Reabilitação de Pacientes com COVID-19 em Hospital de Agudos: Um Estudo Retrospectivo Observacional

Rehabilitation of COVID-19 Patients in the Acute Hospital Setting: An Observational Retrospective Study

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Abstract

Introduction: *COVID-19 has a wide clinical spectrum and, in severe cases, can lead to serious functional impairments. The role of Physical and Rehabilitation Medicine (PRM) in the subacute and chronic phases of this novel disease has become indisputable but remains unclear in the acute phase. Our aim was to describe the impact of a PRM intervention in acute COVID-19 patients.*

Methods: *Observational retrospective study of the COVID-19 patients admitted to the ICU and Internal Medicine wards and referred for inpatient intervention by the PRM department of an acute care Portuguese hospital during April and May of 2020. Recommendations from the Portuguese Society of PRM regarding rehabilitation of COVID-19 patients in the intensive care unit (ICU) were followed. Two assessments were performed by a PRM physician: prior to the intervention and at discharge. Demographic data, comorbidities, Medical Research Council Sum Score (MRC-SS), handgrip dynamometry and Chelsea Critical Care Physical Assessment Tool (CPAx) were recorded in electronic health records and were afterwards retrieved for analysis.*

Results: *Twenty-two patients were eligible. Sixteen (72.7%) were male and six (27.3%) were female with a mean age of 65.36 ± 14.07 years old. Mean duration of hospitalization was 25.64 ± 10.25 days, with 18/22 patients being admitted to the ICU (mean of 11.39 days). At discharge, there was: a mean improvement of 16.96 points in MRC-SS; a difference in median handgrip dynamometry of 10.00 kg, (improvements in 21/22 patients); a difference in median CPAx total score of 24.00 points, (improvements in 21/22 patients); improvements in all CPAx subscores. All results were statistically significant ($p<0.05$). There were no adverse events in patients or infections in the PRM team.*

Conclusion: *A PRM intervention in the acute COVID-19 inpatient is safe both for patients and PRM team. It seems to have a positive effect on physical and functional status of the patients, reflected by improvements in all of the parameters evaluated.*

Keywords: *COVID-19; Intensive Care Units; Physical Therapy Modalities; SARS-CoV-2*

Resumo

Introdução: A COVID-19 tem um espetro clínico variado e, em casos graves, pode levar défices funcionais importantes. O papel da Medicina Física e de Reabilitação (MFR) nas fases subagudas e crónicas desta nova doença tornou-se indicutível, mas não é claro na fase aguda. O nosso objetivo era descrever o impacto de uma intervenção de MFR nos doentes agudos com COVID-19.

Métodos: Realizou-se um estudo observacional retrospetivo dos doentes com COVID-19 admitidos na Unidade de Cuidados Intensivos (UCI) e enfermaria de Medicina Interna e referenciados para intervenção de MFR em internamento num hospital português de cuidados

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médicos agudos durante abril e maio de 2020. Foram seguidas as recomendações da Sociedade Portuguesa de MFR relativas à reabilitação de doentes COVID-19 na UCI. Foram realizadas duas avaliações por um médico fisiatra: antes da intervenção e à data de alta. Foram registados no registo médico eletrónico de cada doente e posteriormente recolhidos para análise os dados demográficos, comorbilidades, o *Medical Research Council Sum Score* (MRC-SS), a dinamometria de preensão palmar e a *Chelsea Critical Care Physical Assessment Tool* (CPAx).

Resultados: Vinte e dois doentes foram elegíveis. Dezasseis (72,7%) eram homens e seis (27,3%) eram mulheres, com uma idade média de 65,36 ± 14,07 anos. A duração média de hospitalização foi de 25,64 ± 10,25 dias, com 18/22 doentes admitidos na unidade de cuidados intensivos (UCI) (média de 11,39 dias). À data de alta, verificou-se: uma melhoria média de 16,96 pontos na MRC-SS; uma diferença na média da dinamometria da preensão palmar de 10,00 kg (melhoria em 21/22 doentes); uma diferença na média da pontuação total do CPAx de 24,00 pontos (melhoria em 21/22 doentes); melhoria em todas as subpontuações do CPAx. Todos os resultados foram estatisticamente significativos ($p<0,05$). Não houve nenhum evento adverso nos doentes ou infecções na equipa de MFR.

Conclusão: A intervenção de MFR no doente agudo internado por COVID-19 é segura tanto para os doentes como para a equipa de MFR. Parece ter efeitos positivos no estado físico e funcional dos doentes, que se reflete em melhoria de todos os parâmetros avaliados.

Palavras-chave: COVID-19; Modalidades de Fisioterapia; SARS-CoV-2; Unidades de Cuidados Intensivos

Introduction

In December 2019, an outbreak of novel coronavirus (SARS-CoV-2) infection took place in Wuhan, China.[1] Since then, the infection has spread globally. On March 11th, the World Health Organization declared COVID-19 a pandemic. That led to unprecedented public health measures, creating enormous pressure on healthcare systems, from primary to critical care.

The coronavirus that causes COVID-19 is a betacoronavirus of the same subgenus as the severe acute respiratory syndrome (SARS) coronavirus. The spectrum of symptomatic infection ranges from mild to critical, with the majority of infections (80%) being mild.[2] Around 15% of the infections caused severe disease, with dyspnea, hypoxia, or >50% lung involvement on imaging within 24 to 48 hours. The disease is critical in 5% of the cases, presenting with respiratory failure, shock or multiorgan dysfunction, thus leading to the need of invasive organ support, namely, mechanical ventilation.[2,3] There is a general consensus that these patients often need a period of mechanical ventilation longer than usual for acute respiratory distress syndrome (ARDS), with reports ranging from 10 days to 3 weeks. In this context, about 5%-15% of the infected patients can potentially need respiratory assistance in the acute state.

Intensive Care Unit (ICU) hospitalizations may lead to multiple serious impairments in physical, cognitive or mental health status after discharge. These are due to multiple factors, including disease severity, patients' comorbidities and the treatment itself, and were termed as postintensive care syndrome.[4] The ICU-acquired weakness (ICU-AW) is one of the physical impairments of postintensive care syndrome and consists of a flaccid, bilateral and symmetrical limb weakness that can affect the respiratory muscles. ICU-AW may prolong ventilatory weaning, lead to long-term deconditioning and functional incapacity and may increase mortality.[5,6]

Previous reports in ICU patients suggest that early rehabilitation addressing both prevention and treatment of ICU-AW, decreases mechanical ventilatory support dependency, the ventilatory support weaning duration and prevents neuromuscular complications secondary to immobilization.[7,8] This not only improves functional outcomes but also decreases intensive care and hospital length of stay.[7-9] This is of particular relevance in the acute hospital setting during a pandemic, when there is a shortage of ICU and Internal Medicine beds. In this context, multiple societies throughout the globe began releasing recommendations addressing the rehabilitation of COVID-19 patients, including the Chinese Association of Rehabilitation Medicine and the Australian Physiotherapy Association.[10,11] In Portugal, a taskforce designated by the Portuguese Society of Physical and Rehabilitation Medicine (SPMFR) also issued recommendations on rehabilitation of COVID-19 patients in the ICU setting that guided our clinical practice (http://www.spmfr.org/taskforce-spmfr-covid-19/ [Accessed 01 April 2020]).

Soon after the first case of COVID-19 was diagnosed in Portugal, our institution had to be drastically reorganized to be able to provide the best care possible to the numerous patients needing hospitalization. In line with the International and National recommendations above mentioned, rehabilitation was considered pivotal in the management of patients suffering from this new disease. Thus, as our colleagues started referring acute COVID-19 inpatients for rehabilitation, our department had to respond in accordance to continue to provide quality rehabilitation to these

individuals, both in the ICU and the Internal Medicine wards. Therefore, the aim of this article is to report the impact of an inpatient PRM intervention in a series of patients diagnosed with COVID-19 in the early phase of the pandemic in Portugal.

Methods

This observational retrospective study took place in a Portuguese acute care hospital center concerning the period of April and May of 2020. Ethical approval for this study (Ethical Committee Nº CA-080/2021-0MP / CC) was provided by the Ethical Committee of our institution on 8 March 2021. This study also respected the World Medical Association Declaration of Helsinki. The data was collected from the electronic health records, ensuring anonymity, confidentiality and that it would not be used for purposes other than this article. This study is reported according to the STROBE statement.[12]

The participants were the adult patients diagnosed with COVID-19 admitted to the ICU and Internal Medicine department that were referred to our PRM department for a comprehensive inpatient intervention. We considered eligible for this study those patients that successfully completed the rehabilitation program upon discharge from the hospital and had two systematic assessments: one immediately before starting the PRM intervention and another upon discharge. Subjects that started the program but passed away or were transferred to another institution during the intervention were excluded.

Every patient referred to the PRM department was evaluated by a PRM physician in order to identify the clinical and functional deficits that our rehabilitation program would address. The rehabilitation program was designed by an experienced PRM team, following the guidelines from the SPMFR taskforce, and was adapted to meet each patient's individual deficits. Generally, the program included joint mobilization, stretching exercises, muscular strengthening, functional mobility training, balance training, gait training and reconditioning exercise. Patients with sustained respiratory symptoms would also perform respiratory rehabilitation (Table 1).

Each intervention session had a duration of 30 minutes and was performed 6 days a week, assisted by a specific multiprofessional and multidisciplinary rehabilitation team, including 5 PRM physicians, 9 physiotherapists, 2 speech therapists and 5 rehabilitation nurses. Every member of the rehabilitation team received training regarding personal protective equipment (PPE) and was given a set of proper PPE to wear each session.

Before and during each session, the safety of the intervention was assessed by a PRM physician, according to the stop criteria advocated by the SPMFR taskforce, as outlined on Table 2.

Table 1 - General outline of the PRM intervention.

Joint mobilization	Passive or active assisted depending on patient collaboration
Stretching exercises	Global, focus on flexor groups
Muscular strengthening	Global, rotating muscular groups every 48 hours, initiating isometrics and progressing to dynamic
Functional mobility training	Including moving within bed training (rollover, bridge, etc.), supine to sitting on the edge of the bed training, transfer training and sit to stand training
Balance training	Both sitting and standing, static and dynamic
Gait training	Promoting safety and assessing the need for a walking aid
Reconditioning exercise	Respecting intensity recommendations of Modified Borg Dyspnea Scale 3-4
Respiratory rehabilitation	Breathing control training and management of airway secretions (passive and/or passive)

Table 2 - Exclusion / Stop criteria for PRM intervention.

Body temperature	. > 38.0℃
Oxygen blood saturation	. ≤ 90% . variation > 4% of baseline value during treatment
Respiratory rate	. > 30 cycles/min
Borg dyspnea scale	. > 3 in 10 (resting or during treatment)
Cardiac frequency	. < 40 beats/min . > 120 beats/min
Systolic blood pressure	. <90 mmHg . > 180 mmHg . variation > 20% of the baseline value during treatment
Mean blood pressure	. < 65 mmHg . > 110 mmHg . variation > 20% of the baseline value during treatment
Others	. shock signs with lactic acid level ≥ 4 mmol/L . loss of conscience or restlessness . active bleeding . venous or pulmonary thrombosis in the last 24 hours without anticoagulation therapy . severe aortic stenosis . symptomatic heart arrhythmia . antiarrhythmic drugs administration in the last 24 hours . vasopressor support . acute myocardial infarction in the last 48 hours . unstable fracture . relevant and progressive kidney or liver failure . chest tightness . dizziness . headache . unclear vision . disconnection from monitoring or treatment catheter . prone positioning

Before starting the PRM intervention and upon discharge, each patient was systematically evaluated by a PRM physician following a standardized protocol, and the information was recorded on the electronic health record. Level of cooperation was assessed by the Standardized 5 Questions (S5Q) which has a score ranging from 0 to 5 upon answering correctly to five commands: “open and close your eyes”; “look at me”; “open your mouth and put out your tongue”; “nod your head”; “raise your eyebrows when I have counted up to five”.[13] Three functional measures were used: Medical Research Council – Sum Score (MRC-SS), maximal handgrip strength dynamometry, and Chelsea Critical Care Physical Assessment Tool (CPAx).

MRC-SS is a manual measure of global peripheral muscle strength and consists in the sum of the muscle strength grades according to the Medical Research Council (MRC) scale of the abduction of the arm, flexion of the elbow, extension of the wrist, flexion of the hip, extension of the knee and dorsiflexion of the foot bilaterally, thus ranging from 0 to 60.[14] This scale has been widely used and an MRC-SS < 48 in two evaluations 24 hours apart is the foundation for the diagnosis of ICU-AW (Table 3).[15]

Table 3 - Diagnostic criteria for ICU-AW15.

Minimum criteria for diagnosing ICUAW is 1 + 2 + 3 or 4 + 5
1. Generalized weakness developing after the onset of critical illness
2. Weakness is diffuse (involving both proximal and distal muscles), symmetric, flaccid, and generally spares cranial nerves
3. MRC-SS < 48 evaluated on 2 occasions separated by 24 hours
4. Dependence on mechanical ventilation
5. Causes of weakness not related to the underlying critical illness have been excluded

Handgrip strength measured by a dynamometer has been proposed as a simple and easy diagnostic method for ICU-AW and a correlation between handgrip dynamometry and the MRC-SS has been reported.[9,14] It has also been proposed that handgrip strength could predict the outcome of intensive care patients regardless of ICU-AW diagnosis.[6] The handgrip dynamometry cutoff proposed for diagnosing ICU-AW is < 11 kg-force for males and < 7 kg-force for females.[6,9]

CPAx is a measure of functional independence that consists in a 6-point Guttman-Scale from complete dependency (0 points) to independency (5 points) the following items: respiratory function; cough; moving within bed; supine to sitting on the edge of the bed; dynamic sitting; standing balance; sit to stand; transferring from bed to chair; stepping; grip strength (predicted mean for age and gender on the stronger hand).[16] These subscores are added to give an overall score out of 50 and higher scores indicate better function / independency. It is a fairly recent tool but its proof of concept and construct validity have been proved.[16,17]

Due to the exceptional context of this period, we were not able to ensure that the same PRM physician would assess the same patient at the start and at discharge. However, an attempt to minimize this possible interobserver bias was made by holding a daily meeting between the PRM physician team to present and discuss every assessment.

All variables were compiled for descriptive analysis. Normality was first assessed using the Shapiro-Wilk test. Frequency tables, measures of central tendency (mean, median) and dispersion measures (standard deviation (SD), interquartile range (IQR)) were used. To assess the patients' evolution during the intervention, we compared final and initial evaluations, using Paired Samples Student's T-test in normally distributed variables and Wilcoxon Signed Ranks Test in non-normally distributed data. To determine whether the mean MRC-SS was significantly different from the cutoff for diagnosing ICU-AW we used the One-sample Student's T-test. *P*-values < 0.05 were considered significant with 95% of confidence interval (CI95). Analysis was performed using IBM® SPSS Statistics version 23 for Windows®.

Results

During April and May of 2020, a total of 136 patients diagnosed with COVID-19 were admitted in the ICU and Internal Medicine wards. Of those, 39 (28.7%) were referred to our PRM department for intervention. Those 39 patients were evaluated and treated as described on the Materials and Methods section. We were only able to perform a final evaluation at discharge in 22 patients due to 4 deaths, 7 transfers to other hospitals while the rehabilitation program was still ongoing and 8 single evaluations. Therefore, only data retrieved from these 22 patients was considered for analysis.

Sample Characteristics

All 22 patients were previously independent on their activities of daily living and their demographic and clinical data is individually described in Table 3.

Table 3 - Demographic data of the 22 patients included in the study.

Patient ID	Sex	Age (years)	Comorbidities[a]	Days in hospital	Days in ICU	Initial S5Q (0-5; points)
1	Male	68	1, 3, 10, 11	25	8	4
2	Male	58	15	27	18	0
3	Female	71	3, 4, 12, 14	16	14	3
4	Male	77	16	24	16	1
5	Male	83	1, 4, 7, 8	23	5	5
6	Female	50	2	20	16	2
7	Male	40	1	11	4	5
8	Male	46	3, 13	24	11	3
9	Male	55	8	38	18	0
10	Female	73	1, 3, 4, 13	35	14	4
11	Male	70	1, 2, 20	27	12	0
12	Male	86	16	15	0	5
13	Male	81	26	38	0	4
14	Male	57	25	31	0	5
15	Male	75	-	10	3	4
16	Female	56	1, 2, 4, 9	25	14	1
17	Male	53	2, 4, 6, 22	25	9	5
18	Female	61	1, 3, 4, 13, 14	17	14	5
19	Male	42	21	10	7	5
20	Female	78	1, 3, 4, 5, 7, 18, 19	37	0	5
21	Male	77	1, 2, 5, 17	40	14	1
22	Male	81	5, 8, 23, 24	46	8	4

ICU: Intensive Care Unit; S5Q: Standardized 5 questions for cooperation. [a] 1: hypertension; 2: type 2 diabetes; 3: obesity; 4: dyslipidemia, 5: chronic obstructive pulmonary disease/emphysema; 6: obstructive sleep apnoea syndrome; 7: previous atrial fibrillation; 8: ischaemic heart disease; 9: active smoker; 10: former smoker; 11: fatty liver; 12: asthma; 13: depression; 14: hypothyroidism; 15: duodenal ulcer; 16: recent orthopaedic surgery; 17: bladder cancer; 18: total hip arthroplasty; 19: total ankle arthroplasty; 20: hyperactive delirium; 21: nephrolithiasis; 22: sarcoidosis; 23: vocal cord cancer; 24: urethral stenosis; 25: L5-S1 spondylodiscitis; 26: sigmoid volvulus

Sixteen (72.7%) were male and 6 (27.3%) were female with mean age of 65.36 (SD 14.07) years old (ranging from 40 to 86 years old). The mean duration of hospital stay was 25.64 (SD 10.25) days (ranging from 10 to 45 days). Eighteen of 22 patients needed admission to the ICU, spending there an average of 11.39 (SD 4.72) days (ranging from 3 to 18 days) before being transferred to an Internal Medicine ward, where they remained until discharge. The mean intervention duration was 10.82 ± 5.52 days, with a minimum of 5 days and a maximum of 26 days.

At the initial evaluation, mean MRC-SS was 34.77 (SD 16.79) points, median maximal handgrip strength measured by dynamometry was 7.00 kg (IQR 0 – 13.00) (female patients 2.50 kg (IQR 0 – 7.25); male patients 10.00 kg (IQR 0.50 – 19.00)) and median CPAx total score was 14.50 points (IQR

3.75 – 26.25). At discharge, mean MRC-SS was 51.73 (SD 7.23) points, median maximal handgrip strength measured by dynamometry was 17.00 kg (IQR 14.00 – 26.50) (female patients 13.00 kg (IQR 9.50 – 15.50); male patients 21.00 kg (IQR 16.00 – 29.50)), and median CPAx total score was 38.50 (IQR 33.00 – 43.25).

Comparison between initial and final assessments (Table 4)

Overall, patients had higher scores at discharge when compared to the initial evaluation and these differences were all statistically significant, both in parametric and non-parametric tests, where applicable. Of note, by the end of follow-up all patients presented at least the same initial values in all outcome measures.

The mean improvement in MRC-SS was 16.96 (SD 15.70) points ($p < 0.001$, CI95 [9.99; 23.92]). The difference in median maximal handgrip strength measured by dynamometry was 10.00 kg ($p < 0.001$), with improvements in 21/22 patients. Regarding CPAx, the difference in median total score was 24.00 points ($p < 0.001$). There were improvements registered in 21/22 patients in the CPAx total score and in all CPAx subscores: respiratory function (18/22), cough (18/22), moving within the bed (18/22), supine to sitting (19/22), dynamic sit (19/22), standing balance (17/22), sit to stand (18/22), transferring from bed to chair (18/22), stepping (19/22), and grip strength (16/22). Progression in median CPAx subscores is also shown in Fig. 1.

ICU-AW identification

At the initial evaluation, 14/22 (63.63%) patients fulfilled the MRC-SS criteria for ICU-AW, with mean MRC-SS being 13.23 points inferior to the cutoff for diagnosing ICU-AW (48 points) (t = -3.70, $p < 0.001$, CI95 [-20.67; -5.78]). At the end

Table 4 - Comparison between initial and final assessments (n=22).

Parameter (range; units)	**Mean (Standard-deviation)**		***p*-values**
	Initial	**Final**	
MRC-SS (0-60; points)	34.77 (16.79)	51.73 (7.23)	<0.001
	Median (Interquartile range)		
	Initial	**Final**	
Handgrip strength dynamometry (Kg)	7.00 (0-13.00)	17.00 (14.00-26.25)	<0.001
CPAx total score (0-50; points)	14.50 (3.75-26.25)	38.50 (33.00-43.25)	<0.001
CPAx – Respiratory function (0-5; points)	3.50 (1.00-4.00)	5.00 (5.00-5.00)	<0.001
CPAx – Cough (0-5; points)	3.00 (1.00-4.00)	4.00 (4.00-4.25)	<0.001
CPAx – Moving within bed (0-5; points)	2.00 (0-4.00)	4.5 (4.00-5.00)	<0.001
CPAx – Supine to sitting (0-5; points)	1.50 (0-2.25)	4.00 (3.00-5.00)	<0.001
CPAx – Dynamic sitting (0-5; points)	1.50 (0-3.00)	4.00 (4.00-5.00)	<0.001
CPAx – Standing balance (0-5; points)	0 (0-2.25)	4.00 (3.00-4.00)	<0.001
CPAx – Sit to stand (0-5; points)	0 (0-2.00)	3.50 (3.00-4.00)	<0.001
CPAx – Transferring from bed to chair (0-5; points)	0 (0-2.00)	4.00 (4.00-4.25)	<0.001
CPAx – Stepping (0-5; points)	0 (0-1.25)	3.00 (2.00-4.00)	<0.001
CPAx – Grip strength (0-5; points)	1.50 (0-2.00)	3.00 (2-3.25)	0.001

MRC-SS: Medical Research Council-Sum Score; CPAx: Chelsea Critical Care Physical Assessment Tool

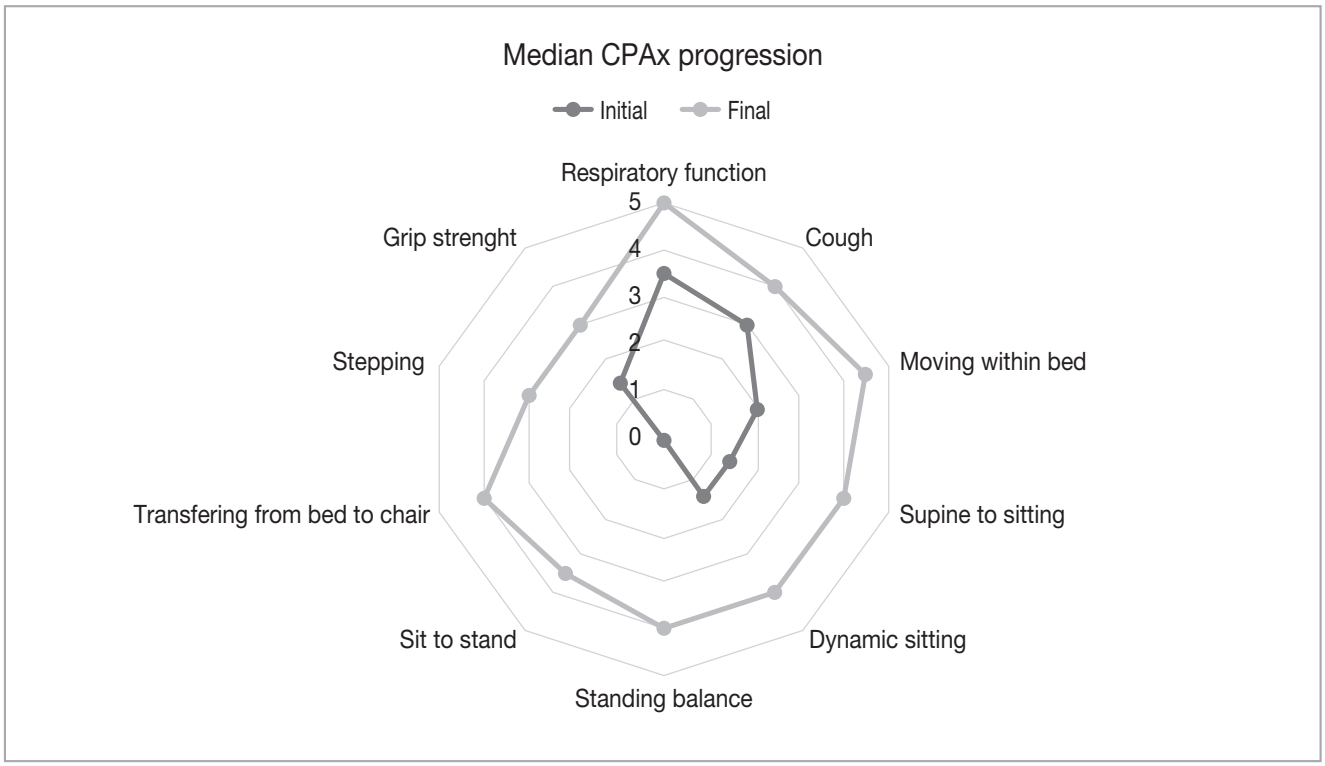

Figure 1 - CPAx progression (median initial and final subscores).

of the program, only 5/22 (22.72%) patients had a MRC-SS inferior to 48 points, with mean MRC-SS being 3.73 points superior to that cutoff value (t = 2.42, *p* = 0.025, CI95%[0.52; 6.93]). There was a 40.91% reduction in the overall prevalence of patients fulfilling the MRC-SS criteria for ICU-AW diagnosis by the end of the program.

Discussion

As we were forced to face a new disease with an epidemiological context that put a tremendous stress on healthcare systems, our aim was to describe the impact of a PRM hospital-based intervention in acute COVID-19 inpatients in the early phase of the pandemic in Portugal.

Overall, our patients showed a significant physical and functional improvement. We report a 40.91% decrease in ICU-AW overall prevalence, with mean improvement in MRC-SS of 16.96 (SD 15.70) points at the end of the inpatient PRM intervention, which is relevant since at the beginning of the program there was a significant prevalence of ICU-AW in our sample.

MRC-SS is widely used to globally assess strength. However, there have been some concerns regarding the clinical applicability of manual volitional muscle strength testing in critically ill patients.[18] Therefore, we also measured handgrip strength by dynamometry, which showed a favorable progression in 21/22 (95.45%) patients at the end of the program. It has also been proposed that ICU-AW can be identified based on dynamometry, with different cutoffs for males and females.[6,9] However, these cutoffs are controversial since handgrip strength also varies with age and dominant hand. In our sample, 4/6 females and 9/16 males had an initial value indicative of ICU-AW. Unfortunately, due to the reduced sample, further exploration of this data was not possible.

MRC-SS and handgrip dynamometry are both impairment-specific tools that measure strength. Strength does not necessarily imply function and a poor functional status can be an obstacle to hospital discharge.

Therefore, other measures are necessary to provide a full and thorough functional evaluation. We used CPAx, which is a tool with a functional approach instead of an impairment-specific approach. This functional measure takes into account not only the motor sequence but also strength through handgrip dynamometry and other domains that potentially need to be addressed in COVID-19 patients, namely respiratory function and cough. In our sample, the initial median CPAx total score was 14.50 points and the final median CPAx total score was 38.50 points, which reflects an improvement of 24.00 points by the end of the PRM intervention. This represents a considerable improvement of the functional status of our patients. It should also be noted that there were improvements in most

patients in all the subscores, with no worsenings to report. As stated before, CPAx is a fairly recent tool and despite having a different rationale than MRC-SS and handgrip dynamometry, patients also improved their CPAx score.

Concerns regarding the safety of rehabilitation treatment in an acute setting were addressed by guaranteeing that only patients that did not meet the exclusion/stop criteria would enroll in the program, and by providing proper PPE to both physicians and physiotherapists. Deaths registered were not attributable to the rehabilitation program but to the global deterioration of the clinical status. To our knowledge, there were no COVID-19 cases among the PRM staff involved.

There is a general consensus that PRM has a key role managing and treating the subacute and chronic sequelae of COVID-19. However, the role of PRM in the acute COVID-19 patient is less clear. Therefore, by addressing this issue, the present study raises awareness for the importance of PRM care also in the acute COVID-19 setting, possibly contributing to improving physical and functional status, thus allowing a safer discharge for both patient and caregivers.

One year after the outbreak, evidence on rehabilitation of COVID-19 is on the rise, both in quantity and quality but the level of evidence is still weak, due to the lack of randomized control trials (RCT) or quasi-RCT.[19]

Li et al. conducted an observational study on the management of COVID-19 patients exclusively in an ICU setting.[20] The authors focused mainly on respiratory rehabilitation which is reflected in the variables studied, thus we can only compare the MRC-SS results. The median MRC-SS was 60 points both at the onset and at the end of their intervention. In our sample, we registered a significant progression from a mean MRC-SS of 34.77 to 51.73 points. However, there was a functional improvement in both samples during the course of each intervention, with no adverse effects associated with them. Gustavson *et al* disclosed preliminary data on a COVID-19 Rehabilitation Unit with an increase of 17 points in the Functional Independence Measure, which reflected an improvement in functional status with a rehabilitation program similar to ours.[21] Similar to our study, Jiandani *et al* described the role of a rehabilitation program in both the ICU and stepdown unit settings. The authors claimed that their program facilitated better outcomes by reducing the need of oxygen support and promoting a progressive improvement in patient mobility.[22] Therefore, even in very different populations and environments, PRM interventions appear to be safe and associated with respiratory, mobility and functional improvements in patients with COVID-19.

Despite encouraging, the results of our study have to be interpreted in the light of certain limitations. First, our sample is relatively small, is a convenience sample made of patients referred to our PRM department and encompasses patients with different degrees of disease severity and therapeutic needs. Hence, the results cannot be generalized and there is a risk of bias by the fact that the patients selected for this rehabilitation intervention were possibly the ones that would benefit more from it. In theory, the inclusion of a control group would have helped to clarify this issue. It could have also allowed us to conclude to what extent our intervention contributed to the improvements reported. Withdrawal of sedatives, cooperation improvement and infection control, among others, also play a role in the results presented in this report. However, it should be stated that recruiting a control group would not be ethical, as it would mean denying a probable beneficial treatment intervention. In the evaluation of ICU-AW, we considered all 22 patients, including 4 that were not admitted to the ICU, because they presented similar deficits to the ICU patients, meeting the criteria for diagnosing ICU-AW, except for the actual stay in a critical care unit. There are even some authors that argue that the term ICU-AW does not describe the condition accurately, because this muscle weakness is not limited to ICU patients, rather possibly being the extreme end of a spectrum of a muscle weakness associated with any severe disease, regardless of care location.[23] Still, in most cases, our intervention began in the ICU and transitioned to the Internal Medicine ward upon ICU discharge, ensuring a continuum of rehabilitative care. The fact that the intervention was not the same to every patient, rather a tailor-made intervention adjusted to each patient's deficits and clinical status, also precludes associating any of the improvements to a specific treatment. We have also to consider the possibility of interobserver variability in the patients' assessment, as mentioned before. Finally, we were not able to retrieve some data that could have improved discussion of results, namely patients' complete medical treatment, the need for ventilator support or tracheostomy, corticosteroids or sedoanalgesia, and complications during hospital stay.

In conclusion, we present encouraging results of a rehabilitation intervention in the acute COVID-19 inpatient based on a systematic assessment protocol performed in the early phase of the pandemic, when the role of PRM was still unclear. Overall, patients significantly improved their physical and functional status. In the future, a follow-up of these patients will provide further details on their clinical and functional evolution, along with more studies with larger samples and more details. At the present date, severe COVID-19 rehabilitation is recommended by several PRM societies, both at the acute and chronic phase. It is also safe for patients and healthcare providers alike, as long as it is a structured rehabilitation program and the stop criteria are respected.

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Referências / *References*

1. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. N Engl J Med. 2020; 382:727-33. doi: 10.1056/NEJMoa2001017.
2. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020; 395:497-506. doi: 10.1016/S0140-6736(20)30183-5.
3. Wang Z, Yang B, Li Q, Wen L, Zhang R. Clinical Features of 69 Cases With Coronavirus Disease 2019 in Wuhan, China. Clin Infect Dis. 2020; 71:769-77.
4. Needham DM, Davidson J, Cohen H, Hopkins RO, Weinert C, Wunsch H, et al. Improving long-term outcomes after discharge from intensive care unit: report from a stakeholders' conference. Crit Care Med. 2012; 40:502-9. doi: 10.1097/CCM.0b013e318232da75.
5. Sharshar T, Bastuji-Garin S, Stevens RD, Durand MC, Malissin I, Rodriguez P, et al. Presence and severity of intensive care unit-acquired paresis at time of awakening are associated with increased intensive care unit and hospital mortality. Crit Care Med. 2009; 37:3047-53. doi: 10.1097/CCM.0b013e3181b027e9.
6. Ali NA, O'Brien JM, Jr., Hoffmann SP, Marsh CB; Midwest Critical Care Consortium. Acquired weakness, handgrip strength, and mortality in critically ill patients. Am J Respir Crit Care Med. 2008; 178:261-8. doi: 10.1164/rccm.200712-1829OC
7. Hashem MD, Parker AM, Needham DM. Early mobilization and rehabilitation of patients who are critically ill. Chest. 2016; 150:722-31. doi: 10.1016/j.chest.2016.03.003.
8. Hashem MD, Nelliot A, Needham DM. Early mobilization and rehabilitation in the icu: moving back to the future. Respir Care 2016; 61:971-9. doi: 10.4187/respcare.04741. E
9. Bragança RD, Ravetti CG, Barreto L, Ataíde TB, Carneiro RM, Teixeira AL, et al. Use of handgrip dynamometry for diagnosis and prognosis assessment of intensive care unit acquired weakness: A prospective study. Heart Lung. 2019; 48:532-7. doi: 10.1016/j.hrtlng.2019.07.001.
10. Thomas P, Baldwin C, Bissett B, Boden I, Gosselink R, Granger CL, et al. Physiotherapy management for COVID-19 in the acute hospital setting: clinical practice recommendations. J Physiother. 2020; 66:73-82. doi: 10.1016/j.jphys.2020.03.011.
11. Zhao HM, Xie YX, Wang C. Recommendations for respiratory rehabilitation in adults with coronavirus disease 2019. Chin Med J.2020; 133: 1595–602. doi: 10.1097/CM9.0000000000000848.
12. von Elm E, Altman DG, Egger M, Yarmolinsky J, Davies NM, Swanson SA, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. J Clin Epidemiol. 2008; 61:344-9.
13. Jang MH, Shin MJ, Shin YB. Pulmonary and physical rehabilitation in critically ill patients. Acute Crit Care. 2019; 34:1-13. doi: 10.4266/acc.2019.00444.
14. Kleyweg RP, van der Meché FG, Schmitz PI. Interobserver agreement in the assessment of muscle strength and functional abilities in Guillain-Barré syndrome. Muscle Nerve. 1991; 14:1103-9.
15. Stevens RD, Marshall SA, Cornblath DR, Hoke A, Needham DM, de Jonghe B, et al. A framework for diagnosing and classifying intensive care unit-acquired weakness. Crit Care Med. 2009; 37:S299-308. doi: 10.1097/CCM.0b013e3181b6ef67.
16. Corner EJ, Wood H, Englebretsen C, Thomas A, Grant RL, Nikoletou D, et al. The Chelsea critical care physical assessment tool (CPAx): validation of an innovative new tool to measure physical morbidity in the general adult critical care population; an observational proof-of-concept pilot study. Physiotherapy. 2013; 99:33-41. doi: 10.1016/j.physio.2012.01.003.
17. Corner EJ, Soni N, Handy JM, Brett SJ. Construct validity of the Chelsea critical care physical assessment tool: an observational study of recovery from critical illness. Crit Care. 2014; 18:R55.
18. Connolly BA, Jones GD, Curtis AA, Murphy PB, Douiri A, Hopkinson NS, et al. Clinical predictive value of manual muscle strength testing during critical illness: an observational cohort study. Crit Care. 2013; 17:R229. doi: 10.1186/cc13052.
19. De Sire A, Andrenelli E, Negrini F, Patrini M, Lazzarini SG, Ceravolo MG. Rehabilitation and COVID-19: a rapid living systematic review by Cochrane Rehabilitation Field updated as of December 31st, 2020 and synthesis of the scientific literature of 2020. Eur J Phys Rehabil Med. 2021;57:181-8. doi: 10.23736/S1973-9087.21.06870-2.
20. Li L, Yu P, Yang M, Xie W, Huang L, He C, et al. Physical Therapist Management of COVID-19 in the Intensive Care Unit: The West China Hospital Experience. Phys Ther. 2021;101:pzaa198. doi: 10.1093/ptj/pzaa198.
21. Gustavson AM, Rud B, Sullivan EK, Beckett A, Gause LR. Role and impact of interdisciplinary rehabilitation in an acute COVID-19 recovery unit. J Am Geriatr Soc. 2021;69:878-81. doi: 10.1111/jgs.17060.
22. Jiandani MP, Salagre SB, Kazi S, Iyer S, Patil P, Khot WY, et al. Preliminary Observations and Experiences of Physiotherapy Practice in Acute Care Setup of COVID 19: A Retrospective Observational Study. J Assoc Physicians India. 2020; 68:18-24.
23. Piva S, Fagoni N, Latronico N. Intensive care unit-acquired weakness: unanswered questions and targets for future research. F1000Res. 2019; 8:F1000 Faculty Rev-508. doi: 10.12688/f1000research.17376.1. eCollection 2019.