

1 **Text word counts:**

2 **Brief Report**

3 **PREDICTORS OF LOW PHYSICAL FUNCTION IN COVID-19 PATIENTS WITH ACUTE**
4 **RESPIRATORY FAILURE ADMITTED TO A SUB-ACUTE UNIT**

5
6 ~~PATIENTS RECOVERING FROM COVID-19 PNEUMONIA AT A SUB-ACUTE ADMISSIONS~~
7 ~~UNIT EXHIBIT PROFOUND PHYSICAL FUNCTION DISABILITY~~

8
9 **Abstract (189)**

10
11 This is a cross-sectional study performed in 184 COVID-19 patients (74±12 years) who were admitted to a
12 sub-acute unit to stabilize their condition and recover from acute respiratory failure due to COVID-19.

13 **Aim.** The aim of the study was to document the level of physical function in COVID-19 patients recovering
14 from Acute Respiratory Failure (ARF) and investigate which patient clinical characteristics could predict
15 physical function assessed by the Short Physical Performance Battery (SPPB) test.

16 **Methods.** At admission patients underwent the SPPB test, represented by the sum of three functional tests:
17 standing balance, 4-meter gait speed (4-MGS), and five-repetition sit-to-stand (5-STSS) motion. Comparison
18 between groups were performed by an unpaired t-test; multivariate stepwise linear regression analysis was
19 employed to detect associations between SPPB score and clinical parameters.

20 **Results.** SPPB score was 3.02±3.87 denoting patients' profound physical dysfunction. Normal physical
21 function was detected in only 12% of patients, whereas low, intermediate and severe impairment was found in
22 65%, 13% and 10% respectively. Age, both invasive and non-invasive ventilation use, and the presence of
23 previous disability were significant predictors of SPPB. Patients without any comorbidities (8%) also exhibited
24 low function (SPPB: 5.67±1.12).

25 **Conclusions.** The majority of COVID-19 survivors experienced ARF due to pneumonia and exhibit substantial
26 physical dysfunction influenced by age, mechanical ventilation need and previous disability. Further studies are

27 needed to evaluate the role of rehabilitation to promote recovery and community reintegration in this
28 population.

29
30 **Keywords:** disability; coronavirus; rehabilitation; outcome; physical function

31
32 **Abbreviation list**

33
34 **ARF:** Acute Respiratory Failure

35 **CIRS:** Cumulative Illness Rating Scale

36 **CPAP:** Continuous Positive Airways Pressure

37 **COVID-19:** Corona Virus Disease 2019

38 **FiO₂:** Inspiratory Fraction of Oxygen

39 **IMV:** Invasive Mechanical Ventilation,

40 **NIV:** Non-Invasive Ventilation

41 **SpO₂:** Percentage of oxygen saturation

42 **SPPB:** Short Physical Performance Battery

43 **4-MGS:** 4-meter gait speed

44 **5-STTS:** five-repetition sit-to-stand

49 **Introduction**

50
51 Studies describe a wide variety of clinical presentations for COVID-19 infectious disease, ranging from
52 absence of symptoms to pneumonia with Acute Respiratory Failure (ARF).^{1,2} ARF is associated with prolonged
53 functional impairment in many individuals and the recovery from this critical illness is fraught with challenges.³

54 **Local unpublished data estimate that approximately 40% of patients with COVID-19 present ARF, with and**
55 **without hospitalisation need.** A recent study by **Belli and colleagues⁴**, showed that 75% of patients entering a
56 COVID-19 ward following acute hospitalization, exhibited very low physical functioning and experienced
57 impaired performance of daily physical activities. Further improvement in our understanding of the factors that
58 influence physical function recovery after critical illness, may help inform survivors of the challenges and
59 milestones of their recovery period⁵, along with the appropriate prescription of rehabilitation interventions.⁶

60 The aim of this pragmatic cross-sectional study was to show the level of physical function in another cohort of
61 COVID-19 patients with ARF due to pneumonia, that were admitted **to a sub-acute unit** to stabilize their
62 condition. The secondary aim was to investigate which clinical characteristics during hospitalisation could
63 predict physical function, assessed by the Short Physical Performance Battery (SPPB) test.⁷

64
65 **Methods**

66 Consecutive patients recovering from ARF due to COVID-19 pneumonia, were admitted from the Emergency
67 Area of several acute hospitals to a **sub-acute Unit of the Lumezzane, Brescia, Lombardy Region** from 10 March
68 2020 to 30 April 2020. **The change of hospital mission was due to the emergency situation of the Covid-19**
69 **pandemic in Italy.** The study was approved by the Local Review Board and Ethics Committee (xxxx).

70 At the point of admission patients underwent the SPPB test, a standardized, objective, rapid and simple to
71 conduct assessment.⁷ The SPPB represents the sum of results from three functional tests: standing balance, 4-
72 meter gait speed (4-MGS), and five-repetition sit-to-stand (5-STs) manoeuvre. Each component is scored based
73 on a subscale, and the three sub-scores are added to obtain a summary score.⁷ Scores between 0-3 denote severe
74 physical function disability, 4-6 low function, 7-9 intermediate function, and 10-12 normal function.⁷ Predicted

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75 values for the SPPB were calculated using normative values for total SPPB score and a European population
76 aged ≥ 40 years, stratified for age and sex.⁸

77 SPPB scores have been previously shown to be highly predictive of disability, hospitalization,
78 institutionalisation, and mortality in older patients.⁹ The Cumulative Illness Rating Scale (CIRS)¹⁰ score was
79 used to assess the number of comorbidities, whereas cognitive deficits were defined using a Mini Mental State
80 Examination score < 20 points. We defined the presence of previous disability through the anamnestic
81 impossibility to walk without assistance or walking aid devices prior to Covid-19 infection.

82 Comparisons between groups were performed using an unpaired t-test. Stepwise multivariate linear regression
83 analysis was employed to investigate predictors of physical function captured by the SPPB score, from patient
84 demographic and clinical characteristics (sex, age, BMI, number of comorbidities, FiO₂ and SpO₂ at admission,
85 use of invasive ventilation, use of non-invasive ventilation or continuous positive airway pressure, presence of
86 tracheostomy, hospital length of stay and previous disability). $P < 0.05$ was considered statistically significant.

89 Results

91 **Table 1** shows demographic and clinical data of all 184 consecutive patients hospitalised in our hospital.

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We defined the presence of previous disability as the inability to walk without assistance or a walking aid prior to COVID-19 infection.

Table 1. Patient characteristics in all population and in subgroups of patients with SPPB score ≤ 3.0 and SPPB score > 3.0 .

Variables	All (n=184)	SPPB ≤ 3.0 (n=118)	SPPB > 3.0 (n=66)	p
Male, %	50	46.61	60.61	0.068
Age, years	74 \pm 12	78 \pm 11	69 \pm 11	0.001
<i>Patients with age < 60 years, %</i>	11.96	22.73	5.93	0.001
<i>Patients with age > 85 years, %</i>	17.39	25.42	3.03	0.001
CIRS score	3.44 \pm 2.16	4.08 \pm 2.35	2.29 \pm 1.75	0.001
BMI score	26.24 \pm 4.80	26.23 \pm 5.10	26.27 \pm 4.36	0.9601
<i>Absence of any comorbidities, %</i>	8.15	5.93	12.12	0.001
<i>More than 2 comorbidities, %</i>	43.48	57.63	18.18	0.001
Previous disability, %	32.61	44.07	12.12	0.001
Cognitive deficits, %	10.87	16.10	1.52	0.002
Length of acute hospital stay, days	14 \pm 10	15 \pm 11	13 \pm 8	0.096
Tracheotomy, % of patients	4.35	5.93	1.52	0.159
Only NIV/CPAP, % of patients	21.74	23.73	18.18	0.382
NIV + IMV, % of patients	8.70	11.02	4.55	0.135
FiO ₂ , %	28.5 \pm 11.72	28.39 \pm 12.46	26.68 \pm 10.35	0.875
SpO ₂ , %	94.97 \pm 2.17	94.76 \pm 2.22	95.35 \pm 2.06	0.079
SPO ₂ /FiO ₂	370 \pm 98	372 \pm 99	365 \pm 97	0.627

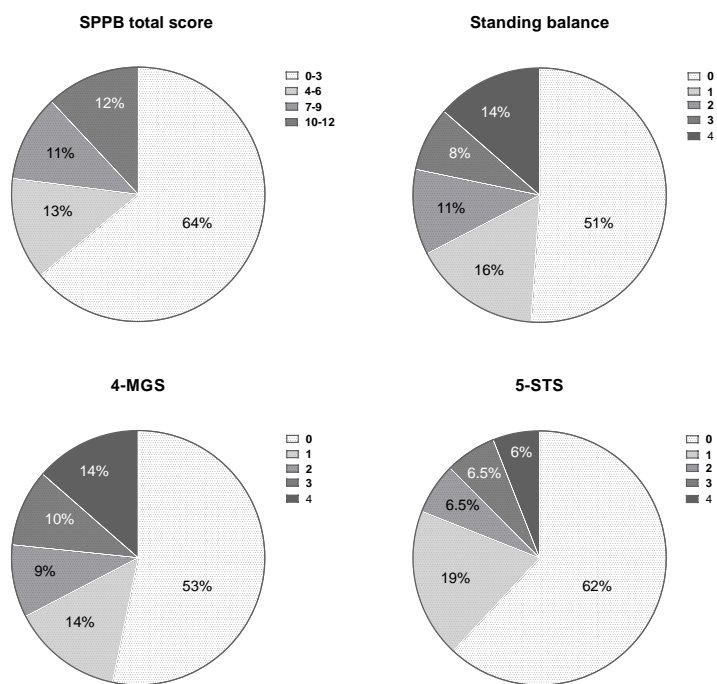
Legend: Values are presented as mean \pm SD or as a fraction. CIRS = Cumulative Illness Rating Scale, NIV = Non-Invasive Ventilation, CPAP= Continuous Positive Airways Pressure, IMV= Invasive Mechanical Ventilation, FiO₂ = Inspiratory Fraction of Oxygen, SpO₂ = Percentage of oxygen saturation.

The total SPPB score was 3.1 ± 3.9 ($26.8 \pm 33.4\%$ predicted normal), with 64% of patients exhibiting SPPB scores ≤ 3.0 . Mean values for the balance score was 1.2 ± 1.5 , 1.2 ± 1.5 for the 4-MGS score and 0.8 ± 1.2 for the 5-STS score. The 4-MGS duration was 7.7 ± 3.8 seconds and the 5-STS duration was 17.76 ± 6.71 seconds.

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Figure 1 depicts the SPPB score distribution in relation to severity levels. Differences between patients with a SPPB score ≤ 3.0 (bedbound patients) and those with SPPB > 3.0 were significant for age, the number of comorbidities, absence of any reported comorbidities, cognitive deficits and the presence of previous disabilities (Table 1).

Figure 1. Physical function disability evaluated by SPPB (as total score, panel A) and for each component of SPPB test (panels B-D).



19 **Legend:** Fractional representation of patients (n=184) relative to the total SPPB score (A), the standing balance
20 score (B), the 4-meter gait speed (4-MGS) score (C), and the five-repetition sit-to-stand (5-STS) score (D).

21
22 On the basis of stepwise linear regression analysis including all baseline variables, a better functional status
23 (higher SPPB score) was directly inversely related to previous disability (B= -2.9839, SE=0.494, p<0.001), age
24 (B= -0.1916, SE=0.021, p<0.001), invasive mechanical ventilation (B= -3.8802, SE=0.9035, p<0.001), use of
25 non-invasive mechanical ventilation (NIV/CPAP) (B=-2.3928, SE= 0.6061, p = 0.001) (R2 of regression model
26 was 0.4292). Nevertheless, patients with comorbidities (n=169, 91.85%) show highest physical impairment
27 [SPPB 2.86 (3.78), 25 (32.58) % predicted normal] when compared to patients without comorbidities (n= 15,
28 8.15%) (SPPB score 5.67±1.12 (47.2 ±36.3% predicted normal) (p <0,001).

29 When compared to patients with comorbidities patients, without any comorbidities were younger [56.47±10.32
30 vs 76.05±10.48 years, P<0.001] but with longer length of hospital stay [19.73±10.74 vs 13.87±9.59 days,
31 P=0.0263], having undergone tracheostomy [26.67% vs 2.37%, p =0.001] and required more invasive
32 mechanical ventilation [46.67% vs 5.33%, p=0.001] and non-invasive ventilation [46.67% vs 19.53%,
33 p=0.015].

36 Discussion

37
38 This pragmatic study highlights that physical function disability is highly prevalent in patients
39 recovering from ARF from COVID-19 infection, being present in approximately 2/3 of patients admitted to a
40 dedicated sub-acute Covid-19 Department. The study confirms recent data from the literature,⁴ demonstrating
41 that age, mechanical ventilation need, and previous disability may strongly influence this functional
42 impairment.

43 In non COVID ARF survivors with SPPB scores ≤3.0, physical function either does not recover within 6
44 months, or it improves initially but survivors remain functionally disabled by 6 months³. Similarly, to patients

45 recovering from severe influenza A (H1N1),¹¹ those with an acute COVID event may have functional damage
46 both in the short and long term periods following discharge. Undoubtedly, patients with comorbidities usually
47 take longer to return to their former condition.³

48 The findings of impaired physical function status in our study population, encompassing severely
49 compromised strength, balance and walking function, validate relevant recommendations on referral to
50 rehabilitation services for COVID-19 survivors. As the effect of muscle activity associated with viral agents is
51 not known, active mobilisation and low intensity exercise are indicated in this post-acute phase, when safe to do
52 so, to improve physical capacity and prevent the development of persistent disability.¹²

53 Variables predicting a pathological SPPB score include age, invasive ventilation and non-invasive
54 ventilation use and physical function status in ARF survivors.³⁻⁵ Interestingly, our study suggests that
55 comorbidities are also predominant in COVID-19 patients with ARF, with significant physical function
56 disability, whereas absence of any comorbidity is associated with better functional status, albeit not completely
57 eliminating the risk of suffering profound functional limitations. Accordingly, alert protocols for the early
58 detection of deterioration in physical performance and early physiotherapy interventions should be considered
59 for all patients, but particularly those with comorbidities.

60 Importantly, our study confirms the value of the SPPB instrument to stratify physical function as part of
61 the onward referral process to rehabilitation services, in the absence of more sophisticated testing due to
62 infection risk. The routine bedside use of a simple and well documented test, such as the SPPB test, has been
63 well accepted and deemed useful in this population.

64 The main limitations of our report are: a) the possible low external validity, as the study only included
65 patients who needed an intermediate care setting, therefore only representing a partial picture of the COVID-
66 19 population discharged from an acute context (we did not take into account patients remained in a high-
67 intensity care setting and patients with mild illness who were discharged home); b) the limited number of
68 variables we included in our regression analysis (due to the lack of other clinical information such as drug
69 therapy performed in the Emergency Area and social status) may limit the amount of valuable information that
70 we could gather from our results; c) the emergency situation in which the study was conducted affecting

71 hospital capacity, patient increase, resources, etc., which could have had a negative impact on patient
72 autonomy.

73 In conclusion, the majority of COVID-19 survivors experienced ARF due to pneumonia exhibit substantial
74 physical dysfunction, **influenced by age, mechanical ventilation need and previous disability**. Screening
75 rehabilitation needs in the acute and sub-acute setting should be performed through simple functional and
76 disability assessments. **Future studies on rehabilitation interventions are mandatory in order to define the role
77 rehabilitation could play in those recovering from COVID-19 pneumonia.**

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