Functional Outcome in an Inpatient Rehabilitation Setting After Post-Intensive Care Syndrome due to COVID-19: A Retrospective Study

Resultados Funcionais num Ambiente de Reabilitação em Regime de Internamento após Síndrome de Cuidados Pós-Intensivos devido à COVID-19: Um Estudo Retrospetivo

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Abstract

Introduction: *Coronavirus disease 2019 (COVID-19) can cause acute respiratory distress syndrome and acute respiratory failure, requiring hospitalization. The complications and functional consequences of hospitalization at intensive-care units (ICU) are called post-intensive care syndrome (PICS). This study aimed to describe functional outcomes in patients with PICS due to COVID-19 and evaluate the factors that could influence or even predict these outcomes.*

Methods: *This retrospective study included all patients admitted to an inpatient rehabilitation facility (IRF) following hospitalization for critical COVID-19. We recorded the potentially useful patient demographics and clinical characteristics.*

Results: *This study included 18 patients, most of them male, with a mean age of 60 years. We noted an important radiological pulmonary involvement by the disease in all patients, and most required oxygen supply upon admission to the IRF. The total functional independence measure (FIM) and medical research council sum scores (MRC-SS) significantly improved from admission to discharge. A higher percentage of radiological pulmonary involvement and a higher fraction of inspired oxygen (FiO2) at admission to the IRF were associated with greater FIM variation between admission and discharge. Additionally, a lower FIM at admission correlated with a greater variation in FIM during the IRF stay. A higher MRC-SS at discharge was associated with a higher FIM. Conversely, a greater need for oxygen support at discharge predicted a lower FIM score.*

Conclusion: *Inpatient rehabilitation was associated with significant motor and functional improvement in our sample. The functional recovery of our patients correlated more with radiological pulmonary involvement, the need for oxygen support, and the overall functionality at admission rather than with the muscle weakness. Cardiopulmonary condition at discharge, as expressed by FiO2, was more important than muscle strength in defining functional outcomes at discharge and even predicted FIM at discharge. According to our study, patients with more severe respiratory/pulmonary involvement by COVID-19 and lower levels of functional independence at admission may benefit the most from integrating an inpatient rehabilitation program into an acute/subacute IRF.*

Keywords: *COVID-19/rehabilitation; Inpatients; Intensive Care Units; Recovery of Function.*

Resumo

Introdução: A COVID-19 pode causar uma síndrome

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respiratória aguda grave com insuficiência respiratória aguda e necessidade de hospitalização. As complicações e consequências funcionais de um internamento numa Unidade de Cuidados Intensivos (UCI) denominam-se de síndrome pós-internamento em UCI (SPICI). Este estudo visa descrever a evolução funcional de doentes com SPICI por COVID-19, avaliando potenciais fatores que podem influenciar ou até predizer essa mesma evolução.

Métodos: Este estudo retrospetivo incluiu todos os pacientes internados num Serviço de Medicina Física e de Reabilitação (MFR) após internamento em contexto de COVID-19 crítica. Foram recolhidos dados relativos às características clínicas e demográficas desses pacientes.

Resultados: Este estudo incluiu 18 pacientes, a maioria do sexo masculino, com uma média de 60 anos de idade. Constatou-se um importante envolvimento radiológico pela doença em todos os pacientes, e a maior parte deles ainda necessitava de oxigénio suplementar à admissão no internamento de MFR. A medida de independência funcional (MIF) total e o *Medical Research Council Sum-Score* (MRC-SS) aumentaram significativamente desde a admissão até à alta do internamento de MFR. Quanto maior a percentagem de envolvimento pulmonar radiológico pela doença e a necessidade de oxigénio suplementar (FiO2) à admissão no internamento de MFR, maior a variação da MIF entre a admissão e a alta. A presença de uma MIF menor à admissão também se correlacionou com uma maior variação da MIF durante o internamento. Quanto maior o MRC-SS à data de alta, maior a MIF nesse momento. Por outro lado, a maior necessidade de suplementação de oxigénio à data de alta prediz uma MIF menor nesse momento.

Conclusão: O internamento no Serviço de Reabilitação esteve associado a uma evolução motora e funcional significativas. A recuperação funcional dos nossos pacientes esteve mais correlacionada com o envolvimento radiológico pela doença, a necessidade de suplementação de oxigénio e a funcionalidade global à admissão, do que propriamente com a força muscular. A condição cardiopulmonar à data de alta, expressa pela FiO2, revelou-se mais importante do que a força muscular para definir o resultado funcional à data de alta, e inclusivamente predisse a MIF à data de alta. Assim, de acordo com o nosso estudo, pacientes com um maior envolvimento respiratório/pulmonar pela COVID-19 e menores níveis de independência funcional à admissão, parecem ser aqueles que mais beneficiam de integrar um programa intensivo de reabilitação em regime de internamento.

Palavras-chave: COVID-19/reabilitação; Doentes Internados; Recuperação da Função, Unidades de Cuidados Intensivos.

Introduction

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is the most recently discovered coronavirus, identified in 2019, and is the causative agent of coronavirus disease 2019 (COVID-19). The spread of COVID-19 led to a global pandemic in March 2020, resulting in significant morbidity and mortality worldwide, with millions of individuals hospitalized due to acute COVID-19.[1]

COVID-19 is most commonly characterized by upper respiratory symptoms, and patients usually do not require hospitalization. However, it can progress to a lower respiratory infection, leading to acute respiratory distress syndrome and respiratory failure, requiring hospitalization.[1] Approximately 5% of unvaccinated patients develop severe hypoxemic respiratory failure and require admission to the intensive care unit (ICU).[2] The risk of severe COVID-19 infection varies with demographics and pre-existing medical conditions, including increased age, diabetes, cardiovascular disease, and underlying lung disease.[2]

The complications and functional consequences of prolonged ICU hospitalization are referred to as post-intensive care syndrome (PICS). PICS involves a constellation of new or worsening impairments in physical, mental, and/or cognitive abilities in individuals who have had a critical illness that requires intensive care. These impairments may persist for months or years after hospitalization.[3-5] Hospitalization due to acute illness caused by COVID-19, regardless of severity, results in new functional impairment after discharge, which is worse in patients requiring intensive care.[6,7] Physical problems experienced by individuals with PICS include impaired pulmonary function, skeletal and respiratory muscle weakness, dysphagia, difficulty walking, fatigue, exercise intolerance, and inability to return to work. Mental health problems include anxiety, stress disorders, post-traumatic stress disorders, and depression. Cognitive problems include impairments in memory, mental processing speed, and executive function.[3-5] According to the literature, patients with PICS benefit from inpatient rehabilitation, with excellent results and important functional recovery.[3,8,9] Its purpose is to improve respiratory function, counteract musculoskeletal deconditioning and immobilization, reduce the onset of complications, improve cognitive status, reduce disability, and improve quality of life in anticipation of the patient's discharge.[4]

There are limited data on the functional outcomes of inpatient rehabilitation in patients with PICS due to COVID-19, as well as on the predictors of these outcomes. Given the global burden of COVID-19 and the particular need for rehabilitation in these patients, identifying the most relevant factors influencing functional outcomes could help clinicians

develop more effective rehabilitation programs. This knowledge would also assist in determining which patients are most likely to benefit from inpatient rehabilitation, ultimately leading to improve patient-centered outcomes.

This study aimed to describe the functional outcomes of patients with PICS due to COVID-19 in an inpatient rehabilitation setting and to evaluate the factors that could influence or potentially predict these outcomes.

Material and Methods

Selection of participants and physical medicine and rehabilitation intervention

This study was approved by the Health Ethics Committee (HEC) of our Hospital. It consisted of a retrospective chart review of all patients admitted to an inpatient rehabilitation facility (IRF) at a District General Hospital (Hospital de Braga – HB) in Portugal between April 2020 and June 2021, following hospitalization for critical COVID-19 requiring admission to the ICU, that is, patients with PICS due to COVID-19. According to the HEC of HB, patient consent was not required for this research,

Patients with symptomatic COVID-19 are usually admitted to HB through the emergency department. If hospitalization is required, they are assigned to a conventional ward (Internal Medicine or Infectious Disease), an Intermediate Care Unit, or to an Intensive Care Unit, depending on the severity of their symptoms and the extent of the disease. During hospitalization, patients may experience a step-up or step-down in the level of care between wards according to their clinical evolution.

All patients admitted to the ICU received standard inpatient rehabilitation care, as long as they were allowed for their clinical condition. A physiatrist prescribed a rehabilitation program tailored to each patient's condition, with a gradual increase in intensity as tolerated. Since there is limited evidence supporting specific treatment approaches to improve functional outcomes after COVID-19, no standardized rehabilitation protocol was used during this phase or the IRF period. Instead, interventions were tailored to each patient's individual needs, following the guidelines of the Portuguese Society of Physical Medicine and Rehabilitation.[10] Rehabilitation interventions during this phase included the management of postural variations, passive and active mobilization, gradual progression to an upright position, eventually reaching seated and standing positions, speech therapy for dysphagia management, and respiratory kinesiotherapy, all adapted to the patient's clinical condition during their ICU stay.

The inclusion criteria for our IRF were hemodynamic stability, the need for low levels of respiratory support (fraction of inspired oxygen [FiO2] < 24%) via nasal cannula, and the ability to participate in a rehabilitation program. Exclusion criteria included failure to meet the aforementioned criteria, as well as the presence of pressure ulcers or the need for continuous ventilation (invasive or non-invasive). The need for nocturnal ventilation (non-invasive or through the tracheostomy) was not an exclusion criterion. This rehabilitation program comprises general and rehabilitation nursing care, including decannulation of tracheostomized patients; respiratory kinesiotherapy, including thoracic expansion, localized expansion and diaphragmatic breathing exercises, posture correction, forced expiratory techniques and cough training; physiotherapy, including endurance training for deconditioning, strength, and balance training; speech therapy, including swallowing evaluations and the management and treatment of swallowing disorders; occupational therapy to help recover from deficits in basic and instrumental activities of daily living (ADL); psychological therapy; and nutritional counseling. Training sessions lasted 30-45 minutes each, with patients receiving at least 2-3 hours of inpatient rehabilitation therapy per day, excluding weekends, which represents about 10-15 hours a week. Patient safety during training was ensured through strict monitoring of peripheral oxygen saturation, adjustment of oxygen supply as needed, and continuous observation and assessment of the patient's well-being using Borg Rating of Perceived Exertion.

Data collection

Patient demographics and clinical characteristics were recorded from individual clinical files using a standardized data extraction form. These characteristics included age, sex, cardiovascular risk factors (high blood pressure, diabetes, dyslipidemia, obesity, obstructive sleep apnea, and smoking status), length of stay in the ICU and inpatient rehabilitation facility, number of days on mechanical ventilation and with a tracheostomy, maximum percentage of radiological pulmonary involvement reported on CT scan (PPI-CT), FiO2 at admission and discharge from the IRF, and destination after discharge. We also assessed functional measures at admission and discharge from the IRF, including the functional independence measure (FIM) and the Medical Research Council Sum Scores (MRC-SS).

The functional independence measure was developed as a measure of disability in various populations (not specific to any diagnosis). It assesses 18 items corresponding to areas of dysfunction that commonly occur in individuals with functional impairments (physical and/or cognitive). It ranges from 18 points (lower level of independence) to 126 points (higher level of independence).[11] MRC-SS represents a measure of global peripheral muscle strength, which ranges from 0 (complete paralysis) to 60 (normal strength).[12]

Study design

We performed descriptive statistics for quantitative continuous variables using mean (M) ± standard deviation

(SD), and categorical variables using frequency (n) and percentage (%).

Comparisons between admission and discharge values were performed using paired sample t-tests or Wilcoxon signed-rank tests, according to the distribution of the data.

The dependent variables used to determine the functional outcome of patients during their stay at the IRF were the FIM variation between admission and discharge from the IRF (FIM_var) and FIM at discharge (FIM_dis). We explored other variables that were collected as independent variables.

First, we established a linear relationship between each independent and dependent variable (FIM_var and FIM_dis) using the Pearson correlation coefficient (r). We then selected all variables that showed an $r > 0.4$, which indicates a moderate to high correlation, and created a multiple linear regression model using these variables to evaluate their statistical significance as predictors of each of the dependent variables in the analysis.

Statistical analyses were performed using the IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp. A *p*-value of less than 0.05 indicated significance of the test performed.

Results

Patient characteristics

This study included 18 patients who survived critical COVID-19 in the ICU and were admitted to the IRF. Tables 1 and 2 present the patients' descriptive characteristics. Most patients were male (78%, n=14), with a mean age of 60 years (SD=9.3). Of the participants, 67% (n=12) had two or more cardiovascular risk factors, with the most common

Table 1 - Population's demographics and comorbidities.

Demographics	Descriptive statistics
Age (years)	
M (*SD*)	60.2 (9.3)
Minimum – Maximum	44 – 78
Sex	
Male – *n* (%)	14 (77.8%)
Female – *n* (%)	4 (22.2%)
Length of stay in ICU (days)	
M (*SD*)	51.4 (35.2)
Minimum – Maximum	13 – 123
Length of stay at the IRF (days)	
M (SD)	35.9 (31.8)
Minimum – Maximum	11 – 142
Background and comorbidities	
Cardiovascular risk factors (number)	
M (SD)	2.2 (1.7)
Minimum – Maximum	0 – 6
List of cardiovascular risk factors	
High blood pressure – *n* (%)	10 (55.6%)
Diabetes – *n* (%)	7 (38.9%)
Dyslipidemia – *n* (%)	7 (38.9%)
Obesity – *n* (%)	9 (50%)
Obstructive sleep apnea – *n* (%)	2 (11.1%)
Ex-smoker – *n* (%)	5 (27.8%)

Table 2 - Population's clinical characteristics.

Clinical characteristics during ICU stay	Descriptive statistics
Radiological pulmonary involvement reported on CT-scan (percentage)	
M (*SD*)	64 (17)
Minimum – Maximum	40 – 90
Number of patients under tracheostomy	
n (%)	11 (61%)
Number of days under tracheostomy (between tracheostomized patients)	
M (*SD*)	29 (11)
Minimum – Maximum	14 – 47
Number of days under intubation	
M (SD)	28.1 (17.6)
Minimum – Maximum	0 – 62

Clinical characteristics at the time of admission to the IRF	
FiO2 (percentage)	
M (*SD*)	23.5 (2.8)
Minimum – Maximum	21 – 28
FIM	
M (*SD*)	80.8 (22.7)
Minimum – Maximum	53 – 121
MRC-SS	
M (*SD*)	43.7 (6.7)
Minimum – Maximum	26 – 48
Clinical characteristics at the time of discharge from the IRF	
FiO2 (percentage)	
M (*SD*)	21.2 (0.3)
Minimum – Maximum	21 – 22
FIM	
M (*SD*)	111.3 (13.1)
Minimum – Maximum	79 – 126
MRC-SS	
M (SD)	50.4 (6.3)
Minimum – Maximum	36 – 59
Destination	
Home – *n* (%)	14 (77.8%)
Rehabilitation Center – *n* (%)	4 (22.2%)

ICU = intensive care unit; M = mean; SD = standard deviation; n = absolute frequency; % = percentage; IRF = inpatient rehabilitation facility; FiO2 = fraction of inspired oxygen; FIM = functional independence measure; MRC-SS = Medical Research Council – sum score.

being high blood pressure (56%, n=10) and obesity (50%, n=9). All patients were completely independent before admission for COVID-19 and required mechanical ventilation. The mean length of intubation was 28.1 days (SD=17.6) and the mean length of stay in the ICU was 51.4 days (SD=35.2). Tracheostomy was performed in 61% (n=11) of the patients and lasted for a mean of 29 days (SD=11). Three patients (27%) were admitted to the IRF with tracheostomy, but were already undergoing decannulation. We reported an important radiological pulmonary involvement in all patients, with a mean involvement of 64% (SD=17) of the pulmonary parenchyma. Ten patients, or 55% of the group, still required oxygen supply upon admission to the IRF, with a mean FiO2 at admission (FiO2_adm) of 23.5% (SD=2.8) across all patients.. At the time of discharge from the IRF, only four patients maintained that need (22% of all patients), and all required a lower percentage of oxygen supply compared to admission, with a mean FiO2 at discharge of 21.2% (SD=0.3). The mean duration of inpatient rehabilitation was 35.9 days (SD=31.8). Most patients (78%, n=14) were discharged home, and the remaining 22% (n=4) had planned admission to a Rehabilitation Center.

Outcomes evolution between admission and discharge

The total FIM score significantly improved from admission to discharge (80.8 *vs* 111.3, respectively; p <0.001), with a mean difference of 31 points. The MRC-SS also improved significantly from admission to discharge (43.7 *vs* 50.4, respectively; p = <0.001), as did the FiO2 (23.5% *vs* 21.2%, respectively; p = 0.002).

Statistical analysis to find correlations and/or predictors of the outcomes under evaluation

FIM variation:

We used the Pearson correlation coefficient to explore the association between each independent variable and the FIM variation during the IRF stay, as shown in Table 3. We found a statistically significant association between the percentage of radiological pulmonary involvement by the disease and FIM variation (r = 0.822 / p = 0.006). These variables showed a direct correlation, indicated by the positive value of 'r'; thus, the higher the percentage of radiological pulmonary involvement by the disease, the greater the FIM variation during IRF stay. Similar results were found for FiO2 at

Table 3 - Analysis of the linear relationship between the independent variables and the dependent variable "FIM variation" through Pearson correlation coefficient, and its statistical significance.

Dependent variable	Independent variable	Test statistics
FIM variation (difference between FIM at discharge and FIM at admission to the IRF)	Age	r = 0.209; *p* = 420
	Sex (0=female; 1=male)	r = 0.347; *p* = 0.172
	Diabetes (0=Absence; 1=Presence)	r = -0.359; *p* = 0.157
	HBP (0=Absence; 1=Presence)	r = -0.219; *p* = 0.398
	Dyslipidemia (0=Absence; 1=Presence)	r = -0.154; *p* = 0.555
	Obesity (0=Absence; 1=Presence)	r = -0.460; *p* = 0.063
	OSA (0=Absence; 1=Presence)	r = -0.047; *p* = 0.859
	Ex-smoker (0=No; 1=Yes)	r = 0.043; *p* = 0.871
	Number of CVRF	r = -0.343; *p* = 0.178
	Length of stay in ICU	r = 0.132; *p* = 0.627
	Percentage of radiological pulmonary involvement on CT-scan	r = 0.822; *p* = 0.006**
	Number of days under tracheostomy	r = 0.287; *p* = 0.454
	Number of days under intubation	r = 0.192; *p* = 0.476
	Total FIM at admission to the IRF	r = -0.813; *p* < 0.001**
	MRC-SS at admission to the IRF	r = -0.322; *p* = 0.208
	FiO2 at admission to the IRF	r = 0.512; *p* = 0.036**
	MRC-SS variation during the stay at the IRF	r = 0.142; *p* = 0.587
	Length of stay at the IRF	r = 0.397; *p* = 0.115
	Destination after discharge (0=Home; 1=RC)	r = -0.304; *p* = 0.236

HBP = high blood pressure; OSA = obstructive sleep apnea; CVRF = cardiovascular risk factors; ICU = intensive care unit; CT = computed tomography; IRF = inpatient rehabilitation facility; FIM = functional independence measure; MRC-SS = Medical Research Council – sum score; FiO2 = fraction of inspired oxygen; RC = rehabilitation center; r = Pearson correlation coefficient (<0.29: weak correlation; 0.30 - 0.49: moderate correlation; 0.5 - 0.99: strong correlation; 1: perfect correlation); *p* = statistical significance of the test performed; ** = test showing statistical significance

admission to the IRF (r = 0.512 / *p*=0.036), which also exhibited a significant positive correlation with the FIM variation. This means that the greater the need for oxygen supply at admission, the higher the FIM variation during the IRF stay.

Considering these results, we analyzed the correlation of these two independent variables with the FIM scores at admission and discharge. We observed that both radiological pulmonary involvement and FiO2 at admission correlated inversely with FIM at admission, as indicated by the negative value of 'r' (r = -0.543 and r = -0.445, respectively). Thus, the higher the percentage of radiological pulmonary involvement by the disease and the higher the need for oxygen supply, the lower the FIM score at admission. However, this association was not statistically significant. The correlation of these independent variables (PPI-CT and FiO2_adm) with FIM at discharge was relatively weak, with despicable values of 'r' (r = 0.303 and r = 0.039, respectively). FIM at admission showed a significant negative correlation with FIM variation during the IRF stay (r = -0.813 / *p* < 0.001), as shown in Table 3. Thus, the lower the FIM score at admission, the greater the FIM variation during the IRF stay.

Among the other independent variables analyzed, "obesity" was the only variable whose correlation coefficient with FIM variation was greater than 0.4 (r = -0.460; *p* = 0.063). This indicates that the more obese the patient, the lower the FIM variation. For this reason, we also included the variable "obesity" in the linear regression model to predict FIM variation during IRF stay (Table 4), although the correlation was not statistically significant. This model showed that the four variables explained 96% of the variation in the FIM_var values during the IRF stay (*p*=0.004). However, only the variable "FIM_adm" was a significant predictor of the FIM variation.

Table 4 - Multiple linear regression model exploring potential predictors of FIM variation (Constant) during the stay at the IRF, and its statistical significance. The variables used are those that showed a Pearson correlation coefficient 'r' >0.40.

				Collinearity statistics	
		Beta	*p* value	Tolerance	VIF
VARIATION OF FIM	Constant				
	Obesity	0.038	0.828	0.35	2.87
	Radiological pulmonary involvement on CT-scan	0.564	0.104	0.13	7.84
	FiO2 at admission to the IRF	-0.069	0.759	0.21	4.80
	Total FIM at admission to the IRF	-0.642	0.005**	0.69	1.45
R^2 = 0.963, *F* = 26.037, *p* = 0.004**					

VIF = variance inflation factor; CT-scan = computed tomography scan; FiO2 = fraction of inspired oxygen; IRF = inpatient rehabilitation facility; FIM = functional independence measure

Table 5 - Analysis of the linear relationship between the independent variables and the dependent variable "FIM at discharge" through Pearson correlation coefficient, and its statistical significance.

Dependent variable	Independent variable	Test statistics
Total FIM at discharge	Age	r = -0.322; *p* = 0.193
	Sex (0=female; 1=male)	r = 0.348; *p* = 0.157
	Diabetes (0=Absence; 1=Presence)	r =0 .126; *p* = 0.618
	HBP (0=Absence; 1=Presence)	r = 0.107; *p* = 0.671
	Dyslipidemia (0=Absence; 1=Presence)	r =0 .063; *p* = 0.803
	Obesity (0=Absence; 1=Presence)	r = 0.022; *p* = 0.931
	OSA (0=Absence; 1=Presence)	r = 0.382; *p* = 0.118
	Ex-smoker (0=No; 1=Yes)	r = 0.406; *p* = 0.095
	Number of CVRF	r = -0.277; *p* = 0.265
	Length of stay in ICU	r = -0.219; *p* = 0.398
	Percentage of radiological pulmonary involvement on CT-scan	r = 0.303; *p* = 0.428
	Number of days under tracheostomy	r = -0.089; *p* = 0.806
	Number of days under intubation	r = -0.241; p = 0.352
	Total FIM at admission to the IRF	r = 0.505; *p* = 0.039**
	MRC-SS at admission to the IRF	r = -0.277; *p* = 0.266
	FiO2 at admission to the IRF	r = 0.039; *p* = 0.879
	MRC-SS at discharge from the IRF	r = 0.564; *p* = 0.015**
	FiO2 at discharge from the IRF	r = -0.666; *p* = 0.003**
	MRC-SS variation during the stay at the IRF	r = 0.260; *p* = 0.298
	Length of stay at the IRF	r = -0.311; *p* = 0.209
	Destination after discharge (0=Home; 1=RC)	r = -0.747; *p* <0.001**

HBP = high blood pressure; OSA = obstructive sleep apnea; CVRF = cardiovascular risk factors; ICU = intensive care unit; CT = computed tomography; IRF = inpatient rehabilitation facility; FIM = functional Independence measure; MRC-SS = Medical Research Council – sum score; FiO2 = Fraction of inspired oxygen; RC = Rehabilitation center; r = Pearson correlation coefficient (<0.29: weak correlation; 0.30 - 0.49: moderate correlation; 0.5 - 0.99: strong correlation; 1: perfect correlation); *p* = statistical significance of the test performed; ** = test showing statistical significance

Table 6 - Multiple linear regression model exploring potential predictors of FIM variation (Constant) during the stay at the IRF, and its statistical significance. The variables used are those that showed a Pearson correlation coefficient 'r' >0.40.

				Collinearity statistics	
		Beta	*p* value	Tolerance	VIF
FIM AT DISCHARGE	Constant				
	Total FIM at admission to the IRF	0.375	0.055	0.699	1.43
	MRC-SS at discharge from the IRF	0.160	0.424	0.59	1.71
	FiO2 at discharge from the IRF	-0.607	0.003**	0.81	1.24
$R^2 = 0.712$, $F = 10.722$, $p = 0.001$**					

VIF = variance inflation factor; FIM = functional independence measure; IRF = Inpatient rehabilitation facility; MRC-SS = medical research council – sum score; FiO2 = fraction of inspired oxygen

FIM at discharge:

The Pearson correlation was also calculated to explore the association between each independent variable and the dependent variable, FIM at discharge from the IRF, as shown in Table 5. We found a statistically significant association between the MRC-SS at discharge and FIM at discharge (r = 0.564 / *p* = 0.015). These variables showed a positive correlation; therefore, the higher the MRC-SS at discharge, the higher was the FIM at discharge. We also found a statistically significant negative correlation between FiO2 and FIM at discharge (r = -0.666 / *p* = 0.003). Thus, the greater the need for oxygen at discharge, the lower the FIM score at that moment. Additionally, there was a statistically significant direct correlation between the FIM scores at admission and discharge (r = 0.505 / *p* = 0.039). Therefore, patients with a higher FIM at admission also tend to have a higher FIM at discharge.

None of the other variables in the analysis showed a significant correlation with FIM at discharge; therefore, we included only the three variables mentioned above in the linear regression model (Table 6). This model showed that these variables explain approximately 71% of the variation in the FIM at discharge, with FiO2 at discharge being a significant predictor of FIM at discharge.

Discussion

In this study, we assessed the clinical characteristics, functional outcomes, and predictors of functional recovery in patients who underwent inpatient rehabilitation at an acute care facility following ICU admission for critical COVID-19.

Our rehabilitation cohort consisted of a relatively young group of patients. However, they presented with a risk profile for comorbidities that have already been reported to be associated with severe manifestations of COVID-19.[1,6] It is important to note that most of the population in Portugal was not vaccinated against this virus during the analysis period (April 2020 to June 2021).[12] Specifically, none of the patients in our cohort had received the vaccine, which may have contributed to the younger age of the group. The severity of lung involvement seems to be important, considering the mean percentage of radiological pulmonary involvement reported on computed tomography (CT) scan (64%, SD=17), as well as the percentage of patients still requiring oxygen supply upon admission to our IRF (55%, n=10) after a mean ICU stay of 51.4 days (SD=35.2).

An expert consensus has established that direct access to physical therapy after ICU discharge is imperative for all patients with PICS, regardless of the underlying disease. The goals are to improve ADL function, mobility, strength, and quality of life.[13] In our study, patient's functional status significantly improved during their stay at the IRF, as demonstrated by the significant improvement in FIM and MRC-SS between admission and discharge. This reflects the increased ability of patients to independently perform daily tasks such as personal hygiene, bathing, dressing, walking, and climbing stairs. Therefore, the data presented in this study highlight the importance of inpatient rehabilitation, which is associated with significant motor and functional improvements in patients who have experienced critical acute illness due to COVID-19.

According to the literature, PICS resulting from COVID-19 frequently leads to persistent physical and cognitive impairment[6]; thus, long-term continuation of rehabilitation is important for achieving optimal recovery. In our study, most patients (78%, n=14) were discharged to continue ambulatory rehabilitation. A total of 22% (n=4) required further inpatient rehabilitation at a specialized Rehabilitation Center.

In our cohort, 22% (n=4) of patients required oxygen supplementation at discharge. This may be attributed to the slow resolution of bilateral interstitial infiltrates in COVID-19 patients, with significant alterations in ventilation-perfusion rates.[3] These respiratory sequelae present additional challenges to the rehabilitation process.

Regarding functional outcomes and their predictors, we identified an association between more severe radiological pulmonary involvement and greater variation in FIM scores between admission and discharge from the IRF. This greater improvement does not appear to be explained by a higher FIM scores at discharge, as we found no association between radiological pulmonary involvement and FIM scores at discharge. Instead, this seems to be attributed to the lower FIM score at admission in these patients. Similarly, we found that a higher need for oxygen supply at admission (FiO2) was associated with a greater improvement in FIM scores during the IRF stay, consistent with findings related to de degree of radiological pulmonary involvement. Therefore, we infer that patients with more severe respiratory failure had lower FIM scores at admission to the IRF, resulting in greater gains in functional independence during their stay. Additionally, we observed a statistically significant negative correlation between FIM scores at admission and FIM variation, with lower admission FIM scores predicting greater gains during the rehabilitation stay. This strong correlation supports the hypothesis that the greater functional improvements seen in patients with more severe radiological pulmonary involvement and respiratory failure are primarily due to their lower FIM scores at admission, rather than the severity of their respiratory/pulmonary involvement. Further studies are needed to investigate these associations.

The independent variable MRC-SS, which measures overall muscle strength, did not correlate with FIM variation or with the other variables analyzed. According to our findings, the functional recovery of inpatients with PICS due to COVID-19 is more strongly associated with the degree of radiological pulmonary involvement, the need for oxygen support, and the overall functionality at admission to the IRF, rather than with muscle weakness. Obesity may also negatively impact FIM improvement, potentially leading to less pronounced functional recovery in these patients. However, further studies are needed to clarify this relationship.

Regarding FIM scores at discharge, our study found an association between higher MRC-SS at discharge and higher FIM scores at discharge. This indicates that functional independence at discharge is linked to overall muscle strength at that time. Other studies on post-intensive care patients (unrelated to COVID-19) have corroborated this finding.[14-16] Patients requiring more oxygen at discharge had lower levels of functional independence, with FiO2 at discharge being a predictor of FIM at discharge. This suggests that cardiopulmonary condition, as reflected by FiO2, is more influential than muscle strength in determining functional outcomes at discharge in patients recovering from critical COVID-19. In fact, the degree of respiratory/pulmonary involvement in this group of patients is crucial for determining autonomy and function acquisition during their stay at the IRF and at discharge, more so than muscle strength or any other variable. While patients with a greater need for oxygen at admission exhibited more significant functional gains during inpatient rehabilitation, maintaining the need for oxygen support at discharge was associated with less substantial functional outcomes. This underscores the importance of respiratory kinesiotherapy and aerobic reconditioning in the rehabilitation of these patients. Studies have suggested that dyspnea and hypoxemia may have distinct mechanisms through which they affect functional capacity, and that exercise-induced desaturation in this group of patients is likely linked to parenchymal and/or pulmonary vascular phenomena.[2,17-18] Further studies are needed to clarify these relationships and their predictive value.

In addition to the findings already discussed, this study highlights the prevalence of persistent functional deficits following severe COVID-19, which often require ongoing rehabilitation after discharge, despite significant improvements during inpatient rehabilitation. These deficits may result in long-term impairments that are beyond the scope of this study. However, further research is needed to investigate the long-term functional effects of COVID-19, as well as other complications.

There are other study limitations in addition to those previously mentioned. The small sample size may have limited our ability to detect significant associations. The single-center, retrospective design, and the absence of a standardized rehabilitation protocol for post-acute severe COVID-19 patients may have influenced our results. These findings are applicable only to critically ill COVID-19 patients and may not be generalizable to hospitalized patients who did not require ICU care. Further studies are necessary to determine whether these associations can be extended to that broader population. We argue that early rehabilitation, advance care planning, and referrals to appropriate therapies are crucial for all inpatients with acute COVID-19 to maximize functional outcomes. However, since we did not include a control group of critically ill COVID-19 patients who only underwent outpatient rehabilitation after ICU discharge, we cannot conclude that our results are solely due to inpatient rehabilitation. Future studies comparing the functional outcomes of critical COVID-19 patients in inpatient versus outpatient rehabilitation settings could help physiatrists determine the most appropriate level of care following ICU discharge.

Although the FIM assesses cognitive function in some important areas, we did not specifically evaluate cognitive impairment or psychiatric complications, including mood disorders, which are associated with severe COVID-19 and can significantly affect participation in rehabilitation programs. These complications, reported in some literature, may affect functional outcomes and represent a limitation and potential source of bias in our study.

We assessed cardiopulmonary involvement based on the percentage of pulmonary parenchyma affected by the disease (as seen on CT-scan) and the need for oxygen supplementation. The use of these variables to evaluate cardiopulmonary function is debatable and represents another limitation. More comprehensive tests, such as spirometry and body plethysmography, could have provided better insights but were not conducted due to resource limitations at that time. Additionally, excluding patients who required oxygen supplementation with FiO2 above 24% also introduces potential bias by excluding more severely ill patients, particularly those with a more fragile cardiopulmonary condition – one of the variables showing significant associations in our study. Nevertheless, it is important to note that all of these excluded patients were eventually admitted to our IRF once their oxygen supplementation levels met our admission criteria (FiO2 <24%), though they had to remain in their original wards for a longer period. Further research should be conducted to address these limitations.

This study has several strengths, including a diverse patient sample, systematic and detailed assessment of important parameters such as functional outcomes, and the inclusion of comprehensive clinical information from patients' hospitalization. It is the first study to analyze the functional outcomes of inpatient rehabilitation in critically ill COVID-19 patients. This highlights the importance of post-acute rehabilitation care in this population and helps identifying which patients may benefit the most from inpatient rehabilitation programs. Additionally, it demonstrates the impact of radiological pulmonary involvement on the functional status of these patients. With further studies and more robust data, it may be possible to better define the actual impact of the studied variables on the functional outcomes of inpatients with post-intensive care syndrome due to COVID-19. We may even define relevant variables or cut-off points that indicate which patients are likely to benefit the most from inpatient rehabilitation programs. In the context of bed shortages, as experienced at the beginning of the pandemic, this knowledge would enable physiatrists to prioritize patient selection for inpatient rehabilitation more effectively. To the best of our knowledge, no similar studies have been published regarding functional outcomes and their predictors in critically ill COVID-19 patients who underwent inpatient rehabilitation, making this a pioneering study in this area.

Conclusion

Our study provides evidence that post-acute multidisciplinary inpatient rehabilitation in individuals with critical COVID-19 is associated with significant improvements in clinical, motor, functional, and cardiorespiratory outcomes. The functional consequences of critical COVID-19 infection appear to be predominantly related to respiratory limitations rather than motor limitations. Our findings underscore the importance of pulmonary rehabilitation for this group of patients. Early post-acute rehabilitation in the ICU may also significantly impact patient recovery by preventing the development of more severe PICS. This study also revealed the prevalence of persistent functional deficits following critical COVID-19, which will require ongoing rehabilitation and may sometimes lead to long-term impairments.

According to our findings, patients with more severe respiratory/pulmonary involvement, which is also associated with lower levels of functional independence at admission, may benefit the most from integrating an inpatient rehabilitation program into acute/subacute IRF. This group of patients demonstrated a strong association with greater functional recovery during their stay in the IRF. This reflects one of the main objectives of an inpatient rehabilitation program: achieving significant functional gains in the shortest possible time. However, further research is needed to determine whether the associations identified in this analysis are truly predictive and to establish more precise parameters that could help physiatrists define prioritized admission criteria for these patients.

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