SHORT COMMUNICATION

Geriatric syndromes and functions in older adults with COVID-19 hospitalized in sub-acute care: a multicenter study

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Abstract

Objective Alternatives to conventional acute hospitalizations have been particularly useful during the COVID-19 pandemic. However, little is known on the management and outcomes of COVID-19 in older patient admitted to non-acute settings. The main aim of this study was to determine the effect of geriatrics syndromes on functional outcomes in older COVID-19 patients cared in sub-acute units.

Methods Prospective multicenter observational cohort study of patients aged 65 years and older with COVID-19, admitted to sub-acute units in Italy and Spain. Multivariable logistic regression models were used to test the association between geriatric syndromes and other clinical variables, and the functional status at discharge, defined by a Barthel Index $> = 80$.

Results A total of 158 patients were included in the study with a median age of 82 [Interquartile Range 81, 83]; of these 102 (65%) patients had a Barthel Index ≥ 80 at discharge. In the main multivariable logistic regression model a higher severity of frailty-measured with the Clinical Frailty Scale—(OR 0.30; CI 0.18–0.47), and the presence of delirium (OR 0.04; CI 0.00–0.35) at admission were associated with lower odds of a higher functional status at discharge. Other variables associated with lower functional status were female gender (OR 0.36; CI 0.13–0.96), and a higher number of comorbidities (OR 0.48; CI 0.26–0.82).

Conclusion The study reports a relatively high prevalence of functional recovery for older COVID-19 patients admitted to sub-acute units. Additionally, it underlines the importance of targeting geriatrics syndromes, in particular frailty and delirium, for their possible effects on functional recovery.

Keywords Delirium · Frailty · Psychoactive drugs · COVID-19 · Elderly

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Introduction

At the end of 2019, the first cases of coronavirus disease-19 (COVID-19) caused by the new SARS-COV-2 infection were identified and progressively overwhelmed the health care system around the world in different waves [1]. Patients have been admitted and cared for this infection especially in acute hospitals. Several factors have been associated with adverse outcomes in older persons including age, the severity of the acute illness, frailty, delirium, and dementia [2, 3]. Few data have been published on the management and effects of COVID-19 in rehabilitation wards and nursing home [4, 5], even though these settings represented complementary alternatives to conventional acute hospitalizations in many cases [6].

Since the beginning of the COVID-19, researchers have investigated the role of geriatric syndromes as predictors of clinical outcomes in older persons besides the impact of chronological age. Frailty and delirium have been studied for their relationship with COVID-19 and for their possible prognostic role, mainly in acute hospital and critical care settings [7–10]. However, few studies have been conducted in rehabilitation and nursing homes [4, 5, 11].

Given the paucity of data on the management and outcomes of COVID-19 in older patients admitted to non-acute settings in northern Italy during the second wave of COVID-19 emergency, we conducted a multicenter prospective cohort study involving four sub-acute care units to determine the effect of geriatric syndromes (in particular, delirium and frailty) on functional outcomes.

Materials and methods

Study population

This is a prospective multicenter observational cohort study of patients aged 65 years and older with a diagnosis of COVID-19, consecutively admitted to four sub-acute units in Italy and Spain between February 2021 and March 2021. The sub-acute units in Cremona and Barcelona were specifically created within a department of rehabilitation, while the sub-acute unit in Milan and in Desio were already existing and were converted into sub-acute COVID-19 units. The main criterion for admission of COVID-19 patients into this unit was the lower severity of the acute illness with a maximum Oxygen requirement of 2 l/min.

Patients aged 65 years and older with a diagnosis of COVID-19 (i.e., positive result at the SARS-CoV-2 naso-pharyngeal swab polymerase chain reaction test) were included. The exclusion criteria were: presence of aphasia; history of major stroke; coma; severe hearing or visual deficits; refusal to provide informed consent. Patients were asked to provide verbal consent to participate in the study, given the low impact of the observational study and limit the diffusion of SARS-CoV2 with the paper material. The study was approved by the local Ethical Committee at each center.

Assessment of geriatric syndromes and use of psychoactive drugs on admission

The presence of delirium at the admission was assessed with the 4AT, and delirium was considered present with a 4AT score ≥ 4. The 4 'A's Test (4AT) is a short (< 2 min) instrument for delirium detection that is used internationally as a standard tool in clinical practice. The 4AT was originally validated in acute geriatric wards and rehabilitation wards [12]. A 4AT score of 0 suggests the absence of dementia or delirium, a score between 1 and 3 suggests a possible cognitive impairment but not delirium, while a score ≥ 4 is strongly suggestive of delirium. A recent systematic review reported a pooled sensitivity of 0.88 (95% CI 0.80–0.93) and specificity of 0.88 (95% CI 0.82–0.92) of the 4AT for delirium detection [13].

Frailty was measured using the well-validated Clinical Frailty Scale (CFS), considering the participant's health status before the COVID-19 infection. CFS score ranges from 1 to 9, where 1 indicates a very fit person and 9 a terminally ill individual [14]. The CFS has been widely used in other studies to define the presence of frailty in multiple settings and especially during the COVID-19 emergency [15, 16].

The presence of undernutrition and obesity were defined according to a clinical evaluation.

The use of psychoactive drugs (i.e., typical and atypical antipsychotics; benzodiazepines; antidepressants) at the time of sub-acute admission was recorded.

All these evaluations were carried out by the attending physicians caring for the patient.

Study outcome

The functional status was assessed using the Barthel Index (BI) as reported by the patient and/or his/her proxy, referring to the level presented on admission and at discharge from the sub-acute care unit. The BI at discharge was identified as the primary outcome and a cut-off ≥ 80 was chosen as indicative of functional independency, according to a previous study [17].

Data collection and clinical assessment

At the sub-acute care unit admission, the following variables were recorded: demographics, smoking status, and the comorbidities (i.e., chronic obstructive pulmonary disease-COPD, diabetes, coronary artery diseases-CAD, chronic heart failure-CHF, liver disease, cerebrovascular disease, solid tumor, Parkinson disease, dementia, psychiatric disease).

Statistical analysis

Continuous variables were described with median and interquartile range (IQR), and categorical data were expressed as frequency and percentage. Three multivariable logistic regression models were created to evaluate the association with the functional outcome including variables selected a priori according to clinical relevance and statistical significance in the univariate analysis: delirium at admission, frailty, gender, undernutrition, obesity, enrollment center, number of comorbidities, psychoactive drugs on admission. In the first model the Barthel Index and the presence of psychoactive drugs at admission were not included. In the second model age, the number of comorbidities and psychoactive drugs on admission were not included. In the third model age, the number of comorbidities was excluded and the Barthel Index and the presence of psychoactive drugs on admission were included. This approach was chosen to avoid the overfitting of the models and to test the association of specific variables with the outcomes, especially the Barthel Index and the presence of psychoactive drugs on admission.

A multivariate linear regression was also modeled with the continuous Barthel Index as the outcome variable and adjusted for including variables selected a priori according to clinical relevance: delirium, frailty, gender, undernutrition, obesity, enrollment center, functional change (difference between the BI before the admission and the BI at the admission).

Statistical analyses were performed with the statistic "R" software (R version 3.6.1 (2019–07-05), Copyright 2015 The R Foundation for Statistical Computing).

Results

A total of 158 patients were included in the study with a median age of 82 years; 44.9% ($N = 71$) were women (Table 1). A total of 102 (65%) patients had a Barthel Index ≥ 80 at discharge. According to the clinical evaluation, 37% ($N = 57$) were undernourished, 11.7% ($N = 18$) were obese. In the univariate analysis patients with a Barthel Index ≥ 80 compared to those with a Barthel Index < 80 were less female (39.3% vs. 63.7%), were younger (76 years, IQR 72–81 vs. 84.5, IQR 79–88), with a lower prevalence of undernutrition (17.9% vs. 48%) and a higher prevalence of obesity (14.3% vs. 10.2%); they had a lower severity of frailty as defined by the CFS (3 IQR 3,4 vs. 6, IQR 4–6). The level of comorbidity, as measured the number of comorbidities (1 IQR 1–2 vs. 2, IQR 2–3) with and the presence of psychoactive drugs (33.9% vs. 52%) was lower in patients with BI ≥ 80. Finally patient with better functional status ad discharge had a higher BI on (BI 90, IQR 76.5–96 vs. BI 35,

Table 1 Characteristics of 158 older patients with COVID-19 infection admitted to four sub-acute units according to the functional status at discharge as measured with the Barthel Index

Variable	All sample $N = 158$	Barthel Index < 80 $N = 56$	Barthel Index ≥ 80 $N = 102$	P value
Sex (Female)	71 (44.9%)	65 (63.7%)	22 (39.3%)	< 0.001
Age	82 [81, 83]	84.5 [79,88]	76 [72,81]	0.005
Clinical Frailty Scale	5 [3, 6]	6 [4, 6]	3 [3, 4]	< 0.001
Nutritional problems				
Absent	79 (51.3%)	41 (41.8%)	38 (67.9%)	< 0.001
Undernutrition	57 (37%)	47 (48%)	10 (17,9%)	
Obesity	18 (11.7%)	10 (10,2%)	8 (14.3%)	
Number of diseases	2 [1, 3]	2 [1, 3]	1 [1, 2]	< 0.001
Psychoactive drugs at admission	72 (45.6%)	53 (52%)	19 (33.9%)	0.004
Barthel Index at admission	45 [20, 80]	35 [15–50]	90 [76.5, 96]	< 0.001
Delirium at admission	37 (24%)	36 (36%)	1 (1.9%)	< 0.001
Enrolling center				0.1
Desio	50 (27.5%)	24 (23.5%)	19 (33.9%)	
Barcelona	47 (25.8%)	26 (25.5%)	8 (14.3%)	
Cremona	30 (16.5%)	14 (14%)	13 (23.2%)	
Milan	55 (30.22%)	38 (37.3%)	16 (28.6%)	

Table 2 A multivariable logistic regression to determine the effect of geriatrics syndromes (delirium, frailty, nutritional problems) on functional outcomes at discharge (defined as Barthel Index ≥ 80)

Variables	Model 1			Model 2			Model 3		
	Odds ratio	Confidence Interval	P value	Odds ratio	Confidence Interval	P value	Odds ratio	Confidence Interval	P value
Female Gender	0.36	0.13–0.96	0.004	0.24	0.05–0.92	0.047	0.23	0.05–0.91	0.046
Age	0.96	0.87–1.05	0.337	–	–	–	–	–	–
Clinical Frailty Scale	0.30	0.18–0.47	< 0.001	0.47	0.26–0.78	0.006	0.47	0.26–0.78	0.006
Undernutrition	2.69	0.74–10.76	0.143	5.96	1.13–40.5	0.047	6.14	1.14–43.16	0.047
Obesity	8.94	1.64–60.06	0.015	9.23	1.28–88.44	0.035	9.39	1.30–91.00	0.035
Number of comorbidities	0.48	0.26–0.82	0.011	–	–	–	–	–	–
Barthel Index on admission	–	–	–	1.10	1.06–1.15	< 0.001	1.10	1.06–1.15	< 0.001
Psychoative drugs on admission*	–	–	–	–	–	–	1.10	0.43–2.89	0.842
Delirium	0.04	0.00–0.35	0.012	0.11	0.12–7.81	0.969	0.11	0.00–2.56	0.194
Ref. Desio	–	–	–	–	–	–	–	–	–
Cremona	0.16	0.03–0.73	0.023	0.96	0.12–7.81	0.053	0.94	0.12–7.74	0.957
Barcelona	0.08	0.01–0.41	0.003	0.16	0.02–0.96	0.969	0.15	0.02–0.96	0.055
Milan	0.03	0.00–0.16	< 0.001	0.35	0.04–2.90	0.341	0.34	0.03–2.88	0.335

*Psychoactive drugs on admission were defined by the presence on admission of one of the following medications: benzodiazepines, typical antipsychotics, atypical antipsychotics

IQR 15–50) and lower prevalence of delirium at admission (1.9% vs. 36%) (Table 1).

In the first multivariable logistic regression model having a higher severity of frailty measured with the Clinical Frailty Scale—(Odds Ratio 0.30; Confidence Interval 0.18–0.47), and the presence of delirium (OR 0.04; CI 0.00–0.35) at admission were associated with lower odds of a higher functional status at discharge. Other variables associated with lower functional status were female gender (OR 0.36; CI 0.13–0.96), and a higher number of comorbidities (OR 0.48; CI 0.26–0.82). In the second and in the third multivariable logistic regression model having a higher severity of frailty, being female, and a higher number of comorbidities were associated with lower odds of a higher Barthel Index at discharge; while higher Barthel Index at admission were associated with a higher Barthel Index on discharge. No association was found in the third Model between the presence of antipsychotics at admission and the Barthel Index at discharge. The findings of the association between obesity and undernutrition should be interpreted with caution given the wide confidence interval related to the small number of patients in the subgroup with a Bathel Index ≥ 80 (Table 2).

The multivariable linear regression model confirmed that higher severity frailty, as measured with the CFS, was inversely correlated with the functional outcome at discharge (point estimate − 9.24, 95% Confidence Interval-CI − 11.85, − 6.62; $p < 0.001$) independent of multiple confounders.

Discussion

The study found a relatively high prevalence of functional recovery for older COVID-19 patients admitted to sub-acute units with 65% of the patient with a Barthel Index ≥ 80 at the time of discharge. The main factors associated with lower odds of functional recovery were the presence of two geriatric syndromes on admission (i.e., delirium and frailly).

Numerous studies have been published to investigate the prevalence of frailty and related outcomes in older patients acutely hospitalized for COVID-19 [7, 8]. However, fewer studies focused on older patients in rehabilitation and post-acute care settings. Sub-acute care, often defined as care for older patients with decompensated well-known chronic conditions, represent expanding healthcare services to face the increase of comorbidity and complex healthcare and social needs, and might be included into the broad category of intermediate care resources [12, 18]. During the pandemic, these services have been predisposed to care for COVID-19 older patients as a complement to the insufficient acute hospital capacity for selected acute patients [4].

In the context of the COVID-19 pandemic, frailty was mainly studied in critical care settings to understand how its measurement could guide intensive care physicians in the acute management of this infection and allocation of resources [5]. Frailty was indeed used to support clinicians in the decision process across the different COVID-19

waves, especially given its association with mortality [5]. To the best of our knowledge, this is the first study to show the association between frailty and functional status in older patients with COVID-19 admitted to sub-acute care units.

Finally, the association between delirium and worse functional outcomes is in line with other studies in non-COVID-19 patients [19]. A recent systematic review reported a high prevalence and incidence of delirium in older patients with COVID-19 in acutely hospitalized patients [8]. However, only a few studies were conducted in rehabilitation and nursing homes [4, 5]. Moreover, several studies have focused on the association between delirium and mortality in COVID-19, but little is known about the relationship between delirium and functional performances [8]. One study reported an interaction of delirium and pre-morbid frailty with worse physical function at the hospital discharge after COVID-19 [20].

The current study has notable strengths but also some limitations. This is the first multicenter international study evaluating a relatively large group of older patients with COVID-19 admitted to sub-acute care units. Patients underwent a comprehensive geriatric assessment to study the association between key geriatric syndromes and functional status at discharge. However, the variability in the management of the patients across the four sites might have influenced the final outcomes and potentially affected the lack of association of delirium with worse functional status. The data included in this study were collected at the end of the second wave and at the beginning of the third wave and the representativeness of the sample might be limited, potentially impacting the generalizability of the study findings. We were unable to monitor the prevalence, the incidence and severity of delirium during the sub-acute stay thus limiting our possibility to study the effect of delirium on the functional outcomes. Finally, the small number of patients with undernutrition and obesity in the group with a higher Barthel Index at discharge limited our ability to investigate the association between these variables and the functional outcomes.

Conclusion

This study showed a relatively high prevalence of functional recovery for older COVID-19 patients admitted to sub-acute units with 65% of the patient with a Barthel Index ≥ 80 at the time of discharge. Additionally it underlines the importance of targeting two main geriatrics syndrome—frailty and delirium—for their possible effects on functional recovery.

Declarations

Conflict of interest The authors declare that they have no conflict of interest.

Statement of human and animal rights All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent The exclusion criteria were: presence of aphasia; history of major stroke; coma; severe hearing or visual deficits; refusal to provide informed consent. Patients were asked to provide verbal consent to participate in the study, given the low impact of the observational study and limit the diffusion of SARS-CoV2 with the paper material. The study was approved by the local Ethical Committee at each center.

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