

Functional Decline in COVID-19 Older Survivors Compared to Other Pneumonia Patients, a Case Control Study

S. Le Gentil¹, S. Prampart¹, M. Karakachoff², M.L. Bureau¹, G. Chapelet¹, L. De Decker¹, A. Rouaud¹, A.-S. Boureau^{1,3}

1. Department of Geriatrics, Nantes University Hospital, Nantes, France; 2. CHU de Nantes, INSERM CIC 1413, Pôle Hospitalo-Universitaire 11, Santé Publique, Clinique des données, Nantes, France; 3. Université de Nantes, CHU Nantes, CNRS, INSERM, l'institut du thorax, Nantes, France

Corresponding Author: Anne-Sophie Boureau, Department of Geriatrics, University Hospital, 44093 Nantes, France; phone: +33 2-40-16-50-46; email: annesophie.boureau@chu-nantes.fr

Abstract

OBJECTIVES: Among patients over 75 years, little is known about functional decline due to COVID-19. The aim of this study was to explore this functional decline, compare to other infectious pneumonia. **DESIGN AND SETTING:** This case-control study included all COVID-19 patients hospitalized from March to December 2020 in Acute Geriatric Ward in Nantes University Hospital matched 1/1 with patients with pneumonia hospitalized in geriatric department between March 2017 and March 2019 (controls) on sex, age. Functional decline was assessed at 3 month follow up as it is routinely done after hospitalization in geriatric ward. We performed multivariable analyses to compare clinical outcomes between patients with COVID-19 vs controls.

RESULTS: 132 pairs were matched on age (mean: 87 y-o), and sex (61% of women). In multivariable logistic regression analysis, there were no statistical significant association between COVID-19 infection and functional decline (OR=0.89 p=0.72). A statistical significant association was found between functional decline and Charlson comorbidity index (OR=1.17, p=0.039); prior fall (OR=2.08, p=0.012); malnutrition (OR=1.97, p=0.018); length of hospital stay (OR=1.05, p=0.002) and preadmission ADL (OR=1.25, p=0.049).

CONCLUSION: COVID-19 does not seem to be responsible for a more frequent or severe functional decline than other infectious pneumonia in older and comorbid population after 3 month follow up. In this population, pneumonia is associated with functional decline in almost 1 in 2 cases. The individual preadmission frailty seems to be a more important predictor of functional decline, encouraging multidimensional care management for this population.

Key words: COVID-19, functional decline, acute lung disease, older patients, geriatric care.

Abbreviations: AF: atrial fibrillation; ADL: Katz Activities of Daily Living; APACHE II: Acute Physiology And Chronic Health Evaluation II; CCI: Charlson Comorbidity Index; CFS: Rockwood Clinical frailty scale; CI: Confidence Interval; CURB-65: Confusion Urea Respiratory rate, Blood pressure, 65 years old; IADL: Instrumental Activity of Daily Living of Lawton; MMSE: Mini Mental State Examination; OR: Odds Ratio; SOFA: Sequential Organ Failure Assessment Score.

Introduction

Since December 2019, Coronavirus disease 2019 (COVID-19) caused by a novel beta-coronavirus, named as Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is responsible for more than 290 million infections, and more than 5 million deaths worldwide (1). Patients aged 75 and older are the most susceptible to severe infection. In Europe, they account for 85% of COVID-linked deaths even though they represent only 9% of global population (2). In this older population, the COVID in-hospital mortality rate vary across cohorts from 20% up to 60%, reflecting differences in variable thresholds for hospitalization and patient's severity (3–5).

Beside high risk of severe COVID-19 pneumonia, many older patients experience persistent symptoms and a decline in health-related quality of life after COVID-19 (6–8). Functional status is a major concern included in health-related quality of life for individuals of all ages with acute or chronic illness. Therefore, optimizing functional status is a central tenet of geriatric practice (9). Recently, interplay between acute infectious disease and functional status has been highlighted. Severe infections can lead to severe functional decline (10), including after COVID-19 (11, 12). However, the specific influence of SARS-CoV-2 infection per se on prognosis remained difficult to establish, since COVID-19 is associated with a high risk of severe infection. In addition, poorer preadmission health status is also linked to severe clinical presentation of infectious disease (13, 14) and could lead to a higher functional decline (15, 16). Because of COVID-19 clinical severity is higher than in other pneumonia and because many older individuals experience persistent symptoms, we expected to observe a higher functional decline in COVID-19 older patients than in other lung infections survivors. The main purpose of this study was to determine whether COVID-19 per se is an independent prognostic factor for functional decline beyond advanced age, associated comorbidities and disease severity.

Methods

Study design and population of patients with COVID-19

Between March the 11st 2020 and December the 31th 2020, all patients aged 75 years and older, consecutively admitted in Acute Geriatric Wards of Nantes University Hospital, in France, for a confirmed SARS-Cov-2 infection were included as cases in this observational prospective case-control study.

Patients hospitalized in that ward were patients aged 75 and older with ICU admission denied or not required following the French guidance published during that inclusion period (17). Inclusion criteria were: i) aged 75 and over ii) COVID-19 diagnosis confirmed biologically (by SARS-CoV-2 PCR test) and/or radiologically (ground-glass opacity and/or crazy paving on chest computed tomography scan) iii) three months' follow-up as it is usually done. The exclusion criteria were patient or legal representative refusal and baseline Katz ADL <1/6. Prior to any data collection, the investigator presented the interest of the study and ensured an oral non-opposition. The study was approved by the local ethics committee, Groupe Nantais d'Ethique dans le Domaine de la Santé (GNEDS), which waived the need for informed consent in accordance to legislation on analyses of anonymized data. All research was performed in accordance with the ethical standards set forth in Helsinki declaration (1983).

Control group

The control group was composed with patients hospitalized for pneumonia in the same Acute Geriatric Ward of Nantes University Hospital between March the 1st 2017 and March the 31st 2019. Eligibility criteria were: i) aged 75 and over at the time of hospitalization ii) hospitalized for an infectious pneumonia based on International Classification of Disease-10 Codes (J-10 to J17 included) iii) three to six months' follow-up as it is routinely done. Patients with inhalation pneumonia or baseline Katz ADL <1/6 were excluded. Controls were selected using a screening algorithm applied to electronic medical records contained in the EDBN (in french, Entrepôt de données biomédicales Nantais), the clinical data warehouse of the Nantes University Hospital. The result of the screening phase was validated by clinical experts and submitted to the matching case-control phase. Cases and Controls were matched (1:1) on age (same year of birth \pm 2 years), sex. In the event of multiple matching, investigators were asked to choose the control with the closest preadmission ADL score.

Baseline Data

Variables of interest among all patients were age, gender, nursing home, pathogen type (SARS-COV2, other respiratory virus, bacteria), clinical severity (maximal oxygen flow, oxygen-requirement duration, Sequential Organ Failure Assessment Score (SOFA) and length of hospital stay),

in-hospital complications (acute atrial fibrillation, acute heart failure, thrombosis, acute renal failure, delirium) and place of discharge.

A quick geriatric assessment was done for each patient as it is routinely done for older patients hospitalized in geriatric ward or during out-patient's examination. This geriatric assessment includes evaluation of comorbidities, nutritional status, cognition, depression, physical performances, functional status and instrumental assessment.

Patient' functional status was assessed by the Katz Activities of Daily Living scale (ADL) including bathing, dressing, toileting, transferring, continence, feeding; and the Lawton instrumental Activities of Daily Living (IADL) including ability to use the telephone, mode of transportation, responsibility for own medications, ability to handle finances. ADL ranges from 0 (severe functional impairment) to 6/6 (full functional status); and IADL from 0 (dependency) to 4/4 (full functional status). The functional status scores were calculated with the patients' abilities 15 days before admission, defined as the preadmission ADL. The complete definition of the geriatric factors and others scores are detailed in Supplementary data.

Study outcomes

The primary outcome was the functional decline defined by a decrease of at least one point on the ADL score.

The other follow-up data collected to describe the population were in-hospital complication, length of hospital stay, place of discharge and data of the geriatric assessment at 3 months as clinical frailty scale, nutritional status, cognition, depression and physical performances.

Statistical analysis

Categorical data are expressed as number (%). Quantitative data are expressed as mean (SD) or median (25th – 75th percentile) according to their distribution. Comparisons between groups are based on data availability within pairs, so if the data were missing for a patient with COVID-19 or his/her control, the matched pair was removed from the comparison. For categorical data, between-group comparisons were tested using McNemar's test for binary data or Fisher's exact test if not applicable. For quantitative data, between-group comparisons were tested using sign tests.

Univariable logistic regression was used to identify factors associated with functional decline. The OR and the confidence intervals (CI) are presented in the charts. Variables in the models were checked for collinearity. All baseline variables with a p-value <0.20 in univariable analysis, the variables already known to be confounding factors and significant baseline differences between COVID-19 patients and controls were included in multivariable logistic regression comparing outcomes between patients with COVID-19 vs controls. A stepwise regression model was also done. A P-value < 0.05 was considered as statistically significant, without correction for multiple testing.

The sample size calculation was not possible at the time

we started the study. Indeed, 3-months functional decline in COVID-19 patients was unknown. In older and frail patients, 3 months' functional decline after hospitalization for acute medical illness is of 22% (16).

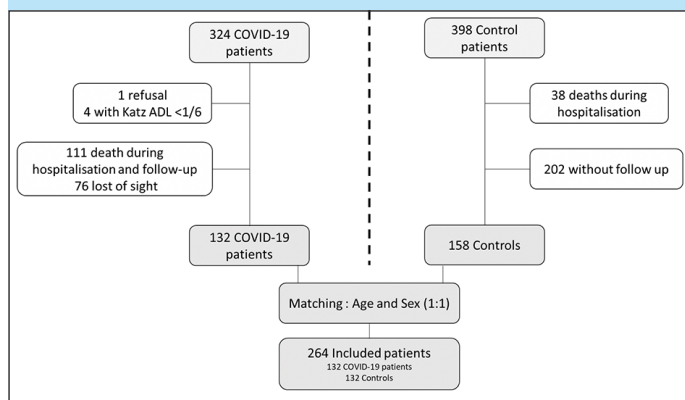
All analyses were performed without imputation, using statistical software R, version 4.0.3 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Study population and baseline characteristics

Between March the 11st 2020 and December the 31th 2020, inclusion was proposed to 326 hospitalized patients with SARS-COV2, in the Acute Geriatric Ward of Nantes University Hospital. One patient refused, two patients were under 75 years old and four had Katz ADL <1/6. On the 319 other patients, 111 (34.2%) died before follow up and 76 patients (23%) were lost of sight (Figure 1). The 132 patients were matched with 132 patients out of the 158 patients of the constituted control group (i.e.controls).

Figure 1. Flow Chart



Indeed, during the study period of the control group, 398 patients were hospitalized in Acute Geriatric Ward for acute infectious pneumonia of whom 38 patients died during hospitalization and 202 patients weren't reassessed during the year following hospitalization. The control group was composed of 113 bacterial pneumonias, 18 influenza pneumonia, of which 12 presented a surinfection, and 1 para-influenza pneumonia.

There were not different for age (87 (83-91) vs 87 (82-90) years) or sex (61% women in both groups) validating an appropriate matching (Table 1). In the COVID-19 group, the median SOFA score was of 2 (IQR=1-3), the median WHO Clinical Progression Scale was of 5 (IQR=4-5) and 53 patients (40,1%) had systemic steroid therapy.

There were statistical significant differences between the COVID-19 group and the control group concerning : living in nursing home (41 (30%) vs 20 (15%) p-value=0.003), CFS (4 (3-5) vs. 5 (4-6), p-value=0.043), cognitive disorders (84 (65%) vs. 100 (76%), p-value=0.032), length of hospital stay in day (11 (7-18) vs. 8 (6-12) , p-value <0.001), length of oxygen supply in day (2 (0-8) vs. 1 (0-3), p-value <0.001), maximal

oxygen supply in L/min (2 (0-4) vs. 1.5 (0-3), p-value=0.025), SOFA score (2 (1-3) vs. 1 (0-2), p-value 0.008), pulmonary oedema (20 (15%) vs. 54 (41%) , p-value <0.001), delirium (34 (26%) vs. 19 (14%), p-value 0.037), and length before follow-up in months (3 (3-3), vs. 4 (3-6), p-value <0.001) (Table 1).

The distribution of the preadmission ADL was comparable in the two groups (Figure 2).

Functional outcomes in patients with COVID-19 and matched controls

At 3-months, 112 out of the 264 included patients (42%) lost one point on the ADL scale. For patients who experimented a functional decline, the ADL score decreased of 2 points in average, without difference between COVID-19 patients or pneumonia patients (-2 vs. -1.99 points). The distribution of the ADL loss was comparable in the two groups (Figure 2).

During the follow-up, there were no differences of acute heart failure and infection occurrences between the two group (each one with a p-value = 0.7), but there was a statistical significant difference for pneumonia recidivism: 1 (1.1%) in the COVID-19 group, and 17 (13%) in the control group (p<0.001). More patients were rehospitalized in the controls group than in the COVID-19 group (47% vs. 20%, p<0.001).

Impact of COVID-19 on functional prognosis

Univariable Analysis

In univariable logistic regression analysis, a statistical significant association was found between functional decline and Charlson comorbidity index (OR=1.17 CI [1.04 ; 1.34], p=0.010) ; major neurocognitive disorder (OR=1.82 CI [1.06; 3.19], p=0.030) ; prior fall (OR=2.06 [1.26 ; 3.40], p=0.004); malnutrition (2.33 [1.40 ; 3.94], p=0.001) ; preadmission IADL (OR=0.75 [0.62 ; 0.90], p=0.002), length of hospital stay (OR=1.05 [1.02 ; 1.08], p<0,001), discharge to rehabilitation center (OR=1.91 CI [1.17 ; 3.14], p=0.009), IADL decline (OR=0.57 CI [0.43 ; 0.73], p<0.001) and increased CFS (OR=3.98 CI [2.74 ; 6.09], p<0.001) (Table 2).

Multivariable analysis

As it was the main interest of our study, we included the COVID-19 status in the multivariable analysis. After reviewing multicollinearity, preadmission ADL, IADL and CSF were found to be correlated. Because of ADL is more frequently used in the current literature on infection and functional decline, we choose to include it in the multivariable analysis. In multivariable logistic regression analysis, there were no statistical significant association between COVID-19 and functional decline (OR=0.76 CI [0.41, 1.40], p=0.38). A statistical significant association was found between functional decline and Charlson comorbidity index (OR=1.16 CI [1.01, 1.35], p=0.039); prior fall (OR=2.08 CI [1.18, 3.72], p=0.012); malnutrition (OR=1.97 CI [1.13, 3.49], p=0.018);

Table 1. Population characteristics according to COVID-19 status

		Population N=264	Control group N=132	COVID-19 group N=132	P value
Demographic	Age	87 (83 ; 90)	87 (83 ; 91)	87 (82 ; 90)	0.50
	Sex	164 (62%)	82 (62%)	82 (62%)	0.70
	Nursing home	60 (23%)	20 (15%)	40 (30%)	0.003
	CFS	5 (3 ; 6)	5 (4 ; 6)	4 (3 ; 5)	0.038
	CCI	3 (2 ; 5)	3 (2 ; 5)	3 (2 ; 5)	>0.99
	Cognitive disorder	184 (70%)	100 (76%)	84 (64%)	0.032
Frailty	Prior fall	126 (48%)	55 (42%)	71 (54%)	0.049
	Malnutrition	156 (60%)	72 (55%)	84 (64%)	0.13
	Number of medication	8 (5 ; 10)	8 (5 ; 10)	8 (5 ; 10)	0.82
	Antidepressive agent	84 (32%)	48 (36%)	36 (27%)	0.11
	Chronic respiratory insufficiency	17 (6.4%)	7 (5.3%)	10 (7.6%)	0.52
Functional status	ADL	5 (4 ; 6)	5 (4 ; 6)	5 (4 ; 6)	>0.99
	IADL	2 (1 ; 3)	2 (1 ; 3)	1 (1 ; 3)	0.31
	Length of stay (day)	9 (7 ; 15)	8 (6 ; 12)	11 (7 ; 18)	<0.001
Severity	Length of oxygen supply (day)	1 (0 ; 5)	1 (0 ; 3)	2 (0 ; 8)	<0.001
	Maximal oxygen supply (L/min)	2 (0 ; 3)	2 (0 ; 3)	2 (0 ; 4)	0.046
	SOFA	1 (0 ; 2)	1 (0 ; 2)	2 (1 ; 3)	0.008
	Cardiovascular complications	82 (31%)	59 (45%)	23 (17%)	<0.001
	Delirium	53 (20%)	19 (14%)	34 (26%)	0.021
In-hospital complications	Acute kidney injury	46 (18%)	24 (18%)	22 (18%)	>0.99
	Peptic ulcer	4 (1.6%)	2 (1.5%)	2 (1.8%)	>0.99
	Thrombosis	15 (5.7%)	7 (5.3%)	8 (6.1%)	>0.99
	Clostridium infection	2 (0.8%)	1 (0.8%)	1 (0.8%)	>0.99
	Time before follow up	3 (3 ; 4)	4 (3 ; 6)	3 (3 ; 3)	<0.001
Follow-up	Rehabilitation center	107 (41%)	50 (38%)	57 (43%)	0.46
	ADL decline	112 (42%)	55 (42%)	57 (43%)	0.89
	IADL decline	86 (34%)	49 (38%)	37 (29%)	0.20
	Rehospitalization	83 (35%)	62 (47%)	21 (20%)	<0.001
	Weight variation	-0.7 (-2.7 ; 0.6)	-0.8 (-2.7 ; 0.4)	-0.4 (-2.2 ; 0.7)	0.07

Data are presented by using no. (%), mean (SD) or median (25th-75th percentile). P-values are calculated using McNemar's or, if not applicable, Fisher's exact test (categorical parameters) or sign test (quantitative parameters); Column "All patients": results are presented in the whole population with available data, after pair selection; CFS: Clinical Frailty Scale; ADL: Katz Activities of Daily Living; CCI : Charlson Comorbidity Index; CFS : Rockwood Clinical frailty scale; IADL : Instrumental Activity of Daily Living of Lawton; SOFA: Sequential Organ Failure Assessment Score

length of hospital stay (OR=1.05 CI [1.02, 1.09], p=0.002) and admission ADL (OR=1.25 CI [1.01, 1.57], p=0.049) (Table 3, Figure 2). To support our study finding, sensitivity analysis with preadmission CFS and preadmission IADL instead of preadmission ADL were done and showed same results (respectively Table 1S. and Table 2S. in Supplementary Data).

Discussion

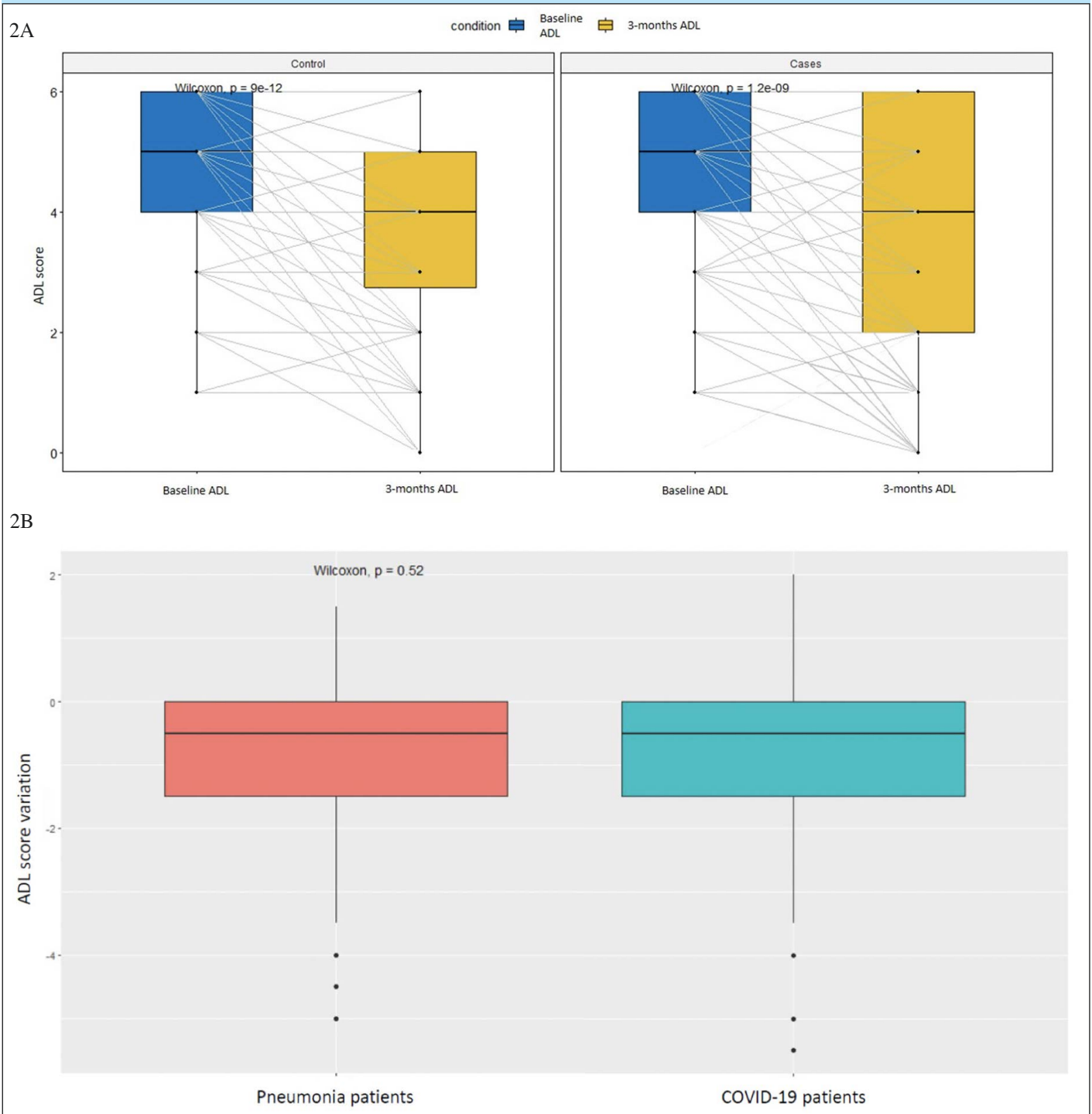
Our study was the first to compare functional prognosis in older survivors after hospitalized COVID-19 infection and other hospitalized patients with infectious lung diseases. We did not demonstrate a different functional prognosis between these two infectious diseases. As described in current published studies,

malnutrition, repeated falls, comorbidities and length of stay were factors associated with functional decline (15, 16, 18, 19).

The few previous studies on long-term COVID-19 functional are mainly descriptive (11, 20–22) or included healthy patients as controls (23). To our knowledge, none of these studies specifically looked at functional impact in older and comorbid population with an index disease as a control group. Because of its predominant respiratory tropism, infectious lung disease seems to us an interesting comparison index, even if bacterial lung infections are not as frequently responsible for systemic inflammatory response and long term persistent symptoms (24).

Despite a significantly more severe initial clinical presentation in the COVID-19 group, the frequency of functional decline in survivors remained comparable in these

Figure 2. ADL repartition (2a) and variation (2b) between preadmission and 3-months follow-up in hospitalized COVID-19 survivors (i.e. cases) and hospitalized pneumonia survivors (i.e. controls)



two groups. According to our study, the factors influencing the functional decline in survivors are more frequently related to the patient's previous frailty as undernutrition, previous falls, comorbidities index rather than to the pathogen or the severity of the infection. The association between comorbidities, frailty and functional decline have already been described in previous studies, in COVID-19 patients and in pneumonia patients, at different time-points (15, 21, 22, 25, 26). This encourages us to favor a global and multidimensional management for older

and comorbid patients rather than a management focused on the pathology.

One unexpected finding in our study was the borderline significant trend towards a higher risk of functional decline in patients with higher preadmission ADL. This data is difficult to analyze as previous studies showed also contradictory results: either prior low functional status nor higher functional status were related to rapid decline after an acute event (27, 28). However, sensitivity analysis with preadmission CFS or

preadmission IADL support our study findings on association between comorbidity, frailty and functional decline.

Table 2. Univariable analysis of factors associated with functional decline in older patients hospitalized for a pneumonia

	OR (95% CI)	P value
COVID-19	0.94 (0.58 ; 1.53)	>0.80
Age	1.04 (0.99 ; 1.09)	0.14
Female	0.99 (0.60 ; 1.64)	0.97
Nursing home	1.25 (0.70 ; 2.23)	0.45
CFS	1.25 (1.04 ; 1.49)	0.015
CCI	1.17 (1.04 ; 1.34)	0.010
Cognitive disorder	1.82 (1.06 ; 3.19)	0.030
Prior fall	2.06 (1.26 ; 3.40)	0.004
Malnutrition	2.33 (1.40 ; 3.94)	0.001
Number of medication	1.02 (0.96 ; 1.09)	0.52
Antidepressive agent	1.46 (0.87 ; 2.47)	0.15
Chronic respiratory insufficiency	1.22 (0.45 ; 3.30)	0.69
ADL	1.03 (0.86 ; 1.24)	0.76
IADL	0.75 (0.62 ; 0.90)	0.002
Length of stay	1.05 (1.02 ; 1.08)	<0.001
Length of oxygen supply	1.01 (0.97 ; 1.05)	0.64
Maximal oxygen supply	0.97 (0.91 ; 1.03)	0.34
SOFA	0.94 (0.79 ; 1.11)	0.48
Cardiovascular complications	1.35 (0.80 ; 2.29)	0.26
Delirium	0.95 (0.51; 1.75)	0.88
Acute kidney injury	0.85 (0.43 ; 1.63)	0.63
Thrombosis	0.90 (0.29 ; 2.57)	0.84
Time before follow up	0.94 (0.83 ; 1.07)	0.35
Subacute care	1.91 (1.17 ; 3.14)	0.009
IADL decline	0.57 (0.43 ; 0.73)	<0.001
CFS rise	3.98 (2.74 ; 6.09)	<0.001
Weight variation	0.98 (0.93 ; 1.04)	0.57

AF : atrial fibrillation; ADL: Katz Activities of Daily Living; CCI : Charlson Comorbidity Index; CFS : Rockwood Clinical frailty scale; CI : Confidence Interval; IADL : Instrumental Activity of Daily Living of Lawton; OR : Odds Ratio; SOFA : Sequential Organ Failure Assessment Score

In our study, 42% of the patients showed a one-point decline in the Katz score whatever the pathogen considered which is consistent with previous studies (22, 29). The proportion of ADL decline among patients with non-COVID-19 pneumonia may varies between studies because of difference in time to endpoint, in the study population or in the activities of daily living assessment. Others studies assessed functional status either with ADL-MSD, a scale on 7 points, 2 months after pneumonia or with a 5 self-care ADL, at different time point (16, 26). In our study, we choose Katz ADL scale as it is the most widely used graded instrument. A one-point decline in the Katz score is clinically important because it might alter the lifestyle of patients and increase the burden on caregivers (25,

30). Pulmonary infection whatever the pathogen considered should therefore be considered as a major element that may be associated with functional decline in this population, justifying a re-evaluation at discharge and at a distance to propose personalized care management (31, 32).

Finally, in-hospital complications revealed that COVID-19 patients experimented less in-hospital acute heart failure than in other pneumonia. This may be related to the prolonged hyperthermia or other symptoms as diarrhea promoting dehydration in COVID-19 patients (33, 34). COVID-19 patients suffered significantly more from delirium. This result was already described and could be related to the severity of the clinical presentations, or to direct brain damage, since the virus passes the blood-brain barrier (34–36). These elements will obviously require further specific studies.

Limitations

Our study had several limitations. First of all, all information on the control group was retrospectively collected. Some elements known to have a significant impact on functional decline in the literature (alcohol consumption, smoking, sensory impairment) could not be retained because of missing data. This choice was necessary to allow a rapid recruitment of control patients. Secondly, the number of loss of sight in the COVID-19 group is also a weakness. It can be explained by the initial difficulty of setting up the follow-up in March 2020 during hospital crisis, but also by the difficulty of organizing it for some patients, socially isolated or with high functional impairment. Third, the COVID-19 disease, by its acute severity in this population (35% of deaths at 3 months) may select the least vulnerable patients, leading to a potential survivorship bias. Fourth, the length before follow-up examination varied significantly between the two groups, which may overestimate the functional decline of patients in the control group. However, as this duration was not significant in the multivariate analysis, we can assume that this impact was minimal. Finally, it is possible that our study presents a lack of statistical power due to an insufficient number of patients. The sample size calculation varies between 182 to 626 patients to include (calculation based on chi-square test and a 2-sided alpha of 0.05; power of 80%). Indeed, post-COVID functional decline varies between 30% to 50% depending on the time of assessment and the settings of recent published studies (16, 21, 22).

Our study also has many strength points. The population studied in the COVID-19 group corresponds to a real life older and comorbid population because of the large inclusion criteria. For example, the death rate of the COVID-19 group was similar to the literature references in older population (33). With the exception of the place of living (nursing home being more frequent in the COVID-19 group), the high CFS status and the cognitive disorders (significantly more frequent in the control group), the two groups remained comparable on many characteristics. These differences are probably explained by recruitment. The Acute Geriatric Ward was privileged interlocutors of the nursing home during the health crisis, but the hospitalization criteria were reviewed due to the hospital

Table 3. Multivariable analysis of factors associated with functional decline in older patients hospitalized for a pneumonia

Variable	Multivariable (Full adjusted model)		Multivariable (Stepwise regression model + COVID-19)	
	OR (95% CI)	P value	OR (95% CI)	P value
COVID-19	0.76 (0.41, 1.40)	0.38	0.78 (0.44 ; 1.35)	0.37
Nursing home	1.56 (0.78, 3.13)	0.21		
CCI	1.16 (1.01, 1.35)	0.039	1.19 (1.04 ; 1.37)	0.012
Cognitive disorder	1.71 (0.91, 3.26)	0.10	1.77 (0.95; 3.36)	0.07
Prior fall	2.08 (1.18, 3.72)	0.012	1.99 (1.13; 3.52)	0.017
Malnutrition	1.97 (1.13, 3.49)	0.018	2.04 (1.17 ; 3.59)	0.012
Preadmission ADL	1.25 (1.01, 1.57)	0.049	1.22 (0.99 ; 1.52)	0.07
Length of stay	1.05 (1.02, 1.09)	0.002	1.04 (1.02 ; 1.09)	0.003
SOFA	0.82 (0.66, 1.02)	0.09	0.86 (0.70 ; 1.05)	0.14
Cardiovascular complications	1.33 (0.70, 2.54)	0.38		
Delirium	1.05 (0.53, 2.08)	0.85		
Time to follow up	0.97 (0.83, 1.13)	0.74		

ADL: Katz Activities of Daily Living; CCI : Charlson Comorbidity Index; CFS : Rockwood Clinical frailty scale; CI : Confidence Interval; OR : Odds Ratio; SOFA : Sequential Organ Failure Assessment Score

overcrowding during the epidemic peaks, with exclusion criteria depending on comorbidities.

Conclusion

Despite a more severe initial clinical presentation than other infectious pneumonias, and despite a high mortality rate, COVID-19 was not responsible of a greater mid-term functional decline than other infectious pneumonias in older and comorbid survivors. This study confirms that the individual preadmission frailty and the length of hospital is a more important prognostic factor concerning functional decline than the pathogen involved. Therefore, a global and multidimensional care management for this population is essential. In future studies, it would be interesting to register ADL score at discharge and at mid-term, in order to describe hospitalization-associated disability and functional loss secondary to long-term symptoms. This information is necessary to develop appropriate multidimensional readaptation care plan. Furthermore, studies are needed to confirm these results in vaccinated patients. Indeed, vaccination decrease COVID-19 mortality but long term symptoms and functional status in that case are still unknown.

Ethical standards: The study was approved by the local ethics committee, Groupe Nantais d'Ethique dans le Domaine de la Santé (GNEDS), which waived the need for informed consent in accordance to legislation on analyses of anonymized data. All research was performed in accordance with the ethical standards set forth in Helsinki declaration (1983).

Conflicts of interest: Sylvain Le Gentil: None. Simon Prampart: None. Matilde Karakachoff: None. Marie Laure Bureau: None. Guillaume Chapelet: None. Laure De Decker: None; Agnès Rouaud: None; Anne-Sophie Bureau: None.

Acknowledgements: We are indebted to Pamela Hublain and Carole Agasse for their assistance in patient enrollment and for their assistance in research organization.

Funding Source: None.

References

1. <https://covid19.who.int/>.
2. <https://dc-covid.site.ined.fr/fr/presentation/q7/>.
3. Zehra Z, Luthra M, Siddiqui SM, Shamsi A, Gaur NA, Islam A. Corona virus versus existence of human on the earth: A computational and biophysical approach. *International Journal of Biological Macromolecules* 2020;161:271–281.
4. 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;324:782–793.
5. Rod JE, Oviedo-Trespalacios O, Cortes-Ramirez J. A brief-review of the risk factors for covid-19 severity. *Rev Saude Publica* 2020;54:60.
6. Logue JK, Franko NM, McCulloch DJ, McDonald D, Magedson A, Wolf CR, Chu HY. Sequelae in Adults at 6 Months After COVID-19 Infection. *JAMA Network Open* 2021;4:e210830–e210830.
7. Garrigues E, Janvier P, Kherabi Y, Le Bot A, Hamon A, Gouze H, Doucet L, Berkani S, Oliosi E, Mallart E, Corre F, Zarrouk V, Moyer J-D, Galy A, Honsel V, Fantin B, Nguyen Y. Post-discharge persistent symptoms and health-related quality of life after hospitalization for COVID-19. *J Infect* 2020;81:e4–e6.
8. Rai DK, Kumar S, Sahay N. Post-COVID-19 pulmonary fibrosis: A case series and review of literature. *J Family Med Prim Care* 2021;10:2028–2031.
9. Bierman AS. Functional status: the six vital sign. *J Gen Intern Med* 2001;16:785–786.
10. Prescott HC, Angus DC. Enhancing Recovery From Sepsis: A Review. *JAMA* 2018;319:62–75.
11. Zhu S, Gao Q, Yang L, et al. Prevalence and risk factors of disability and anxiety in a retrospective cohort of 432 survivors of Coronavirus Disease-2019 (Covid-19) from China. *PLoS One* 2020;15:e0243883.
12. Maltese G, Corsonello A, Di Rosa M, Soraci L, Vitale C, Corica F, Lattanzio F. Frailty and COVID-19: A Systematic Scoping Review. *J Clin Med* 2020;9. doi:10.3390/jcm9072106.
13. Owen RK, Conroy SP, Taub N, Jones W, Bryden D, Pareek M, Faull C, Abrams KR, Davis D, Banerjee J. Comparing associations between frailty and mortality in hospitalised older adults with or without COVID-19 infection: a retrospective observational study using electronic health records. *Age Ageing* 2021;50:307–316.
14. Büla CJ, Ghilardi G, Wietlisbach V, Petignat C, Francioli P. Infections and functional impairment in nursing home residents: a reciprocal relationship. *J Am Geriatr Soc* 2004;52:700–706.
15. Davydow DS, Hough CL, Levine DA, Langa KM, Iwashyna TJ. Functional disability, cognitive impairment, and depression after hospitalization for pneumonia. *Am J Med* 2013;126:615–624.e5.
16. Boyd CM, Landefeld CS, Counsell SR, Palmer RM, Fortinsky RH, Kresevic D, Burant C, Covinsky KE. Recovery of activities of daily living in older adults after hospitalization for acute medical illness. *J Am Geriatr Soc* 2008;56:2171–2179.
17. Azoulay É, Beloucif S, Guidet B, Pateron D, Vivien B, Le Dorze M. Admission decisions to intensive care units in the context of the major COVID-19 outbreak: local guidance from the COVID-19 Paris-region area. *Crit Care* 2020;24:293.
18. Stuck AE, Walthert JM, Nikolaus T, Büla CJ, Hohmann C, Beck JC. Risk factors for functional status decline in community-living elderly people: a systematic literature review. *Soc Sci Med* 1999;48:445–469.

19. Huggan PJ, Akram F, Er BHD, Christen LSJ, Weixian L, Lim V, Huang Y, Merchant RA. Measures of acute physiology, comorbidity and functional status to differentiate illness severity and length of stay among acute general medical admissions: a prospective cohort study. *Intern Med J* 2015;45:732–740.
20. AR Mohamed Hussein A, Galal I, Saad MM, Zayan HEE, Abdelsayed MZ, Moustafa MM, Ezzat AR, Helmy RE, Abd Elaal HK, Aly K, Abdelrheem SS. Post-COVID-19 Functional Status: Relation to age, smoking, hospitalization and comorbidities. medRxiv:2020.08.26.20182618.
21. Carrillo-García P, Garmendia-Prieto B, Cristofori G, Montoya IL, Hidalgo JJ, Feijoo MQ, Cortés JJB, Gómez-Pavón J. Health status in survivors older than 70 years after hospitalization with COVID-19: observational follow-up study at 3 months. *Eur Geriatr Med* 2021;12:1091–1094.
22. Hosoda T, Hamada S. Functional decline in hospitalized older patients with coronavirus disease 2019: a retrospective cohort study. *BMC Geriatrics* 2021;21:638.
23. Rooney S, Webster A, Paul L. Systematic Review of Changes and Recovery in Physical Function and Fitness After Severe Acute Respiratory Syndrome–Related Coronavirus Infection: Implications for COVID-19 Rehabilitation. *Physical Therapy* 2020;100:1717–1729.
24. El Moussaoui R, Opmeer BC, de Borgie CAJM, Nieuwkerk P, Bossuyt PMM, Speelman P, Prins JM. Long-term symptom recovery and health-related quality of life in patients with mild-to-moderate-severe community-acquired pneumonia. *Chest* 2006;130:1165–1172.
25. Andrew MK, MacDonald S, Godin J, McElhaney JE, LeBlanc J, Hatchette TF, Bowie W, Katz K, McGeer A, Semret M, McNeil SA. Persistent Functional Decline Following Hospitalization with Influenza or Acute Respiratory Illness. *J Am Geriatr Soc* 2021;69:696–703.
26. Griffith MF, Levy CR, Parikh TJ, Stevens-Lapsley JE, Eber LB, Palat S-IT, Gozalo PL, Teno JM. Nursing Home Residents Face Severe Functional Limitation or Death After Hospitalization for Pneumonia. *J Am Med Dir Assoc* 2020;21:1879–1884.
27. Baker DW, Hays RD, Brook RH. Understanding changes in health status. Is the floor phenomenon merely the last step of the staircase? *Med Care* 1997;35:1–15.
28. Bindman AB, Keane D, Lurie N. Measuring Health Changes among Severely Ill Patients: The Floor Phenomenon. *Medical Care* 1990;28:1142–1152.
29. Loyd C, Markland AD, Zhang Y, Fowler M, Harper S, Wright NC, Carter CS, Buford TW, Smith CH, Kennedy R, Brown CJ. Prevalence of Hospital-Associated Disability in Older Adults: A Meta-analysis. *J Am Med Dir Assoc* 2020;21:455–461.e5.
30. Suijker JJ, van Rijn M, ter Riet G, van Charante EPM, de Rooij SE, Buurman BM. Minimal important change and minimal detectable change in activities of daily living in community-living older people. *J Nutr Health Aging* 2017;21:165–172.
31. Martínez-Velilla N, Sáez de Asteasu ML, Ramírez-Vélez R, Zambom-Ferraresi F, García-Hermoso A, Izquierdo M. Recovery of the Decline in Activities of Daily Living After Hospitalization Through an Individualized Exercise Program: Secondary Analysis of a Randomized Clinical Trial. *The Journals of Gerontology: Series A* 2021;76:1519–1523.
32. Ortiz-Alonso J, Bustamante-Ara N, Valenzuela PL, Vidán-Astiz M, Rodríguez-Romo G, Mayordomo-Cava J, Javier-González M, Hidalgo-Gamarrá M, Lopéz-Tatis M, Valades-Malagón MI, Santos-Lozano A, Lucia A, Serra-Rexach JA. Effect of a Simple Exercise Program on Hospitalization-Associated Disability in Older Patients: A Randomized Controlled Trial. *Journal of the American Medical Directors Association* 2020;21:531-537.e1.
33. Zerah L, Baudouin É, Pépin M, et al. Clinical Characteristics and Outcomes of 821 Older Patients With SARS-Cov-2 Infection Admitted to Acute Care Geriatric Wards. *J Gerontol A Biol Sci Med Sci* 2021;76:e4–e12.
34. ISARIC Clinical Characterisation Group. COVID-19 symptoms at hospital admission vary with age and sex: results from the ISARIC prospective multinational observational study. *Infection*; 2021. doi:10.1007/s15010-021-01599-5.
35. Bougakov D, Podell K, Goldberg E. Multiple Neuroinvasive Pathways in COVID-19. *Molecular Neurobiology* 2021;58:564–575.
36. Divani AA, Andalib S, Biller J, Di Napoli M, Moghimi N, Rubinos CA, Nobleza CO, Sylaja PN, Toledano M, Lattanzi S, McCullough LD, Cruz-Flores S, Torbey M, Azarpazhooh MR. Central Nervous System Manifestations Associated with COVID-19. *Curr Neurol Neurosci Rep* 2020;20:60.

How to cite this article: S. Le Gentil, S. Prampart, M. Karakachoff, et al. Functional Decline in COVID-19 Older Survivors Compared to Other Pneumonia Patients, a Case Control Study. *J Nutr Health Aging*.2022;26(9):896-903; <https://doi.org/10.1007/s12603-022-1845-1>