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Brief Report

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

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

Abstract (189)

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

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

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

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

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

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

Keywords: disability; coronavirus; rehabilitation; outcome; physical function

Abbreviation list

ARF: Acute Respiratory Failure

CIRS: Cumulative Illness Rating Scale

CPAP: Continuous Positive Airways Pressure

COVID-19: Corona Virus Disease 2019

FiO_2: Inspiratory Fraction of Oxygen

IMV: Invasive Mechanical Ventilation,

NIV: Non-Invasive Ventilation

SpO_2: Percentage of oxygen saturation

SPPB: Short Physical Performance Battery

4-MGS: 4-meter gait speed

5-STS: five-repetition sit-to-stand

Introduction

Studies describe a wide variety of clinical presentations for COVID-19 infectious disease, ranging from absence of symptoms to pneumonia with Acute Respiratory Failure (ARF).[1,2] ARF is associated with prolonged functional impairment in many individuals and the recovery from this critical illness is fraught with challenges.[3] Local unpublished data estimate that approximately 40% of patients with COVID-19 present ARF, with and without hospitalisation need. A recent study by Belli and colleagues[4], showed that 75% of patients entering a COVID-19 ward following acute hospitalization, exhibited very low physical functioning and experienced impaired performance of daily physical activities. Further improvement in our understanding of the factors that influence physical function recovery after critical illness, may help inform survivors of the challenges and milestones of their recovery period[5], along with the appropriate prescription of rehabilitation interventions.[6]

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

Methods

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

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

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

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

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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.

Comparisons between groups were performed using an unpaired t-test. Stepwise multivariate linear regression analysis was employed to investigate predictors of physical function captured by the SPPB score, from patient demographic and clinical characteristics (sex, age, BMI, number of comorbidities, FiO_2 and SpO_2 at admission, use of invasive ventilation, use of non-invasive ventilation or continuous positive airway pressure, presence of tracheostomy, hospital length of stay and previous disability). $P < 0.05$ was considered statistically significant.

Results

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

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±12	78±11	69±11	0.001
Patients with age < 60 years, %	11.96	22.73	5.93	0.001
Patients with age > 85 years , %	17.39	25.42	3.03	0.001
CIRS score	3.44±2.16	4.08±2.35	2.29±1.75	0.001
BMI score	26.24±4.80	26.23±5.10	26.27±4.36	0.9601
Absence of any comorbidities, %	8.15	5.93	12.12	0.001
More than 2 comorbidities, %	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 ±10	15±11	13±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±11.72	28.39±12.46	26..68±10.35	0.875
SpO_2, %	94.97±2.17	94.76±2.22	95.35±2.06	0.079
SPO_2/FiO_2	370±98	372±99	365±97	0.627

Legend: Values are presented as mean±SD or as a fraction. CIRS = Cumulative Illness Rating Scale, NIV = Non-Invasive Ventilation, CPAP= Continuous Positive Airways Pressure, IMV= Invasive Mechanical Ventilation, FiO_2 = Inspiratory Fraction of Oxygen, SpO_2 = Percentage of oxygen saturation.

The total SPPB score was 3.1±3.9 (26.8± 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. **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).

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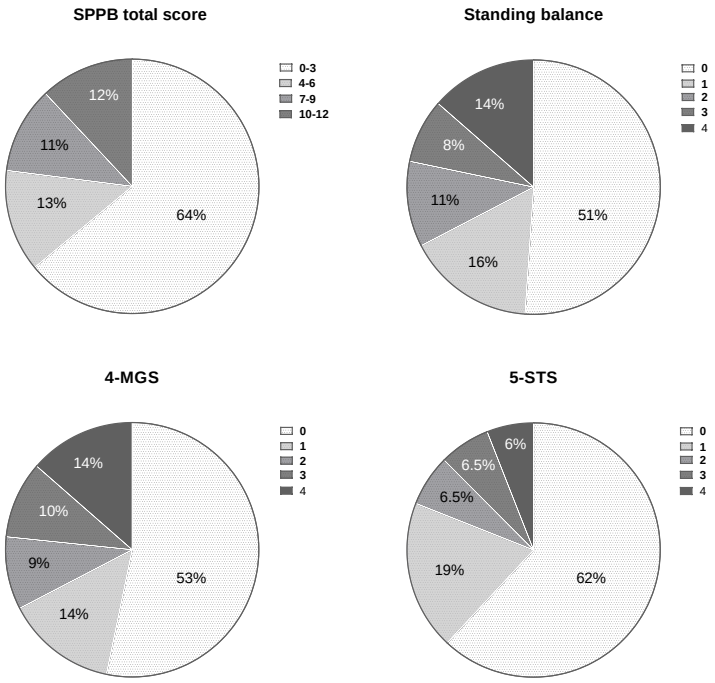
Figure 1. Physical function disability evaluated by SPPB (as total score, panel A) and for each component of SPPB test (panels B-D).



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

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

When compared to patients with comorbidities patients, without any comorbidities were younger [56.47±10.32 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, P=0.0263], having undergone tracheostomy [26.67% vs 2.37%, p =0.001] and required more invasive mechanical ventilation [46.67% vs 5.33%, p=0.001] and non-invasive ventilation [46.67% vs 19.53%, p=0.015].

Discussion

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

In non COVID ARF survivors with SPPB scores ≤3.0, physical function either does not recover within 6 months, or it improves initially but survivors remain functionally disabled by 6 months[3]. Similarly, to patients

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

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

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

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

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

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

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

REFERENCES

1. Lian J, Jin X, Hao S, et al. Analysis of Epidemiological and Clinical features in older patients with Corona Virus Disease 2019 (COVID-19) out of Wuhan. *Clin Infect Dis.* 2020;71(15):740-747.
2. Wang CY, Calfee CS, Paul DW, et al. One-year mortality and predictors of death among hospital survivors of acute respiratory distress syndrome. *Intensive Care Med* 2014; 40(3):388-396.
3. Gandotra S, Lovato J, Case D, et al. Physical Function Trajectories in Survivors of Acute Respiratory Failure. *Ann Am Thorac Soc* 2019; 16(4):471-477.
4. Belli S, Balbi B, Prince I, et al. Low physical functioning and impaired performance of activities of daily life in COVID-19 patients who survived the hospitalisation. *Eur Respir J.* 2020 Aug 6:2002096. doi: 10.1183/13993003.02096-2020.
5. Herridge MS, Chu LM, Matte A, et al.; RECOVER Program Investigators (Phase 1: towards RECOVER); Canadian Critical Care Trials Group. The RECOVER program: disability risk groups and 1-year outcome after 7 or more days of mechanical ventilation. *Am J Respir Crit Care Med* 2016;194(7):831–844.
6. Brown SM, Wilson EL, Presson AP, et al. Understanding patient outcomes after acute respiratory distress syndrome. Identifying subtypes of physical, cognitive and mental health outcomes. *Thorax* 2017; 72(12):1094-1103.
7. Guralnik JM, Simonsick EM, Ferrucci L, et al. A short physical performance battery assessing lower

extremity function: association with self-reported disability and prediction of mortality and nursing home admission. *J Gerontol*. 1994; 49(2):M85-M94.

8. Bergland A, Strand B. Norwegian reference values for the Short Physical Performance Battery (SPPB): the Tromsø Study. *BMC Geriatr*. 2019;19:216.

9. Studenski S, Perera S, Wallace D, et al. Physical performance measures in the clinical setting. *J Am Geriatr Soc* 2003;51(3)**:**314–322.

10. Salvi F, Miller MD, Grilli A, et al. A manual of guidelines to score the modified Cumulative Illness Rating Scale and its validation in acute hospitalized elderly patients. *J Am Geriatr Soc* 2008;56(10):1926–1931.

11. Luyt CE, Combes A, Becquemin MH, et al. Long-term outcomes of pandemic 2009 influenza A(H1N1)-associated severe ARDS. *Chest.* 2012;142(3):583–592.

12. Vitacca M, Carone M, Clini EM, et al; on behalf of the Italian Thoracic Society (ITS - AIPO), the Association for the Rehabilitation of Respiratory Failure (ARIR) and the Italian Respiratory Society (SIP/IRS). Joint statement on the role of respiratory rehabilitation in the COVID-19 crisis: the Italian position paper. *Respiration.* 2020;99(6):493-499.