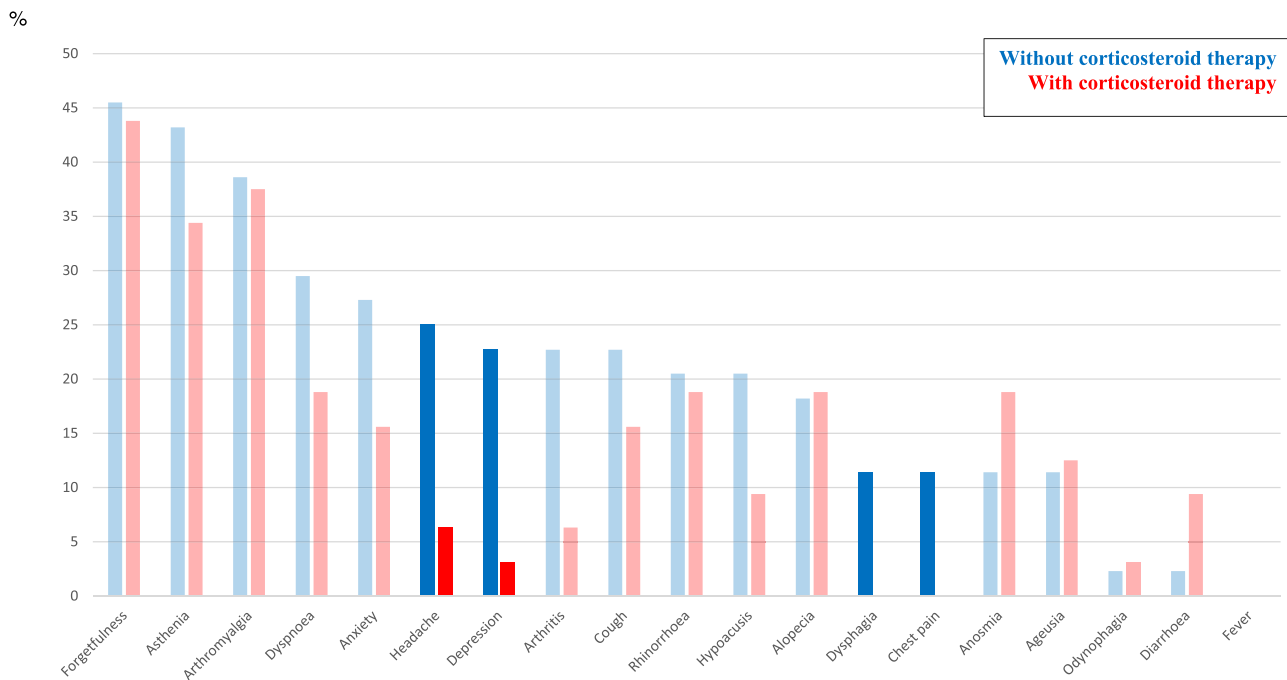


FIGURE 1 Presence of symptoms at one year from admission for COVID-19, according to administration of corticosteroids

TABLE 3 Results of SF-36 quality of life surveys at 1 year, according to administration of corticosteroids during admission for COVID-19

SF-36 domain (%), median, (IQR)	No steroids (N = 44)	Steroids (n = 32)	p
Physical functioning	95 (46.2–100)	92.5 (75–92.5)	0.81
Physical role limitations	100 (31.2–100)	100 (100–100)	0.30
Bodily pain	75 (57–100)	100 (72.5–100)	0.017
General health perceptions	67.5 (40–78.7)	72.5 (55–80)	0.27
Energy/vitality	62.5 (40–85)	80 (56.2–85)	0.12
Social functioning	100 (75–100)	100 (87.5–100)	0.100
Emotional role limitations	100 (100–100)	100 (100–100)	0.23
Mental health	76 (54–88)	86 (69–92)	0.027

Abbreviation: IQR, interquartile range.

Overall, our results suggest that treatment with corticosteroids in patients hospitalized for COVID-19 not only improves the short-term prognosis; it also attenuates the presence of symptoms and improves the quality of life in the long term. More studies are necessary to confirm or reject this hypothesis.

ACKNOWLEDGMENTS

We are grateful to the professionals in the Internal Medicine Service and the Infectious Diseases Unit at the Castellón General University

Hospital for their invaluable cooperation during the performance of the study, without which it would not have been possible. We also express our thanks to Meggan Harris for her assistance in editing.

CONFLICT OF INTERESTS

The authors declare that they have no conflict of interest.

AUTHOR CONTRIBUTIONS

Ignacio Pérez Catalán: conception and design of the study, writing of the manuscript, bibliographic search, data collection and analysis, and interpretation of data. Celia Roig Martí: conception and design of the study, writing of the manuscript, bibliographic search, data collection and analysis and interpretation of data. Daniela Palomo de la Sota: data collection and bibliographic search. Alejandro Cardenal Álvarez: data collection and bibliographic search. María José Esteve Gimeno: data collection and bibliographic search. Sergio Fabra Juana: data collection and bibliographic search. Germán Herrero Rodríguez: data collection and bibliographic search. Elena Domínguez Bajo: data collection and bibliographic search. Nuria Tornador Gaya: conception and design of the study. Jorge Usó Blasco: conception and design of the study. Jose Manuel Ramos Rincón: conception and design of the study, writing of the manuscript, bibliographic search and analysis and interpretation of data.

DATA AVAILABILITY STATEMENT

Author elects to not share data.

ORCID

Ignacio Pérez Catalán  <http://orcid.org/0000-0002-2146-378X>

REFERENCES

1. Ministerio de Sanidad. consumo y bienestar social; 2021. Accessed April 27, 2021. <https://www.msbs.gob.es/profesionales/saludPublica/ccayes/alertasActual/nCov/situacionActual.html>
2. Johns Hopkins Coronavirus Resource Center. Accessed April 27, 2021. <https://coronavirus.jhu.edu/map.html>
3. Menni C, Valdes AM, Freidin MB, et al. Real-time tracking of self-reported symptoms to predict potential COVID-19. *Nat Med.* 2020; 26(7):1037-1040. <https://doi.org/10.1038/s41591-020-0916-2>
4. Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall RS, Manson JJ, HLH Across Speciality Collaboration, UK. COVID-19: consider cytokine storm syndromes and immunosuppression. *Lancet.* 2020;395(10229):1033-1034. [https://doi.org/10.1016/S0140-6736\(20\)30628-0](https://doi.org/10.1016/S0140-6736(20)30628-0)
5. Wiersinga WJ, Rhodes A, Cheng AC, Peacock SJ, Prescott HC. Pathophysiology, transmission, diagnosis, and treatment of coronavirus disease 2019 (COVID-19): a review. *JAMA.* 2020;324(8):782-793. <https://doi.org/10.1001/jama.2020.12839>
6. Garcia-Vidal C, Moreno-García E, Hernández-Meneses M, et al. Personalized therapy approach for hospitalized patients with COVID-19. *Clin Infect Dis.* 2020:ciaa964. <https://doi.org/10.1093/cid/ciaa964>
7. Horby P, Lim WS, et al, RECOVERY Collaborative Group. Dexamethasone in hospitalized patients with Covid-19. *N Engl J Med.* 2021;384(8):693-704. <https://doi.org/10.1056/NEJMoa2021436>
8. COVID-19 rapid guideline: managing the long-term effects of COVID-19. London: National Institute for Health and Care Excellence (UK); 2020.
9. Brito-Zerón P, Conangla L, Kostov B, et al. Manifestaciones persistentes de la COVID-19. Guía de práctica clínica [Internet]. 1st ed. Barcelona: Sociedad Catalana de Medicina Familiar i Comunitària (CAMFIC), 2020. 1-43. Accessed April 27, 2021. <https://www.semfyec.es/formacion-y-recursos/manifestaciones-persistentes-de-la-covid-19-guia-de-practica-clinica/>
10. Ware JE Jr., Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care.* 1992;30:473-483.
11. Chopra V, Flanders SA, O'Malley M, Malani AN, Prescott HC. Sixty-day outcomes among patients hospitalized with COVID-19. *Ann Intern Med.* 2021;174(4):576-578. <https://doi.org/10.7326/M20-5661>
12. Wang X, Xu H, Jiang H, et al. Clinical features and outcomes of discharged coronavirus disease 2019 patients: a prospective cohort study. *QJM.* 2020;113(9):657-665. <https://doi.org/10.1093/qjmed/hcaa178>
13. Halpin SJ, McIvor C, Whyatt G, et al. Postdischarge symptoms and rehabilitation needs in survivors of COVID-19 infection: a cross-sectional evaluation. *J Med Virol.* 2021;93(2):1013-1022. <https://doi.org/10.1002/jmv.26368>
14. Carfi A, Bernabei R, Landi F, Gemelli against COVID-19 Post-Acute Care Study Group. Persistent symptoms in patients after acute COVID-19. *JAMA.* 2020;324(6):603-605. <https://doi.org/10.1001/jama.2020.12603>
15. Moreno-Pérez O, Merino E, Leon-Ramirez JM, et al, COVID19-ALC research group. Post-acute COVID-19 syndrome. Incidence and risk factors: a Mediterranean cohort study. *J Infect.* 2021;82(3):378-383. <https://doi.org/10.1016/j.jinf.2021.01.004>

SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

How to cite this article: Catalán IP, Martí CR, Sota DPdl, et al. Corticosteroids for COVID-19 symptoms and quality of life at 1 year from admission *J Med Virol.* 2022;94:205-210. <https://doi.org/10.1002/jmv.27296>