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ORIGINAL RESEARCH

Factors associated with readmission to the Emergency Department in a cohort of COVID-19 hospitalized patients

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Abstract

Introduction: The aim of this study was to describe the symptomatology and main factors associated with readmission to the Emergency Department (ED) in COVID-19 patients discharged from hospital during the first wave of the pandemic at the San Cecilio University Hospital, Granada, Spain.

Methods: An observational longitudinal study was conducted in a cohort of 441 patients admitted to our hospital with confirmed SARS-CoV-2 polymerase chain reaction (PCR) from 1 March to 15 April 2020. Patients were followed up through medical records 6 months after discharge. Sociodemographic, clinical and symptomatologic variables were collected. Descriptive, bivariate and multivariate logistic regression analyses were performed.

Results: The mean age of patients in the cohort was 66.4 years (s = 15.3), with 55.1% men. In-hospital mortality was 18.1%. The presence of persistent symptomatology was high (64.5%), especially respiratory (53.2%), systemic (46.3%) and neurological (31.0%). A total of 75 (20.8%) patients were readmitted to the ED during the 6 months following hospital discharge. The main factors associated with readmission to the ED were polymedication ($P = 0.031$), living in a care home ($P = 0.014$), fever ($P = 0.047$), general malaise ($P < 0.001$), thoracic pain ($P < 0.001$), headache ($P = 0.012$), hematological symptoms ($P = 0.011$), nephrological symptoms ($P = 0.047$), depressive symptoms ($P = 0.009$), syncope or hypotension ($P = 0.006$) and superinfection ($P = 0.018$). After multivariate adjustment analysis, thoracic pain (OR: 4.45, 95% CI: 1.88–10.52), general malaise and hematological symptoms (OR: 3.95, 95% CI: 1.12–13.89) remained as risk factors.

Conclusions: The presence of persistent symptomatology after hospital discharge in our cohort was common and varied. Polymedication and living in a care home made up the most vulnerable profile of COVID-19 patients for returning to the ED. Thoracic pain, general malaise and hematological symptoms were identified as potential markers of severity, along with others predictors. These findings might be useful for optimizing follow-up strategies. Future studies conducted in other geographical areas are necessary to corroborate our results.

Keywords

COVID-19; Symptoms; Emergency; Hospitalization; Post-discharge

1. Introduction

Since the identification of the first cases of COVID-19 [1–3], the rapid spread of the virus led to great efforts to identify the main prognostic factors of the disease and optimize preventive and therapeutic strategies during the pandemic. Rapid human-to-human transmission [2] along with high initial mortality and hospitalization rates [4] generated great concern and led to the development of unprecedented sanitary and economic measures worldwide. Older age and previous severe diseases have been reported to be the main prognostic factors, making up the most vulnerable population profile which is especially frequent in care homes [4]. Hypertension, diabetes mellitus, stroke or chronic lung disease represented the most frequent comorbidities of severe cases during the first wave of the pandemic [5].

The identification of factors associated with negative outcomes (e.g., in-hospital mortality, admission to Intensive Care

Unit (ICU), sequelae, readmission to emergency care services, hospitalization or post-discharge death) is emerging as a specific field of research aim at individualizing follow-up strategies in these patients [6]. However, to date there is a lack of scientific literature on patient outcomes after discharge. Preventive strategies focused on reducing these outcomes should be based on follow-up studies. Apart from the most commonly known prognostic factors (age and comorbidities), recognizing less frequent risk factors is still needed [7], especially if they are modifiable and, consequently, preventable. Treatment-related factors are also becoming a major field of ongoing research to improve patient management [8].

Emergency Departments in Spain have played an important role in the early identification of severe COVID-19 cases, although in times of great healthcare pressure they have been overloaded [4, 8]. Identification of factors that may predict readmission to emergency care settings could help improve the follow-up of these patients in Primary Care services and the criteria for hospital discharge. For instance, sequelae or persistent symptomatology, also known as post-discharge syndrome [9], could help identify these recurrent cases. Several studies point to the presence of specific symptoms in the short to medium term, including neurological [10–12], cardiovascular [13, 14] or thrombotic [15] sequelae, which were described in the first follow-up studies. Nonetheless, the number of studies with longer follow-up periods is very low. In fact, to the best of our knowledge, only one study conducted in China has completed a 6-month follow-up to date [16]. In Spain, no studies analyzing long-term symptomatology following hospital discharge in COVID-19 patients have been conducted so far.

The aim of this study was twofold: to describe the symptomatology of COVID-19 patients after hospital discharge in our institution; and to analyze the factors (including symptoms) associated with readmission to the ED during the 6 months following discharge.

2. Materials and methods

2.1 Design and setting

This is an observational longitudinal retrospective study, conducted in a cohort of 441 patients who required hospitalization due to COVID-19 in the San Cecilio University Hospital (Granada, Spain) during the first wave of the pandemic, from 1 March to 15 April 2020. According to the inclusion criteria, only patients with confirmed positive polymerase chain reaction (PCR) to SARS-CoV-2 were considered in the study. The sample was followed up for 6 months from the date of discharge, thus follow-up finished on 10 January 2021.

2.2 Data source and variables

Information was collected from medical records of hospitalization and follow-up reports from Primary Care institutions during the 6 months following hospital discharge. All data were gathered by the same researcher (AR-D) to avoid heterogeneity of information and reviewed by two experienced researchers (MR-I and AC-C). The variables considered for the analyses were:
- Sociodemographic variables: sex, age, residence, dependence in activities of daily living.
- Clinical variables: comorbidities, laboratory workup, prognostic scores (CURB-65), treatment received, in-hospital mortality.
- Post-discharge symptomatology: information on symptoms during the 6 months after discharge were collected by means of periodic telephone consultations in Primary Care centers. These symptoms were classified into the following categories:
  - Systemic symptoms: fever, asthenia, muscle weakness, musculoskeletal pain, general malaise.
  - Respiratory symptoms: dyspnea, rib pain, thoracic pain, persistent cough, pharyngeal symptoms.
  - Neurological symptoms: polyneuropathy, headache, sensitivity disorders, movement disorders, confusion, persistent anosmia or dysgeusia.
  - Mental health symptoms: depressive, anxiety or sleep disorders.
  - Hematological symptoms: anemia, thrombotic disorders.
  - Dermatological symptoms: eczema, exanthema, pruritus, alopecia.
  - Nephrological symptoms: renal failure.
  - Urological symptoms: voiding syndrome.
  - Ophthalmologic symptoms.
  - Digestive symptoms: nausea, vomiting, diarrhea, constipation, anorexia, abdominal pain.
  - Syncope or hypotension.
  - Infectious symptoms: superinfections.
- Outcome: readmission to the ED within 6 months after hospital discharge.

2.3 Statistical analyses

First, a univariate descriptive analysis was performed. Then, bivariate analyses were applied using Pearson's chi-squared and Student's *T*-tests if the assumptions of parametric testing were met (otherwise, non-parametric tests were applied, e.g., Fisher's exact test). The dependent variable of our study was the primary outcome, i.e., readmission to the ED during 6 months after discharge. Finally, multivariate analyses for predicting the outcome were performed using logistic regression models. The estimates of strength of association were calculated as odds ratios (ORs). All analyses were performed using the SPSS ® version 22.0 statistical software.

2.4 Ethical considerations

This study complies with the principles of the Declaration of Helsinki. A completely anonymized database was used for the analyses. No identification data were used. The study was approved by the Provincial Research Ethics Committee of Granada on 1 October 2020 (code 1585-N-20).

3. Results

3.1 Descriptive analysis

Of the total sample of hospitalized patients (n = 441; mean age, 66.4 years; 55.1% men), 361 (81.9%) survived and were

T A B L E 1. Sociodemographic and clinical variables collected at baseline (hospital admission) in the followed sample.

Sociodemographic variables	Total followed-up cohort (n = 361)	Readmission to the ED (n = 75)	No readmission to the ED (n = 286)	*P*-value[a]
	N (%)/x (s)	N (%)/x (s)	N (%)/x (s)	
Age	63.4 (14.7)	62.4 (15.5)	63.7 (14.4)	0.495
Men	191 (52.9)	39 (52.0)	152 (53.1)	0.859
Hypertension	163 (45.2)	28 (37.3)	135 (47.2)	0.126
Diabetes mellitus	70 (19.4)	16 (21.3)	54 (18.9)	0.633
Chronic kidney disease	28 (7.8)	7 (9.3)	21 (7.3)	0.566
Cardiovascular disease	59 (16.3)	14 (18.7)	45 (15.7)	0.541
COPD	17 (4.7)	2 (2.7)	15 (5.2)	0.348
Asthma	30 (8.3)	9 (12.0)	21 (7.3)	0.193
Autoimmune disease	22 (6.1)	8 (10.7)	14 (4.9)	0.063
Active neoplasm	6 (1.7)	2 (2.7)	4 (1.4)	0.608
Polymedication	130 (36.0)	35 (46.7)	95 (33.2)	0.031*
Dependence for ADL	65 (18.0)	19 (25.3)	46 (16.1)	0.064
Living at home	307 (85.0)	57 (76.0)	250 (87.4)	0.014*
Living in RCH	39 (10.8)	12 (16.0)	27 (9.4)	0.103
Living in RCD	18 (5.0)	5 (6.7)	13 (4.5)	0.453
Clinical variables				
CRS	127 (35.2)	24 (32.9)	103 (36.1)	0.603
Concomitant infection	70 (19.4)	19 (25.7)	51 (18.3)	0.160
CURB-65 score				
0	106 (29.4)	22 (30.6)	84 (30.2)	
1	150 (41.6)	28 (38.9)	122 (43.9)	0.845
2	82 (22.7)	19 (26.4)	63 (22.7)	
3	12 (3.3)	3 (4.2)	9 (3.2)	
Not candidate for CPR	71 (19.7)	18 (25.0)	53 (19.0)	0.258
Hospitalization days	16.1 (13.3)	18.6 (14.7)	15.4 (12.9)	0.062
ICU admission	32 (8.9)	9 (12.0)	23 (8.0)	0.283

*Data are presented as absolute frequencies (N) and relative frequencies (%) for qualitative variables, and as mean (x) and standard deviation (s) for quantitative variables. ED, Emergency Department; ADL, activities of daily living; COPD, chronic obstructive pulmonary disease; RCH, residential care homes for the elderly; RCD, residential care homes for adults with disability; CRS, cytokine release syndrome; CPR, cardiopulmonary resuscitation; ICU, intensive care unit. [a]P-values are calculated as T-test for quantitative variables and chi-square test for qualitative variables. When conditions of application were not met, Fisher exact test was used. * P < 0.05.*

discharged. This group comprised the sample followed (mean age, 62.4 years; 52.9% men). A total of 75 (20.8%) patients were readmitted to the ED within 6 months after hospital discharge. The main characteristics of the subgroups of the cohort are described in Fig. 1. Table 1 shows the distribution of the sociodemographic and clinical variables of the followed sample, where the 'total followed-up cohort' column presents all the patients who were discharged alive, 'readmission to the ED' explores the subgroup of patients who were readmitted to the ED within the 6-month follow-up after discharge, and 'no readmission to the ED' describes the subgroup of patients who did not return to the ED during the said follow-up.

3.2 Bivariate analyses

As shown in Table 1, no significant differences in most of the sociodemographic or clinical variables at baseline were associated with readmission to the ED at 6 months, although a higher presence of comorbidities in the cohort of patients readmitted to the ED is observed for most of the analyzed variables. Conversely, not living at home and polymedication were significantly associated with the primary outcome. Table 2 shows the presence of symptoms during the 6-month follow-up after discharge of survivors (n = 361), stratified by the primary outcome. The 'readmission to the ED' column explores the subgroup of patients who returned to the ED during follow-up, and 'no readmission to the ED' describes the subgroup of
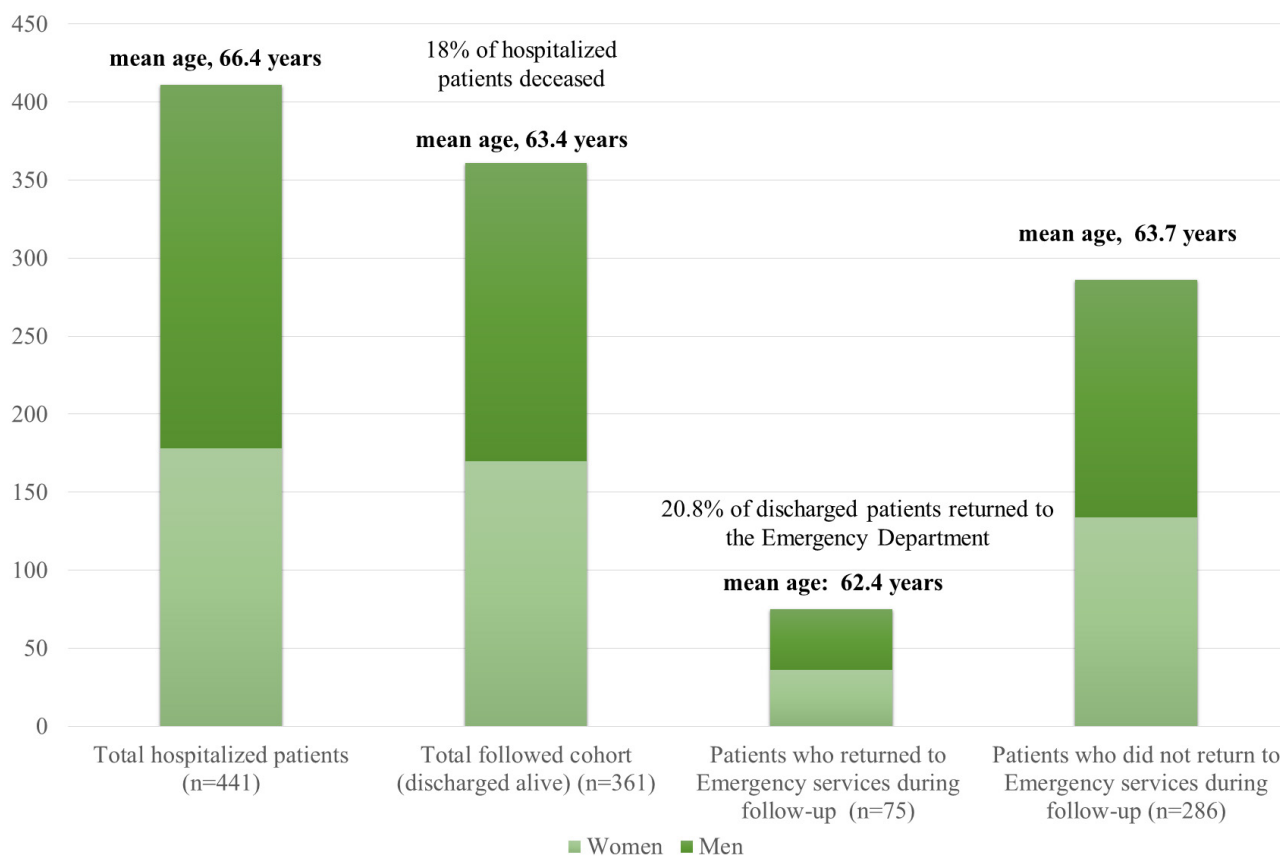
F I G U R E 1. Main characteristics (percentage, sex and age) of the subgroups of the cohort.

patients who were not readmitted to the ED during follow-up.

As shown in the table, the most frequent symptoms were respiratory, systemic, neurological, and digestive.

Bivariate analyses showed that the factors potentially associated with readmission to the ED were fever, general malaise, thoracic pain, headache, hematological and nephrological symptoms, syncope or hypotension and superinfection. On the other hand, anosmia or dysgeusia and asthenia were associated with a lower frequency of readmission to the ED at 6 months.

3.3 Multivariate analysis

Multivariate logistic regression models were applied for predicting readmission to the ED (dependent variable). Models were adjusted for sex, age and the variables resulting from the bivariate analyses (Table 3). The 'cOR' column shows the crude associations between each variable and the odds of returning to the ED during follow-up, and the 'aOR' column shows the adjusted associations in the multivariate models.

After adjustment of the models, the variables that remained as risk factors for readmission to the ED at 6 months following hospital discharge were polymedication, not living at home, general malaise and thoracic pain. Fig. 2 shows the distribution of the main factors associated with readmission to the ED in the multivariate analysis.

4. Discussion

In this study we described the frequency of symptoms during 6 months after discharge of COVID-19 patients in a tertiary hospital from Granada, Spain. We detailed the observed symptomatology and variables associated with readmission to the ED. Statistically significant associations were found between polymedication and living in residential care homes, and a higher frequency of readmission to the ED, which remarks the necessity of strengthening the follow-up of this group of vulnerable patients after hospital discharge during the pandemic.

Regarding the symptomatology analyzed in the cohort, general malaise and thoracic pain were associated with a higher frequency of readmission to the ED. In addition, bivariate analyses showed that headache, syncope or hypotension and superinfection were also associated with higher ED readmission rates. Accordingly, we suggest that these symptoms should serve as guidance for physicians in the follow-up of post-discharge COVID-19 patients to avoid hospital readmission or negative outcomes.

The mean age (63.4 years) and sex distribution (52.9% of men) of our sample are very similar to other previous studies conducted in our environment [4, 8]. The in-hospital mortality of our cohort (18.1%) is also in agreement with data from large cohorts in other countries during the first wave of the pandemic, such as the United States [17]. However, it is slightly lower compared to data from studies published in Wuhan [18]. This difference might be partially explained by

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T A B L E 2. Symptomatology during the 6 months after hospital discharge of COVID-19 patients.

Symptoms	Total followed cohort (n = 361)	Readmission to the ED (n = 75)	No readmission to the ED (n = 286)	P-value[a]
	N (%)/x (s)	N (%)/x (s)	N (%)/x (s)	
Any symptom	233 (64.5)	52 (69.3)	182 (63.6)	0.670
Systemic symptoms	167 (46.3)	40 (53.3)	127 (44.4)	0.168
Fever	32 (8.9)	11 (14.7)	21 (7.3)	0.047*
Asthenia	110 (30.5)	16 (21.2)	94 (32.9)	0.053
Muscle weakness	27 (7.5)	8 (10.7)	19 (6.6)	0.238
Musculoskeletal pain	69 (19.1)	19 (25.3)	50 (17.5)	0.124
General malaise	18 (5.0)	10 (13.3)	8 (2.8)	<0.001*
Respiratory symptoms	192 (53.2)	45 (60.0)	147 (51.4)	0.184
Dyspnea	137 (38.0)	32 (42.7)	105 (36.7)	0.344
Rib pain	19 (5.3)	7 (9.3)	12 (4.2)	0.076
Thoracic pain	30 (8.3)	15 (20.0)	15 (5.2)	<0.001*
Persistent cough	83 (23.0)	15 (20.0)	68 (23.8)	0.489
Pharyngeal symptoms	39 (10.8)	10 (13.3)	29 (10.1)	0.428
Neurological symptoms	112 (31.0)	26 (34.7)	86 (30.1)	0.444
Headache	28 (7.8)	11 (14.7)	17 (5.9)	0.012*
Sensitivity disorders	19 (5.3)	7 (9.3)	12 (4.2)	0.076
Movement disorders	18 (5.0)	5 (6.7)	13 (4.5)	0.453
Confusion	13 (3.6)	5 (6.7)	8 (2.8)	0.109
Anosmia or dysgeusia	46 (12.7)	4 (5.3)	42 (14.7)	0.031*
Mental health symptoms	67 (18.6)	18 (24.0)	49 (17.1)	0.173
Depressive symptoms	24 (6.6)	10 (13.3)	14 (4.9)	0.009*
Anxiety	33 (9.1)	10 (13.3)	23 (8.0)	0.157
Sleep disorders	32 (8.9)	9 (12.0)	23 (8.9)	0.283
Hematological symptoms	12 (3.3)	6 (8.0)	6 (2.1)	0.011*
Thrombotic signs	9 (2.5)	4 (5.3)	5 (1.7)	0.076
Dermatological symptoms	38 (10.5)	11 (14.7)	27 (9.4)	0.189
Exanthema	10 (2.8)	4 (5.3)	6 (2.1)	0.129
Nephrological symptoms	32 (8.9)	11 (14.7)	21 (7.3)	0.047*
Urological symptoms	15 (4.2)	2 (2.7)	13 (4.5)	0.468
Ophthalmologic symptoms	21 (5.8)	7 (9.3)	14 (4.9)	0.144
Digestive symptoms	81 (22.4)	22 (29.3)	59 (20.6)	0.108
Diarrhea	54 (15.0)	11 (14.7)	43 (15.0)	0.937
Abdominal pain	21 (5.8)	7 (9.3)	14 (4.9)	0.144
Syncope or hypotension	17 (4.7)	8 (10.7)	9 (3.1)	0.006*
Superinfection	29 (8.0)	11 (14.7)	18 (6.3)	0.018*
Post-discharge mortality	4 (1.1)	2 (2.7)	2 (0.7)	0.147

*Data are presented as absolute frequencies (N) and relative frequencies (%) for qualitative variables, and as mean (x) and standard deviation (s) for quantitative variables. [a]P-values are calculated as T-tests for quantitative variables and chi-square tests for qualitative variables. When conditions of application were not met, Fisher's exact test was applied. * P < 0.05.*

the design of the studies. We conducted a complete follow-up of a cohort of patients who had been hospitalized, while studies on mortality published during the first months of the pandemic such as [18] only considered the primary outcomes (death or discharge) with no complete follow-up. Accordingly, these studies likely underestimated cases of long-hospital stay and overestimated the mortality rates. Other studies [19] have attempted to characterize COVID-19 patients who returned to
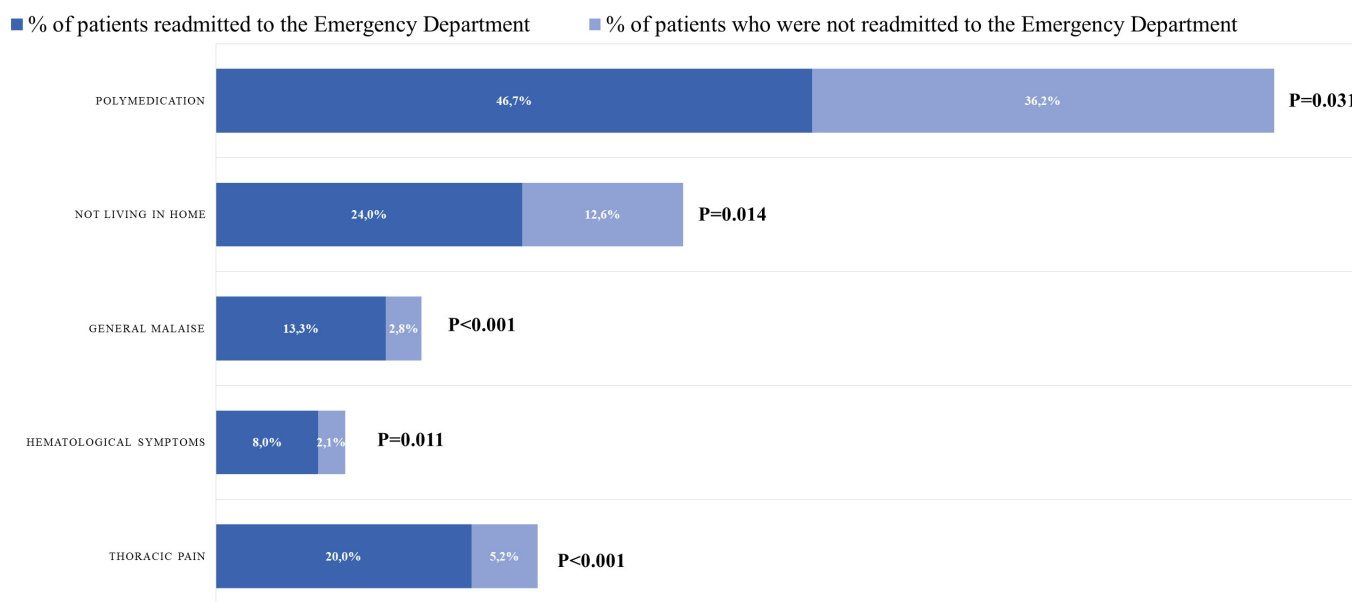
■ % of patients readmitted to the Emergency Department   ■ % of patients who were not readmitted to the Emergency Department

POLYMEDICATION | 46,7% | 36,2% | **P=0.031**

NOT LIVING IN HOME | 24,0% | 12,6% | **P=0.014**

GENERAL MALAISE | 13,3% | 2,8% | **P<0.001**

HEMATOLOGICAL SYMPTOMS | 8,0% | 2,1% | **P=0.011**

THORACIC PAIN | 20,0% | 5,2% | **P<0.001**

F I G U R E 2. Main factors associated with readmission to the Emergency Department in the multivariate analysis. Percentage distribution and *P*-values.

T A B L E 3. Multivariate logistic regression analysis for the outcome 'readmission to the Emergency Department during 6 months after hospital discharge'.

Variable	cOR (95% CI)	aOR (95% CI)
Age	0.99 (0.98–1.01)	0.98 (0.95–1.00)
Sex (reference: men)	1.05 (0.63–1.74)	0.85 (0.48–1.51)
Polymedication	1.75 (1.11–2.76)	2.12 (1.16–3.89)*
Not living at home	2.19 (1.16–4.14)	2.51 (1.16–5.48)*
Fever	2.17 (1.00–4.73)	1.37 (0.56–3.32)
General malaise	5.34 (2.03–14.08)	5.24 (1.72–15.94)*
Thoracic pain	4.52 (2.09–9.74)	4.45 (1.86–10.63)*
Headache	2.72 (1.21–6.09)	1.79 (0.68–4.68)
Depressive symptoms	2.99 (1.27–7.03)	2.38 (0.88–6.47)
Hematological symptoms	4.06 (1.27–12.97)	3.95 (1.12–13.89)*
Nephrological symptoms	2.17 (1.00–4.73)	1.33 (0.446–3.85)
Syncope or hypotension	3.67 (1.37–9.88)	1.44 (0.42–4.89)
Superinfection	2.56 (1.15–5.68)	1.98 (0.71–5.51)

cOR, crude odds ratio (unadjusted); aOR, odds ratio adjusted for all the variables shown in the table.

hospital following discharge. These authors found a 3.6% rate of return to the ED and agreed that the most frequent causes were comorbidities (especially hypertension and respiratory conditions) and respiratory distress. Conversely, we did not find associations with respiratory symptoms but with thoracic pain. Other authors found that 8.6% of patients were readmitted to hospital or ED in the 72 hours after discharge [20]. The main factors associated with readmission were older age, hypoxia, fever, obesity and hypertension. We observed no association between respiratory symptoms and readmission, which contrasts with the results of studies conducted in the United States [19, 20]. This could be partially explained by the subjective report of symptoms in our study (self-reported rather than measurement of hypoxia, as was the case in previous studies). However, we agree that patient vulnerability (older age, comorbidities, dependence or polymedication) increases the frequency of post-discharge readmission to the ED and might be a potential risk factor for improving preventive follow-up strategies.

4.1 Symptomatology

The frequency of persistent symptoms during 6 months after hospital discharge in our study was surprisingly high. Almost

two thirds of the patients (64.5%) showed at least one symptom at follow-up. The most frequent symptoms identified in this study were respiratory (63.0%), especially dyspnea (44.9%); systemic (54.9%), especially asthenia (36.1%); neurological (36.7%); digestive (26.6%), especially diarrhea (17.7%); and related to mental health (22.0%).

The high frequency of potentially severe symptoms such as superinfection (8.0%), hypotension (4.7%) and hematological (3.3%) symptoms should also be considered.

In addition, the high frequency (10.5%) of dermatological symptoms associated with COVID-19 is in agreement with other studies [21, 22].

4.2 Factors associated with readmission to the Emergency Department

Readmission to the ED is an important concern which, considering the state-of-the-art literature on COVID-19, merits further research due to a number of reasons. First, during the pandemic, EDs have been overloaded due to an excessive healthcare demand. Second, readmission to the ED during the 6 months after hospital discharge might be a marker of severity in the short-to-medium term and possibly requires an optimization of the criteria used for hospital discharge or follow-up protocols of these patients by Primary Care physicians. We believe that the identification of factors associated with this severity might be useful for individualizing medical advice and information to the community.

According to the results of bivariate analyses, the main factors associated with readmission to the ED in our study were polymedication ($P = 0.031$), living in a residential care home ($P = 0.014$), fever ($P = 0.047$), general malaise ($P < 0.001$), thoracic pain ($P < 0.001$), headache ($P = 0.012$), depressive symptoms ($P = 0.009$), hematological symptoms ($P = 0.011$), nephrological symptoms ($P = 0.047$), syncope or hypotension ($P = 0.006$) and superinfection ($P = 0.018$). On the other hand, our results point to persistent anosmia or dysgeusia as a possible protective factor for readmission to the ED ($P = 0.031$). It is possible that these symptoms are more frequent in less severe cases of COVID-19. However, studies specifically aimed at contrasting this hypothesis should be conducted.

We believe that polymedication (more than six drugs per day) and living in residential care homes point to a vulnerable profile of patients that might require strengthening and individualizing post-discharge follow-up strategies. Both factors were confirmed by multivariate analyses (OR: 2.12, 95% CI: 1.16–3.89 and OR: 2.51, 95% CI: 1.16–5.48, respectively).

Regarding symptoms, multivariate analyses confirmed the associations between higher frequency of readmission to the ED and general malaise (OR: 5.24, 95% CI: 1.72–15.94), thoracic pain (OR: 4.45, 95% CI: 1.86–10.63) and hematological symptoms (OR: 3.95, 95% CI: 1.12–13.89). However, given the limitations our study data, headache, depressive symptoms, nephrological symptoms, syncope or hypotension and superinfection should also be cautiously considered as possible markers of severity.

4.3 Limitations of the study

The primary aim of this study was to offer a global description of symptomatology during 6 months after discharge of COVID-19 in our institution. However, we could not gather information on the time of symptom onset, thus it was not possible to distinguish between early or late symptoms, and survival analyses or Cox regression models could not be performed. We used medical records for data gathering. Nevertheless, many potentially relevant variables such as obesity or smoking were not systematically collected in the reports and, therefore, could not be analyzed. We tried to minimize this limitation by collecting all available sociodemographic variables and including them in the multivariate analysis adjustments. It should also be noted that data were obtained from a single institution, thus the external validity of our results should be interpreted cautiously. Finally, possible biases associated with the retrospective nature of this study should be considered. We believe that the detailed information on symptoms and factors associated with readmission to the ED after 6 months of follow-up may contribute significantly to improving future follow-up of COVID-19 patients discharged from hospital.

5. Conclusions

The frequency of symptoms after hospital discharge in COVID-19 patients is high and variable. The most common symptoms were respiratory, systemic, neurological, digestive and related to mental health. Variables associated with readmission to the ED included polymedication, living in residential care homes, general malaise, thoracic pain and hematologic symptoms. These factors, along with headache, depressive symptoms, nephrological symptoms, syncope or hypotension, and superinfection might be used as markers of severity for improving follow-up of patients after hospital discharge. However, considering the limitations of our study, these results should be confirmed by long-term longitudinal studies conducted in other countries.

AUTHOR CONTRIBUTIONS

ARD and MRI designed the research study and wrote the first draft of the manuscript. ARD, MRI, AJLRB, PRG and ACC conducted the research and advised on methodology. ACC mentored the work. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study complies with the principles of the Declaration of Helsinki. A completely anonymized database was used for the analyses. No identification data were used. The study was approved by the Provincial Research Ethics Committee of Granada on 1 October 2020 (code 1585-N-20).

CONFLICT OF INTEREST

The authors declare no conflict of interest. Antonio Jesús Láinez-Ramos-Bossini is a Guest Editor of this journal.

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