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Predictors of readmission requiring hospitalization after discharge from emergency departments in patients with COVID-19

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ARTICLE INFO

Article history:

Received 7 January 2021

Received in revised form 29 March 2021

Accepted 18 April 2021

Keywords:

COVID-19

Predictors

Readmission

Emergency department

ABSTRACT

Introduction: Little is known on prevalence of early return hospital admission of subjects with COVID-19 previously evaluated and discharged from emergency departments (EDs). This study aims to describe readmission rate within 14 days of patients with COVID-19 discharged from ED and to identify predictors of return hospital admission.

Methods: We performed a retrospective cohort study of adult patients with COVID-19 discharged from two EDs. Return hospital admission was defined as an unscheduled return ED visit within 14 days after initial ED evaluation and discharge. We compared the group of patients who had a return hospital admission to those who did not. We also evaluated selected clinical characteristics (age, neutrophilia, SOFA, lactate dehydrogenase, C-reactive protein and D-dimer) associated with return hospital admission.

Results: Of 283 patients included in the study, 65 (22.9%) had a return ED visit within 14 days. 32 of those patients (11%) were then hospitalized, while the remaining 33 were again discharged. Patients requiring a return hospital admission was significantly older, had higher pro-calcitonin and D-dimer levels. Major predictors of return hospital admission were cognitive impairment (OR 17.3 [CI 4.7–63.2]), P/F < 300 mmHg (OR 8.6 [CI 1.6–44.3]), being resident in geriatric care facility (OR 7.6 [CI 2.1–26.4]) and neutrophilia (OR 5.8 [CI 1.6–22.0]).

Conclusion: Several factors are associated with 14-day return hospital admission in COVID-19 subjects. These should be considered when assessing discharge risk in ED clinical practice.

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1. Introduction

In December 2019, an outbreak of novel coronavirus disease (COVID-19), occurred in China, and, thereafter, it has dramatically spread worldwide [1,2]. Italy was the first western country experiencing the unexpected, devastating impact of this pandemic, with an outstanding number of infected patients admitted to emergency departments (ED) in a relatively small amount of time. Due to the high pressure to healthcare systems over those weeks, some of them, deemed as less severe, were discharged home [3]. Although several studies have reported readmission rate after hospitalization and relative predictors, little is not known on prevalence of early hospital return of patients non-hospitalized [4–7]. The aim of this study is to describe

short-term return hospital admission (within 14 days) of patients with mild and moderate COVID-19 discharged from two major EDs within the Marche region (an Italian region of 1,5 million of inhabitants) during the first wave, and to identify predictors of return hospital admission.

2. Methods

We conducted a retrospective cohort study of adult patients with COVID-19 discharged from the two EDs of major hospitals of the Marche Region ("Ospedali Riuniti" Ancona, the coordinator centre; "Marche Nord" Hospital, Pesaro, Italy) from March 1 to April 28, 2020. This date range was based on volume. The annual census is approximately 60,000 and 40,000 respectively in Ancona's ED and Pesaro's ED. The whole inpatient capacity for COVID patients was 160. The decision to obtain imaging, and/or discharge was determined by the attending physician at his/her discretion. A specific hospital algorithm was not available. Anonymized data of patients were collected from electronic medical records. Patients were included in the study cohort if they

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tested positive for SARS-CoV-2 by real-time reverse transcription polymerase chain reaction testing from nasopharyngeal swab specimens within 7 days before or after the ED encounter [8] and were discharged from ED. We collected for all cases: i) demographic factors: sex, age, duration of symptoms before ED visit; ii) comorbidities: hypertension, diabetes, dyslipidemia, cognitive impairment (determined by the review of the anamnesis) and others; iii) risk factors: being resident in care facility, fever, tachycardia, pulse oximetry on room air (SatHb \leq 94% vs $>$ 94%), PaO₂/FiO₂ (P/F $<$ 300 mmHg vs 300–400 mmHg or vs $>$ 400 mmHg or vs not available), pro-calcitonin, chest radiograph (abnormal vs normal or vs not performed), age $>$ 65 years, neutrophilia, lactate dehydrogenase $>$ 100 U/L, C-reactive protein $>$ 3 mg/L and D-dimer $>$ 1000 μ g/mL, the last five known to be associated with a poor prognosis [9,10].

Return hospital admission was defined as an unscheduled return ED visit requiring hospitalization within 14 days. We compared the group of patients who had a return hospital admission vs the group of patients who had not. The latter group included both patients who had not unscheduled return ED visit and those who had unscheduled return ED visit within 14 days, but were then discharged again.

Descriptive statistics were used to summarize covariates and unadjusted outcomes. Continuous variables were assessed with the unpaired Welch's *t*-test if normally distributed and the Mann Whitney *U* test if not, using NCSS v20.0.2. A *p* value $<$ 0.05 was considered statistically significant.

3. Results

During the study period, there were 4773 patients attending the two EDs and 442 patients tested positive for SARS-CoV-2 with an admission percentage of 36%. A total of 283 subjects were discharged and included in the present study. Overall, the mean age was 57 years (range 18–95 years), there was a slight predominance of male gender (51.2%) and the median duration of symptoms was 9 days (range 1–25 days). Sixty-five patients (22.9%) had an unscheduled return ED visit within 14 days, with the majority of whom (94%) within 10 days. Of these, 32 patients (11% [95% CI 9–17]) were then hospitalized (defining a return hospital admission), while the remaining 33 were again discharged. Demographic and clinical characteristics at baseline (i.e. on first hospital admission), for all patients and according to the need of return hospital admission, are summarized in Table 1. Patients requiring a return hospital admission were significantly older (55.64 years [95% CI 53.77–57.51] vs 68.09 [95% CI 62.97–73.20] years, $p <$ 0.0001), had higher pro-calcitonin (0.11 [95% CI 0.04–0.18] vs. 0.07 [95% CI 0.03–0.10] ng/mL, $p <$ 0.005) and D-dimer levels (1259 [95% CI 445–2074] vs. 660 [95% CI 529–730] μ g/mL, $p <$ 0.05). Major predictors of return hospital admission were cognitive impairment (OR 17.3 [95% CI 4.7–63.2], $p <$ 0.001), P/F $<$ 300 mmHg (OR 8.6 [95% CI 1.6–44.3], $p =$ 0.02), neutrophilia (OR 5.8 [95% CI 1.6–22.0], $p =$ 0.02), and being resident in geriatric care facility (OR 7.6 [95% CI 2.1–26.4], $p =$ 0.001) (Table 1). The presence of 3 to 5 well known risk factors, the absence of gas blood analysis, age \geq 60 years and the presence of 1 to 3 comorbidities were also found to be predictive. Finally, patients with P/F $>$ 300 mmHg had lower odds (OR 0.1 [95% CI 0.1–0.5], $p =$ 0.001) of return hospital admission compared to the group with hypoxia, as well as those with no comorbidities (OR 0.3 [95% CI 0.1–0.7], $p =$ 0.008) compared to those with almost one comorbidity (Table 1).

4. Discussion

To our knowledge, this is the first study assessing prevalence and predictors of return hospital admission of patients with COVID-19 following an initial ED discharge in Italy during the first wave. The prevalence was 11%, approximately two-times higher than those reported in three previous non-European cohorts [5–7]. However, in two of these studies, readmission rate was assessed within the first 72 h from ED

discharge. In the study by Kilaru et al. [5], indeed, the rate of readmission increased to 8.2% when recorded at 7 days.

Older age (\geq 60 years), cognitive impairment, residence in geriatric care facility, comorbidities, hypoxia and neutrophilia were associated with a higher probability of subsequent return hospital admission. Age-related conditions, in particular presence of dementia, seem to play a relevant role, likely due to the challenging assessment of initial clinical impairment as well as to the difficulties related with management and monitoring of these patients, even in dedicated settings. In addition, our finding about neutrophilia and consequent lymphopenia corroborates data suggesting an association between neutrophil-to-lymphocyte ratio and disease severity [1,6]. Of note, the presence of hypoxia at arterial blood gas analysis was a significant predictor of return hospital admission, while having a saturation \leq 94% was not, underlining the importance of a proper gas analysis assessment for a more precise risk stratification. Not performing an arterial blood gas analysis was, indeed, significantly associated with a higher risk of return hospital admission. On the other hand, it would be reasonable to speculate that a patient who was well enough to not require a blood gas analysis, would not have expected to return to hospital.

In times of significant pressure to healthcare systems, it may not be feasible to admit all patients at first presentation, even when they present with not negligible clinical features. Therefore, it is crucial to safely discharge subjects with low risk for readmission, in order to prioritize bed availability. In this context, identifying major predictors for return hospital admission might be a useful tool to develop and validate an algorithm for risk stratification [5–7].

This study has several limitations. First, the small sample size of this study is a limitation. Second, the limited representativeness of data, that came from two EDs only, as indications to admission and discharge might be different according to hospitals, being influenced by internal guidelines and the entity of pressure to health systems. Moreover, we could miss a number of return hospital admissions, because some patients could subsequently go to other hospitals or died at home. However, it was unlikely that patients went elsewhere because there were no other hospitals in nearby radius. A further limitation is that we did not include the full range of potential risk factors as covariates associated with readmission, such as obesity or discharge medications. Lastly, due to the retrospective nature of the study, more detailed data on comorbidities or treatments prescribed at home were not available.

5. Conclusion

In conclusion, we found that approximately 11% of patients with COVID-19, initially discharged from the ED, returned for an unscheduled ED visit with hospitalization within 14 days. Selected epidemiological and clinical characteristics, such as older age, hypoxia defined by P/F, and cognitive impairment were independently associated with an increased likelihood of return hospital admission. Further investigations are needed to develop risk stratification tools, which help physicians to choose the better disposition for patients with COVID-19 in the ED.

Author contributions

VGM, FF and AS conceived this study. MB and FM provided statistical advice on study design. FF, VGM, UG and SG conducted data collection. FF was responsible for data management. VGM, AS and MB analyzed all data. VGM drafted the article, and all authors contributed substantially to its revision. VGM takes responsibility for the paper as a whole.

Disclosure of potential conflicts of interest

The authors declare that they have no conflict of interest.

Table 1

Demographic and clinical characteristics of study cohort, overall and according to the need of readmission requiring hospitalization. # group "yes" vs group "no". * $p < 0.05$. § mean \pm SD (range). ° Neutrophils $>85\%$. & Five risk factors known to be associated with a poor prognosis: age > 65 years, neutrophilia, lactate dehydrogenase >100 U/L, C-reactive protein >3 mg/L and D-dimer >1000 $\mu\text{g/mL}$.

Characteristics	Overall No. (%) N = 283	Return hospital admission No. (%)		OR (95% CI)	p-value#
		Yes n = 32	No n = 251		
Age, years				3.94 (1.78–8.68)	<0.001*
18–39	40 (14.1)	0 (0)	39 (15.5)		
40–59	133 (47.0)	10 (31)	122 (48.6)		
≥ 60	110 (38.9)	22 (69)	90 (35.9)		
Sex				2.98 (1.4–6.38)	0.006*
Male	145 (51.2)	20 (62.5)	125 (49.8)		
Female	138 (48.8)	12 (37.5)	126 (50.2)		
Comorbidities					
History of hypertension				1.1 (0.5–2.4)	0.1
No	199 (70.3)	22 (68.7)	177 (70.5)		
Yes	84 (29.7)	10 (31.3)	74 (29.5)		
History of diabetes				1.6 (0.5–5.2)	0.6
No	259 (91.5)	28 (87.5)	231 (92.0)		
Yes	24 (8.5)	4 (12.5)	20 (8.0)		
Dyslipidemia				1.7 (0.6–5.0)	0.5
No	254 (89.8)	27 (84.4)	227 (90.4)		
Yes	29 (10.2)	5 (15.6)	24 (9.6)		
Cognitive impairment	272 (96.1)	25 (78.1)	247 (98.4)	17.3 (4.7–63.2)	< 0.001*
No	11 (3.9)	7 (21.9)	4 (1.6)		
Yes					
Number of comorbidities	128 (45.2)	7 (21.9)	121 (48.2)	0.3 (0.1–0.7)	0.008*
0	135 (47.7)	21 (65.6)	114 (45.4)	2.3 (1.1–5.0)	< 0.05*
1–3	20 (7.1)	4 (12.5)	16 (6.4)	2.1 (0.6–6.7)	0.4
≥ 4					
Risk factors				7.6 (2.1–26.4)	0.001*
Resident in care facility					
No	272 (96.1)	27 (84.4)	245 (97.6)		
Yes	11 (3.9)	5 (15.6)	6 (2.4)		
Fever	207 (73.1)	22 (68.7)	185 (73.7)	1.3 (0.6–2.8)	0.7
No	76 (26.9)	10 (31.3)	66 (26.3)		
Yes					
Tachycardia on arrival	216 (76.3)	24 (75.0)	192 (76.5)	1.1 (0.5–2.5)	0.9
No	67 (23.7)	8 (25.0)	59 (23.5)		
Yes					
SatHb				3.3 (0.6–17.5)	0.4
$> 94\%$	274 (97.0)	30 (93.8)	5 (98.0)		
$\leq 94\%$	9 (3.0)	2 (6.2)	5 (2.0)		
P/F mmHg				0.1 (0.1–0.5)	0.001*
> 400	104 (36.8)	3 (9.4)	101 (40.2)		
300–400	146 (51.5)	17 (53.1)	129 (51.4)		
P/F < 300	6 (1.5)	3 (9.4)	3 (1.2)	8.6 (1.6–44.3)	0.02*
Not available	27 (9.5)	9 (28.1)	18 (7.2)	5.1 (2.0–12.5)	< 0.001*
Dimer [§] $\mu\text{g/mL}$	722 \pm 836 (58–5692)	1259 \pm 1411 (98–4942)	660 \pm 727 (58–5692)		< 0.05*
Pro-calcitonin [§] ng/mL	0.07 \pm 0.17; (0.01–1.77)	0.11 \pm 0.09 (0.02–1.27)	0.07 \pm 0.18 (0.01–1.77)		< 0.005*
Neutrophilia [°]				5.8 (1.6–22.0)	0.02*
No	273 (96.5)	28 (87.5)	245 (97.6)		
Yes	10 (3.5)	4 (12.5)	6 (2.4)		
CRP > 3.0 mg/dL				2.1 (0.9–5.0)	0.1
No	99 (35.0)	7 (21.9)	92 (36.7)		
Yes	184 (65.0)	25 (78.1)	159 (63.3)		
Number of risk factors ^{&}					
0	61 (21.6)	3 (9.4)	58 (23.1)	0.3 (0.1–1.2)	0.1
1–3	214 (75.6)	26 (81.2)	188 (74.9)	1.4 (0.6–3.7)	0.6
4–5	8 (2.8)	3 (9.4)	5 (2.0)	5.1 (1.2–22.4)	0.05*
Chest radiograph					
Normal					
Abnormal	58 (20.5)	8 (25.0)	50 (20.0)	1.34 (0.6–3.1)	0.5
Not performed	156 (55.1)	16 (50.0)	140 (55.8)	0.8 (0.4–1.7)	0.7
Not performed	69 (24.4)	8 (25.0)	61 (24.2)	1.04 (0.4–2.4)	0.9

Prior presentations

None.

Declarations of Competing Interest

None.

Acknowledgments

None.

Funding Sources/Disclosures

None.

We disclose any grants or other financial support for this article.

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