

BRIEF REPORT

Risk factors for later hospitalization of patients discharged from an emergency department with non-severe COVID-19 symptoms

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Objectives. To describe the clinical course of patients discharged from the emergency department (ED) with nonsevere coronavirus disease 2019 (COVID-19) and explore possible risk factors for later hospitalization.

Methods. Patients with nonsevere COVID-19 who were discharged from the ED were included prospectively. We explored risk factors for hospitalization after discharge.

Results. Seventy-four patients were included; 17 (23%) were hospitalized after discharge. Three (4%) of the 17 patients died. Age, lymphopenia, a high Charlson Comorbidity Index, and a shorter delay between the onset of symptoms and the first visit to the ED were associated with hospitalization afterwards, although on multivariate analysis only time less than 6 days between symptom onset and the first ED visit was associated with later hospitalization (odds ratio, 4.62; 95% CI, 1.08–19.7).

Conclusion. More than 20% of ED patients with nonsevere COVID-19 require hospitalization later.

Keywords: COVID-19. Emergency department. Observation. Hospitalization.

Factores de riesgo de rehospitalización en pacientes con COVID-19 leve tras el alta desde el servicio de urgencias

Objetivo. Describir la evolución clínica de pacientes con COVID-19 leve tras el alta de urgencias y analizar los posibles factores de riesgo para una posterior hospitalización.

Método. Pacientes con COVID-19 leve dados de alta desde urgencias fueron prospectivamente incluidos. Los factores de riesgo de hospitalización fueron evaluados.

Resultados. Se incluyeron 74 pacientes y 17 (23%) requirieron hospitalización, de los cuales 3 (4%) fallecieron. La edad, la linfopenia, un mayor índice Charlson y un menor tiempo desde el inicio de los síntomas hasta la primera consulta a urgencias se asociaron a hospitalización, aunque en el análisis multivariado únicamente un tiempo desde el inicio de síntomas a la consulta a urgencias < 6 días se asoció a hospitalización (OR: 4,62; IC 95%: 1,08-19,7).

Conclusiones. Más del 20% de pacientes con COVID-19 leve dados de alta desde urgencias requiere hospitalización.

Palabras clave: COVID-19. Urgencias. Vigilancia. Rehospitalización.

Introduction

SARS-CoV-2 (COVID-19) disease comprises a wide range of clinical manifestations. Risk factors of death and admission to the intensive care unit (ICU) have been previously described¹, but the outcome of the mild disease is more unknown. At our hospital, at the beginning of the pandemic, a telephone surveillance service was established for patients with mild COVID-19 discharged from the emergency department (ED). The objectives of this study are: 1) to describe the clinical evolution of a cohort of patients with mild COVID-19 discharged from the ED and 2) to analyze possible predictors of re-hospitalization.

Method

This is a prospective cohort study that included patients with confirmed COVID-19 and respiratory symp-

toms discharged from the ED from March 16 to April 5, 2020. The center's ethics committee approved the study and consent was obtained from all participants. A confirmed case was considered when there was a positive real-time polymerase chain reaction (PCR) result for SARS-CoV-2 from respiratory samples. Patients were discharged if they had mild respiratory tract infection or low-risk pneumonia with low comorbidity (Charlson index < 4) and no immunosuppression. Low-risk pneumonia was defined as the presence of infiltrates or consolidations on plain chest radiography in the absence of severe COVID-19 criteria¹: peripheral oxygen saturation (measured by pulse oximetry -SpO₂-) 93%, respiratory rate (RR) < 30/min, and a PAFI index (ratio of oxygen blood pressure to inspired oxygen fraction -PaO₂/ FIO₂-) > 300. Demographic data, pathologic history, clinical findings (including SpO₂, RR, PAFI), laboratory values (including leukocyte count and formula, lactate dehydrogenase, dimer, and C-reactive protein), radiologic findings, and ED length of stay were recorded for all patients.

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Table 1. Single checklist used in the telephone follow-up of patients with mild COVID-19 treated and discharged from the emergency department

• How are you doing compared to yesterday? Same/Better/Worse
• Have you had fever? Yes/No
• In case of fever, what was the highest body temperature reached?
• How many days have you had fever?
• Have you had a cough? Yes/No
• Do you have difficulty breathing? Yes/No
• Have you had vomiting or diarrhea? Yes/No
• Any other symptoms? Yes/No

Regarding the telephone monitoring service, three doctors (AH, AN and LBP) were in charge of making the telephone calls. The protocol included a single questionnaire, as a checklist, that investigated the presence of fever, respiratory symptoms and other symptoms (Table 1). A daily telephone call was made to the patient during the first 7 days and on the 10th and 14th days from the onset of symptoms. In case of persistence of symptoms, the telephone monitoring service was extended for as long as necessary. In case of worsening of symptoms or presence of signs suggesting aggravation of the disease, patients were recommended to visit the emergency department again.

The quantitative variables were expressed as mean and standard deviation (SD) or as median and interquartile range (IQR). Qualitative variables were expressed as frequencies and percentages. The differences between patients who required or did not require re-hospitalization were calculated with the Student T test, the Mann-Whitney test or the Fisher exact test, de-

pending on the case. Multiple logistic analysis was performed with those variables that showed statistical significance in the bivariate analysis, after categorization of the continuous variables. SPSS software version 19.0 for Windows (IBM, Armonk, New York, USA) was used.

Results

From March 16 to April 5, 687 patients with confirmed diagnosis of COVID-19 were treated in the ED: 570 were admitted and 117 were discharged. Of these 117 patients, 43 did not meet inclusion criteria and 74 eventually made up the study population. At discharge, only symptomatic treatment was prescribed in 30 patients and the rest were also treated with amoxicillin (A), azithromycin (AZ) and/or hydroxychloroquine (H) in a single regimen (10 patients A, 9 AZ) or in combination (3 patients A/AZ, 11 H/AZ). Of the 74 patients included, after an average of 3 days from discharge and 7 days from the onset of symptoms, 19 (26%) consulted the emergency department again (5 on their own initiative and 14 on the advice of the physician who was monitoring by telephone) and 17 (23%) required admission. Of these, 3 (4%) required admission to the ICU and died (all 3 cases from acute respiratory failure refractory to treatment, which in one case was associated with stroke of the left internal cerebral artery). No patient was lost to follow-up. Table 2 shows the clinical characteristics of all patients, as well as the differences between those who required re-hospitalization and those who did not: the former were older, had more

Table 2. Demographic data and clinical characteristics of the study population in general and separated by groups according to whether or not re-hospitalization was required

Variable	Patients discharged from the ED (N = 74) n (%)	Required rehospitalization (N = 17) n (%)	Did not require rehospitalization (N = 57) n (%)	P
General characteristics				
Age (years) [mean (SD)]	54.6 (14.2)	65.5 (11.1)	51.4 (13.4)	< 0.001
Sex (men)	35 (47.3)	9 (25.7)	26 (45.6)	0.783
Time since symptom onset (days) [median (IQR)]	6 (3-8)	4 (3-6)	7 (3-9)	0.002
Time in the emergency department (hours) [median (IQR)]	19 (7-41)	13 (8-22)	22 (7-45)	0.171
Charlson Index (units) [median (IQR)]	1 (0-3)	2 (2-4)	1 (0-2)	< 0.001
Respiratory parameters				
SpO ₂ (%) [median (SD)] Respiratory parameters	96.4 (2.1)	95.7 (1.4)	96.6 (2.2)	0.102
Respiratory frequency (respirations per minute) [median (IQR)]	18 (16-24)	18 (16-22)	18 (16-24)	0.342
PAO ₂ /FIO ₂ ratio (kPa) [median (SD)]	400.3 (72.7)	373 (75)	407 (71)	0.145
Presence of infiltrates on chest radiograph	41 (55)	6 (35.3)	35 (61.4)	0.094
Laboratory parameters				
Hemoglobin (g/L) [mean (SD)]	13.9 (17)	13.7 (1.7)	14.0 (1.7)	0.545
Erythrocyte volume (%) [mean (SD)]	12.9 (12.3-13.8)	13.4 (12.6-14.1)	12.8 (12.3-13.6)	0.137
Leukocyte count (x 10 ⁹ /L) [mean (SD)]	5.9 (2.5)	5.9 (3.2)	5.9 (2.4)	0.984
Lymphocyte count (x 10 ⁹ /L) [mean (SD)]	1.2 (0.6)	1.0 (0.3)	1.3 (0.6)	0.008
Lymphopenia (< 1 x 10 ⁹ /L)	30 (40.5)	11 (64.7)	19 (33.3)	0.027
Neutrophil/lymphocyte index [mean (SD)]	4.1 (3.1)	5.2 (4.7)	3.8 (2.4)	0.100
Plasma urea (mg/dL) [mean (SD)]	31.7 (13.1)	31.1 (9.8)	31.9 (14.0)	0.825
Plasma C-reactive protein (mg/L) [median (IQR)]	30 (11-55)	31 (13-50)	26 (9-56)	0.537
D-dimer (ng/mL) [median (IQR)]	366 (261-664)	310 (270-528)	403 (256-681)	0.439
Plasma lactate dehydrogenase (mg/L) [mean (SD)]	238 (50)	227 (40)	241 (52)	0.554

SD: standard deviation; IQR: interquartile range.

Table 3. Multivariate analysis and odds ratio [odds ratio (OR)] and 95% confidence interval (95% CI) of the predictor variables of rehospitalization

Variable	OR	95% CI	p
Age > 60 years	3.51	0.47-26.3	0.220
Charlson index ≥ 2	2.86	0.31-26.2	0.353
Time from symptom onset to first ED visit < 6 days	4.62	1.08-19.7	0.039
Lymphopenia ($< 1 \times 10^9/L$)	1.69	0.41-7.03	0.469

comorbidities (evaluated according to the Charlson index), had less time from the onset of symptoms and the first ED visit, and had more lymphopenia. In the multivariate analysis, only a time from symptom onset to ED visit of less than 6 days obtained statistical significance as a prognostic factor for re-hospitalization (OR: 4.62; 95% CI: 1.0819.7; P = 0.039).

Discussion

In our series 1 out of 5 patients with mild COVID-19 discharged from the emergency department required hospitalization and 4% died. Patients who consulted within 6 days of the onset of symptoms had a higher rate of hospitalization. These data suggest that the persistence of mild symptoms in the second week of the disease could predict a benign outcome. Considering the high percentage of admissions, postal surveillance programs should be included in the protocols for the care of COVID-19 patients, not only for patients discharged from conventional hospitalization, but also from the emergency department.

Hospitalization and death rates for COVID-19 vary from country to country. In a series that included over 47,000 cases in New York State, they were 13% and 2%², respectively. In Spain, according to data from the National Network of Epidemiological Surveillance (RENAVE)³, more than half (53%) of patients required hospitalization with a death rate of 8.2%. In our study, 85.7% of patients were admitted, a very high figure, even more considering that it was carried out during the first weeks of the pandemic, when the management of the mild patient was less conservative. In a situation of hospital collapse, it is essential to optimize admissions through risk stratification. Unfortunately, little is known about the course of the disease when it presents mild symptoms. During the epidemic in China, many patients with mild COVID-19 were admitted to field hospitals, more for epidemiological (infection control) purposes than as a medical indication. Wang et al.⁴ described their experience in one such hospital. In their study, in a population of 1,012 patients very similar to our cohort, about 10% of cases presented clinical worsening requiring referral to a referral hospital. Our rate of worsening was even higher and highlights the need to establish surveillance systems in this type of patients. Telephone call monitoring programs have the

advantage of economizing on human resources and avoiding contagion compared to face-to-face home visits. However, they have the disadvantage of depending on the subjectivity of the patient when referring symptoms. From our experience we have learned that COVID-19 patients, in comparison with other pathologies, present greater tolerance to hypoxemia. Providing patients with portable pulse oximeters could be an alternative to this problem.

COVID-19 is considered to develop in two phases: a first phase, during the first week since the beginning of the symptoms, which corresponds to the viral replication phase, and a second phase, from the second week on, where prothrombotic and inflammatory phenomena may appear and where the disease may worsen. This hypothetical model of the disease course has been validated in patients with moderate and severe COVID-19 by Zhou et al.¹. These authors described a series of 191 patients admitted and reported that most of the severe complications occurred during the second week since the beginning of the symptoms. According to RENAVE3 data, in Spain the median number of days from the onset of symptoms to hospital admission is 6 days (IQR 39) and 9 days (IQR 612) for ICU admission. Our study confirms this theoretical model in mild disease, as most patients worsened during the second week from the onset of symptoms.

In summary, a high proportion of patients with mild COVID-19 who are discharged from the emergency department become clinically worse and have to be admitted later, especially those who consulted the emergency department in the first week after the onset of symptoms. Telemonitoring systems in patients with COVID-19 discharged from the ED are useful regardless of the severity of symptoms and should be part of the action protocols of the centers.

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