



Article Impact of Physiotherapy on Patients Suffering from COVID-19: An Observational Study

Ilie Onu ^{1,2,3,†}, Daniel-Andrei Iordan ^{4,5,*,†}, Daniela Matei ^{1,†}, Oana-Diana Hrisca-Eva ^{1,†}, Ioana Buculei ^{1,6,*,†}, Anca-Irina Galaction ^{1,2,†}, Ionela Lăcrămioara Serban ^{7,†}, Mona-Elisabeta Dobrin ^{8,9,†}, Ovidiu Popa-Velea ^{10,†}, Dan Eugen Costin ^{4,†}, George Dănuț Mocanu ^{4,†}, Andreea-Georgiana Dobre ^{4,†} and Robert Gherghel ^{3,7,†}

- ¹ Department of Biomedical Sciences, Faculty of Medical Bioengineering, University of Medicine and Pharmacy "Grigore T. Popa" Iasi, 700454 Iasi, Romania; ilie.onu@umfiasi.ro (I.O.); daniela.matei@umfiasi.ro (D.M.); oana.hrisca@umfiasi.ro (O.-D.H.-E.); anca.galaction@umfiasi.ro (A.-I.G.)
- ² Doctoral School of the Faculty of Chemical Engineering and Environmental Protection "Cristofor Simionescu", Technical University "Gheorghe Asachi" Iasi, 700050 Iasi, Romania
- ³ Department of Physiotherapy, Micromedica Clinic, 610119 Piatra Neamt, Romania; robert.ghergel@umfiasi.ro
- ⁴ Department of Individual Sports and Kinetotherapy, Faculty of Physical Education and Sport, "Dunarea de Jos" University of Galati, 800008 Galati, Romania; dan.costin@ugal.ro (D.E.C.);
- george.mocanu@ugal.ro (G.D.M.); andreea.dobre@ugal.ro (A.-G.D.)
- ⁵ Center of Physical Therapy and Rehabilitation, "Dunarea de Jos" University of Galati, 800008 Galati, Romania
- ⁶ Doctoral School of the Faculty of Medicine, University of Medicine and Pharmacy "Grigore T. Popa" Iasi, 700454 Iasi, Romania
- ⁷ Faculty of General Medicine, University of Medicine and Pharmacy "Grigore T. Popa" Iasi, 700115 Iasi, Romania; ionela.serban@umfiasi.ro
- ⁸ Medical Science Department, University of Medicine and Pharmacy "Iuliu Haţieganu" Cluj-Napoca, 400347 Cluj-Napoca, Romania; mona.cioroiu@ymail.com
- ⁹ Clinical Hospital of Pulmonary Diseases Iași, 700115 Iași, Romania
- ¹⁰ Department of Medical Psychology, Faculty of Medicine, University of Medicine and Pharmacy "Carol Davila", 050474 Bucharest, Romania; ovidiu.popa-velea@umfcd.ro
- * Correspondence: daniel.iordan@ugal.ro (D.-A.I.); buculei.ioana@umfiasi.ro (I.B.)
 - + These authors contributed equally to this work.

Abstract: Introduction: COVID-19 was the turning point of 2020, endangering the health of the entire population around the world. Among other therapeutic methods and supportive measures, physiotherapy represents a useful intervention applied on COVID-19 patients suffering from respiratory symptoms, this being supported by recent literature data. Materials and Methods: The study was performed on 45 patients diagnosed with COVID-19 (28 men, 17 women, mean age = 65.03, standard deviation = 14.83). They participated for 2 weeks (the required period of hospitalization) to a series of 14 physiotherapy sessions, which included: position changing, respiratory control, passive joint movements, bed workout, and walking exercises. Depending on the status of the patient, two distinct types of physiotherapy were performed (mild and active). The status of the patients was assessed through a basic assessment of the vital signs, range of motion, degree of dyspnea, and also through the UZ Leuven Start To Move protocol (STMP). The statistical analysis of the data was performed using the Statistica 10 program and included the Spearman correlations (for measuring the strength and direction of association between the ranked variables), the Mann-Whitney test (for measuring the significance of the differences between the groups of patients who undergone light vs. active physiotherapy) and factor analysis (for assessing the changes of the clinical parameters investigated in the study, depending on the type of applied therapy). All differences were considered significant at p < 0.05. Results: The majority of patients (n = 38) benefited from physiotherapy, with the complete disappearance of symptoms met only in the group of patients who followed active physiotherapy. These effects depended on the applied type of physiotherapy (mild vs. active, p = 0.47). In contrast, all patients who were unable to perform physiotherapy (n = 7) remained symptomatic at discharge. Conclusions: The results of this study point out the significant additional role of physiotherapy for a better management of COVID-19 patients. More studies are needed to investigate not only the impact



Citation: Onu, I.; Iordan, D.-A.; Matei, D.; Hrisca-Eva, O.-D.; Buculei, I.; Galaction, A.-I.; Serban, I.L.; Dobrin, M.-E.; Popa-Velea, O.; Costin, D.E.; et al. Impact of Physiotherapy on Patients Suffering from COVID-19: An Observational Study. *Appl. Sci.* 2022, *12*, 5795. https://doi.org/ 10.3390/app12125795

Academic Editors: Francesco Cappello and Akikazu Sakudo

Received: 21 April 2022 Accepted: 4 June 2022 Published: 7 June 2022

Publisher's Note: MDPI stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.



Copyright: © 2022 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https:// creativecommons.org/licenses/by/ 4.0/). that physiotherapy has on the symptoms of this disease, but also its effects on effort capacity, muscle strength and lung capacity.

Keywords: COVID-19; physiotherapy; rehabilitation; interleukin 6; C-reactive protein

1. Introduction

The SARS-CoV-2 (severe acute respiratory syndrome coronavirus) outbreak in 2019 affected every aspect of people's lives all around the world [1]. The corresponding infection is commonly referred as the COVID-19 disease, and is currently known to be able to harm many organs and systems in the body (e.g., the nervous system, heart, kidney, liver, spleen, large vessels, and muscles), with a special propensity for the respiratory function [2]. The virus is easily spread from person to person (through coughing, sneezing, hand-to-mouth contact, and also contact with the eyes after touching contaminated surfaces); this process is further facilitated by living or working together and by the lack of specific immunity [3].

The main cause of COVID-19 mortality is the acute respiratory distress syndrome initiated by epithelial infection and activation of alveolar macrophages in the lungs [4]. The most common clinical symptoms of COVID-19 are fever, dry cough, fatigue, muscle pain, dyspnea, anosmia, and ageusia, which can occur a few days after infection. One of the most common symptoms and dysfunctions present in this category of patients is a decreased exercise capacity, explained mainly by the dysfunction of the cardiovascular and pulmonary systems and, in some cases, by extensive immobilization [5,6].

Risk factors for severe COVID-19 forms include age, male gender, and comorbidities (e.g., severe asthma, hypertension, chronic obstructive pulmonary disease, and diabetes) [7,8]. Generally, people over 65 and patients with comorbidities have a higher risk of developing severe forms of COVID-19, but young patients without underlying medical conditions may be affected as well [9,10].

This important individual and societal consequence of COVID-19 offered legitimacy to the World Health Organization to declare it as a global public health problem and categorize it as a pandemic [11]. Previous research aimed to better understand how the disease is transmitted and to obtain new information about the prevention, treatment, and follow-up of the patients suffering from it [12,13].

The treatment of COVID-19 has been subject to many changes, as it was the first time that the professionals in the medical field had to handle this kind of infection. This eventually led to the use of new methods and to the building of new and improved treatment guidelines [14,15]. Among these methods, respiratory rehabilitation (RR) has been brought into the discussion, due to its previously proven efficacy [16]. As an evidence-based therapeutic method, RR is generally developed by a multidisciplinary team and is applied mainly to patients suffering from dyspnea and decreased tolerance to respiratory stress. This type of intervention includes exercise training and interventions, such as psychological and nutritional support, with an emphasis on education and behavioral changes [17]. Over the years, RR has gained increasing relevance due to studies showing its usefulness in chronic and debilitating respiratory diseases, such as chronic obstructive pulmonary disease and asthma [18–22]. In these particular diseases, RR is able to decrease the burden of symptoms, increase effort tolerance, and significantly increase the self-reported quality of life.

Considering this, the relevance of RR for COVID-19 patients is a legitimate point of discussion, even if the long-term impact of COVID-19 infection is not clear yet. According to experts from the World Confederation for Physical Therapy and Associations of Physical Therapy, about a quarter of patients cured after SARS-CoV-2 infection may remain with pulmonary sequelae, with a decrease of the lung capacity of about 20–30% [23]. Patients hospitalized with moderate to severe forms of COVID-19 may suffer from long-term deficiencies, such as decreased respiratory function, reduced resistance of the respiratory

and limbs muscles, reduced ability to perform activities in daily life, and reduced walking distance [24,25]. In this context, RR may be able to reduce the symptoms of dyspnea, improve lung capacity, and reduce the risk for COVID-19 complications [26].

The authors suggest that the short-term goals of RR for COVID-19 patients should include the decrease of the respiratory symptoms, anxiety, and depression, while the long-term goals should be represented by the maintenance of the patients' lung function and quality of life, and their reintegration into society [17]. Before the RR interventions can be conducted, patients have to be comprehensively evaluated, through an extensive assessment of their clinical status, lab tests, chest Rx and CT, and a measurement of their self-reported quality of life and psychological and nutritional statuses. These evaluations are all needed to calculate the RR risk-benefit ratio. This may be supplemented with the assessment of their aerobic endurance, muscle strength, balance, and flexibility, which are all used to establish an individualized and progressive rehabilitation program [17,27].

In terms of timeline, RR could be used in the acute and post-acute phase, but also for the long-term management of this disease [28]. Specifically, in critically ill patients, the long-term benefits of RR seem to be linked to the decrease of atelectasis and the subsequent improvement of lung function. In all cases, RR should be conducted by a multidisciplinary team and should contain neuromuscular, cardiological, and respiratory interventions, with the provision of psychological support when needed [29,30].

The aim of this study was to investigate the impact of RR on the evolution of COVID-19, specifically whether early physiotherapy can be considered effective in addressing the respiratory symptoms and in improving the effort capacity of COVID-19 patients. The importance of this study stems from the relative scarcity of data in current literature regarding RR, and also from the anticipated high benefit-risk ratio of RR. The latter could make RR suitable to be added in the management plan of COVID-19 patients, especially in those clinical settings where other therapeutic tools are expensive or inaccessible.

2. Materials and Methods

2.1. Study Design and Setting

The current study was conducted in 2020 in Romania in the Piatra Neamt Emergency Hospital, on patients diagnosed with COVID-19, in collaboration with the Department of Physiotherapy Micromedica Clinic from Piatra Neamt. The design of the study was longitudinal and included 45 patients diagnosed with COVID-19 (28 men, 17 women, mean age = 65.03, standard deviation = 14.83). They participated for 2 weeks (the required period of hospitalization) in a series of 14 physiotherapy sessions, which included position changing, respiratory control, passive joint movements, bed workout, and walking exercises. Depending on the status of the patient, two distinct types of physiotherapy were performed (mild and active). Throughout the study, the patients were monitored by an interdisciplinary team, composed of 5 medical doctors, 14 nurses, and one physiotherapist. During hospitalization, all patients included in the study received the same pharmacological treatment for COVID-19 according to the guidelines available at the time of admission.

2.2. Participants and Tools

Before starting, a comprehensive assessment of patients was performed, including a Basic Assessment (BA) and the UZ Leuven Start To Move protocol (STMP).

BA included:

- (BA1) basic vital signs: blood oxygen saturation, respiratory rate, heart rate, blood pressure, and temperature;
- (BA2) range of motion (passive and active);
- (BA3) the degree of dyspnea.

STMP was created to be used in the evaluation of patients hospitalized in Intensive Care Units (this type of patients is exposed to prolonged time spend at bedrest and other factors that can have a direct or indirect impact on the muscle and the body, causing weakness and a decrease in functional performance). It consists of six levels of assessment, each of them being determined through objective measurements [31]. This type of protocol was used in this study because the vast majority of hospitalized patients with COVID-19 became physically deconditioned fairly quickly, and this imposed bed rest for them. According to the STMP guidelines, an STMP level of 0 corresponds to a patient who does not cooperate, so no physiotherapy procedures are applied; at level 1, the patient may cooperate by performing passive mobilizations of the lower and upper limbs and the passive bicycle; at level 2, the patient is able to perform active mobilizations, resistance exercises, and active hand and foot cycling; at level 3, imposed ADL movements (ambulating, feeding, dressing, personal hygiene, continence, and toileting) are possible; at level 4, the patient can walk using a frame in the hospital room; and at level 5, the patient can walk assisted by a medical professional.

Inclusion criteria comprised patients aged over 18, with respiratory symptoms (cough and dyspnea) and a confirmed RT-PCR test of COVID-19, with an STMP level between 3 and 5. Patients who did not corresponded to the above mentioned criteria, who were transferred to the ICU ward and whose health had deteriorated or who had various comorbidities such as hepatic, kidney, and circulatory diseases, stroke, or other serious neurological diseases, as well uncooperative patients and those who did not want to perform physiotherapy were excluded.

Electronic medical records of all patients admitted in the study were retrospectively screened, and relevant data were independently extracted. The relevant data extracted was included in a de-identified form in an excel spreadsheet. All data was stored in password-protected electronic documents, with access only for the authors of the study.

Patient demographic data and baseline clinical characteristics, including age, gender, and comorbidities were recorded. Clinical data consisted of the length of hospital stay, medical treatment, symptoms, and types of physiotherapy. Lab tests included blood levels of C-reactive protein (CRP), IL-6 (interleukin 6), and ferritin, and were also recorded.

Sample preparation

The blood samples were collected on admission for all study participants. Taking all aseptic precautions, about 6 mL of blood was drawn by venipuncture from a peripheral vein with a disposable syringe, then collected in a clean dry glass tube (clot activator tube) that allowed it to stand for 10 min at room temperature for the retraction of the clot. This was centrifuged at 4000 rpm for 10 min to separate the serum. All tests were performed in the biochemical laboratory, following standard procedures for clinical biochemistry purposes. The biological parameters measured were: CRP, ferritin, and IL-6.

Biochemical assay

Serum parameters (CRP and ferritin) were measured using a Cobas Integra 400 plus (Roche) biochemical autoanalyzer, while IL-6 was assayed by Cobas E411, fully automated analyzer that uses a patented electrochemiluminescence (ECL) technology for immunoassay analysis. Result quality is validated with internal quality control and the laboratory participates in an external quality control scheme.

They were selected considering that:

- CRP was selected for being measured, as it represents a valuable indicator of inflammation. Literature has associated mild COVID-19 with CRP values < 22 mg/L, while severe forms of COVID-19 have been associated with CRP > 80 mg/L [32];
- IL-6 is a cytokine representing an early indicator of acute inflammation, with very high values of this parameter being associated with more severe forms of COVID-19 [33]. It has been observed that the decrease in IL-6 levels is closely related to the effectiveness of the treatment, while the increase in IL-6 levels indicates the worsening of the disease. For this reason, elevated serum IL-6 levels may be an ideal marker for disease monitoring [34];
- Ferritin was monitored for a similar reason (its concentrations have also been associated with the severity of the disease and it may also serve as a predictive biomarker, as well as in the triage of COVID-19 patients) [35].

The study was run in accordance with the principles of the World Medical Association Helsinki Declaration [36] with approval no. 263/11.05.2020, from Ethics Committee of Micromedica Clinic. All participants offered their written informed consent to participate in the study and to the use of their extracted medical data, in accordance with the GDPR regulations.

2.4. Intervention

The participants received a set of instructions related to bed mobilization, as well as light exercises and were asked to perform them during the hospitalization. Patients were trained by a physiotherapist at the time of hospitalization, received a written physiotherapy program and had the possibility to contact the team members by telephone or internet-connected smartphone applications for questions and for the communication of their health status. Patients were encouraged to report any adverse events during exercises, such as dizziness, dyspnea, and oxygen deprivation. Depending on the evolution of the patient's state of health, the physiotherapist gave indications to the patient to introduce new exercises from the list or to decrease the number of exercises.

The RR plan through physiotherapy included systematic posture changes that optimized ventilation and improved gas exchange by promoting alveolar interdependence, passing through lateral decubitus and semi-dorsal decubitus positions. The RR plan also included dyspnea control techniques, slow exhalation techniques for patients who did not easily desaturate, techniques that reduce respiratory rate, breathing coordination techniques, and musculoskeletal exercises for upper and lower limbs.

During the 14 days of hospitalization, the patients underwent a program of respiratory physiotherapy and physical reconditioning, with a minimum duration of 15 min per day but not exceeding 60 min, depending on dyspnea, oxygen saturation, heart rate and respiratory rhythm. Each phase of RR was performed under the supervision of the medical team, with the aim of gradually achieving the level of independence during the exercise.

The physiotherapy program included:

- (PT1) Patients were advised to change their body positions every two hours during the day, going through prone, semi-dorsal, and lateral decubitus. Changing the patient's position reduces the development of bedsores and can reduce the degree of dyspnea. Prone position ventilation: patients with severe COVID-19 with PaO2/FiO2 less than 150 mmHg at 16 h per day;
- (PT2) Lying on the bed (supine position) with head on the pillow at a 45-degree position of the bed, the patient slowly performs the clenching of the fist and fingers and relaxes, and the planar-dorsal flexion of the ankles (10 times slowly);
- (PT3) From the supine position with head on the pillow at a 45-degree position of the bed, the patient slowly performs the flexion-extension of the elbows (10 times slowly);
- (PT4) From the supine position with head on the pillow at a 45-degree position of the bed, the patient slowly performs the flexion-extension of the knees, without lifting the sole of the floor (10 times, slowly);
- (PT5) From the supine position, with head on the pillow at a 45-degree position of the bed, the patient slowly performs lifting and lowering the shoulders, abduction, and adduction of the scapula (5 times);
- (PT6) Belly Breathing (Diaphragmic Breathing): the patient is in a supine position, with a pillow under his head or with his bed at a 45-degree position and bent knees. The patient puts one of his hands on the chest and the other one on the abdomen, just below the rib cage, inhaling slowly through the nose, letting the air go deep into the lower abdomen. The hand on the chest should remain still, while the hand on the belly should rise. The patient contracts the abdominal muscles and lets them fall inward, exhaling through tight lips. The hand on the abdomen should move back to the starting position. The exercise is performed with a progressive increase of the duration time from 1 to 5 min, considering the distress and the fatigue that can appear;

- (PT7) Pursed Lip Breathing: the patient is in a sitting position, with the muscles of the shoulders and neck relaxed. The patient inhales slowly through the nose for two seconds, keeping the mouth closed, but breathing normally. They are advised that it may be helpful to count for themselves: inspire, one, two. After this, they have to wrinkle or "squeeze" their lips, as if they are whistling or lightly flickering the flame of a candle, then exhale slowly through their tight lips as they count to four. It may be helpful to count: exhale, one, two, three, four. The exercise is performed with a progressive increase of the duration time, from 1 to 5 min, considering the distress and fatigue that can appear;
- (PT8) General exercises. The patients are advised to: squeeze their shoulder blade (8 to 12 times); strengthen the lower legs (10–20 times); raise the heels (20 times); lift the knees, hold for 10 s (3–5 times); shift weight, hold for 10 s (3–5 times); get a single leg balance.

Out of the 45 included patients, 20 were unable to fill the whole protocol and were assigned to the group of mild physiotherapy (from them, 7 followed only PT1–PT3, while 13 followed PT1–PT5). The remaining 25 patients followed the complete protocol (PT1–PT8), being assigned to the group of active physiotherapy.

2.5. Statistical Analysis

The statistical analysis of the data was performed using the Statistica 10 program and included the Spearman correlations (for measuring the strength and direction of association between the ranked variables), the Mann-Whitney test (for measuring the significance of the differences between the groups of patients who underwent mild vs. active physiotherapy) and factor analysis (for assessing the changes of the clinical parameters investigated in the study depending on the type of applied physiotherapy). All differences were considered significant at p < 0.05.

3. Results

In this observational study, laboratory variables and clinical characteristics of 45 patients diagnosed with COVID-19 were evaluated, considering the two physiotherapeutic procedures (mild physiotherapy vs. active physiotherapy). The median age of the patients was 65.03 years old. Forty-four percent of the male patients participated in light physiotherapy and 24% in active physiotherapy. In the case of females, 35% participated in light physiotherapy and 28% in active physiotherapy.

Following clinical examination, it was observed that 53% of the total number of patients included in the study had symptoms of dry cough on admission and 66% of dyspnea. The investigated patients display a series of comorbidities, the most common being gastric ulcer (n = 14), duodenal ulcer (n = 18), and cirrhosis (n = 10) (Table 1).

Table 1. Demographic and clinical characteristics of study participants.

Characteristics	Patients (N = 45)	Mild Physiotherapy	Active Physiotherapy (%)	No Physiotherapy (%)	p
Male	28	49	24	27	0.13
Female	17	35	28	37	0.14
Median age (years)	65	66	68	58	0.54
Dry cough at admission	25	40	28	32	0.50
Dry cough at discharge	6	0	0	100	-
Dyspnea at admission	30	42	31	27	0.10
Dyspnea at discharge	5	4	0	96	-
Gastric ulcer	14	22	15	63	0.62
Duodenal ulcer	18	33	26	41	0.23
Cirrhosis	10	22	8	70	0.03

The biochemical parameters of the patients included in the study showed values above the reference range for ferritin, IL-6, and CRP, but which significantly decreased from hospital admission to discharge (Table 2).

Parameter	Phase of Treatment	Mean	Median	Standard Deviation	Min.	Max.
Ferritin (ng/mL)	hospitalization	1933.88	856.00	2420.94	45.00	9801.00
	discharge	85.97	69.50	73.21	12.30	475.00
IL-6 (pg/mL)	hospitalization	181.68	78.50	322.77	4.56	1491.00
	discharge	19.57	12.50	21.31	5.09	89.54
CRP (mg/L)	hospitalization	104.60	95.58	79.01	12.30	486.00
	discharge	16.60	8.90	17.18	1.06	73.37
Pulse	hospitalization	100.37	96.00	19.04	69.00	145.00
	discharge	74.50	72.00	10.70	56.00	100.00
Oxygen saturation	hospitalization	94.19	95.00	3.73	85.00	98.00
	discharge	97.77	98.00	1.11	94.00	99.00

Table 2. Biological parameters of study participants.

With the help of the statistical processing program of experimental data Statistica 10, the biochemical profile and the clinical variables for the patient included in the study (that participated or did not in physiotherapy procedures) were followed. The discriminant analysis regarding 45 investigated patients and 14 characteristics highlighted 4 representative parameters for this model, which significantly contribute to the separation of the investigated classes: mild physiotherapy/active physiotherapy/no physiotherapy. Based on the statistical results, it can be concluded that IL-6 at admission (F = 23.61; p = 0.0001), CRP at discharge (F = 7.19; p = 0.003), dyspnea at discharge (F = 5.95, p = 0.05), and dry cough on discharge (F = 92.27; p = 0.000) were the parameters with the greatest importance for discriminating the three investigated classes (mild physiotherapy/active physiotherapy/no physiotherapy/no physiotherapy) in patients with COVID-19 (Table 3).

Table 3. Discriminant function analysis summary (grouping mild physiotherapy/active physiotherapy/no physiotherapy).

Biological Parameters	Wilks'–Lambda	Partial–Lambda	F	p	Tolerance	1-Tolerance (R-Square)
Ferritin at admission	0.019	0.998	0.034	0.966	0.294	0.706
Ferritin at discharge	0.021	0.920	1.259	0.299	0.543	0.457
IL-6 at admisson	0.050	0.380	23.615	0.001	0.313	0.687
IL-6 at dischcarge	0.021	0.899	1.632	0.213	0.500	0.500
CRP at admission	0.021	0.929	1.113	0.342	0.416	0.584
CRP at discharge	0.028	0.668	7.195	0.003	0.320	0.680
Dyspnea at admission	0.019	1.000	0.004	0.996	0.870	0.130
Dyspnea at discharge	0.023	0.831	5.954	0.051	0.450	0.550
Pulse at admission	0.022	0.878	2.020	0.151	0.357	0.643
Pulse at discharge	0.020	0.958	0.635	0.537	0.380	0.620
Oxygen saturation on admission	0.023	0.842	2.720	0.083	0.237	0.763
Oxygen saturation on discharge	0.021	0.900	1.607	0.218	0.589	0.411
Dry cough at admission	0.022	0.883	1.916	0.165	0.549	0.451
Dry cough at discharge	0.140	0.136	92.277	0.001	0.296	0.704

Figure 1 shows the classes by representing the individual scores of the subjects investigated during the main discriminating functions. Scatterplot of canonical scores, expressing clinical and biological variables (independent variable) against the type of physiotherapy performed (grouping variable): mild physiotherapy, active physiotherapy, and no physiotherapy patients.



Figure 1. Scatterplot of canonical scores, expressing clinical and biological variables in mild physiotherapy, active physiotherapy, and no physiotherapy patients.

In case of Figure 1, Root 1 and Root 2 represent the discriminant functions Function 1 and Function 2, respectively, corresponding to Table 4 with standardized coefficients for canonical variables generated in discriminant analysis.

Table 4. Standardized coefficients for canonic	al variables generated in discriminant analysis.

Variables	Standardized Coefficients for Canonical Variables					
	Function 1 (Root 1)	Function 2 (Root 2)				
IL-6 at admission	-0.550	0.918				
Ferritin at discharge	-0.526	0.731				
Dyspnea at discharge	-0.983	-0.320				
CRP at discharge	-0.680	-1.071				
Oxygen saturation at admission	0.935	0.457				
CRP at admission	0.741	0.064				
Ferritin at admission	0.564	-0.266				
Pulse at discharge	-0.336	0.290				
IL-6 at discharge	-0.365	-0.147				

In terms of the efficacy of the two physiotherapeutic procedures, the performed nonparametric statistical tests showed that the analyzed data were not normally distributed (p < 0.05) with the Spearman correlation coefficients revealing statistical significance between the investigated parameters of r = 0.30–0.91 (p < 0.05). Statistically significant correlations were found between the groups of patients undergoing mild vs. active PT parameters evaluated at discharge for cough (r = 0.50; p < 0.05), dyspnea (r = 0.39; p < 0.05), oxygen saturation (r = 0.59; p < 0.05), pulse (r = 0.44; p < 0.05), CRP (r = 0.35; p < 0.05), and IL-6 (r = 0.40; p < 0.05) (Figure 2).



Figure 2. Spearman correlations plot between biological parameters in patients with SARS-CoV-2 infection who participated in mild physiotherapy versus active physiotherapy.

The statistical results showed statistically significant differences between the groups of patients undergoing mild vs. active PT for IL-6 at admission (p < 0.01), IL-6 at discharge (p < 0.02), CRP at discharge (p < 0.04), pulse on admission (p < 0.02), dry cough on discharge (p < 0.003), and dyspnea on discharge (p < 0.009) (Table 5).

Variables	Rank Sum Mild PT	Rank Sum Active PT	u	Z	р	Z Adjusted	<i>p</i> Adjusted
Ferritin at admission	502.500	532.500	177.500	-1.645	0.100	-1.645	0.100
Ferritin at discharge	544.000	491.000	219.000	-0.697	0.486	-0.697	0.486
IL-6 at admisson	459.500	575.500	134.500	-2.627	0.009	-2.627	0.009
IL-6 at dischcarge	471.500	563.500	146.500	-2.353	0.019	-2.354	0.019
CRP at admission	496.500	538.500	171.500	-1.782	0.075	-1.782	0.075
CRP at discharge	488.500	546.500	163.500	-1.964	0.049	-1.964	0.049
Dyspnea at admission	517.000	518.000	192.000	-1.313	0.189	-1.600	0.110
Dyspnea at discharge	512.500	522.500	187.500	-1.416	0.157	-2.601	0.009
Pulse at admission	476.000	559.000	151.000	-2.250	0.024	-2.253	0.024
Pulse at discharge	554.000	481.000	229.000	-0.468	0.640	-0.470	0.639
Oxygen saturation on admission	666.000	369.000	159.000	2.067	0.039	2.093	0.036
Oxygen saturation on discharge	655.500	379.500	169.500	1.827	0.068	1.905	0.057
Dry cough at admission	549.000	486.000	224.000	-0.582	0.560	-0.668	0.504
Dry cough at discharge	500.000	535.000	175.000	-1.702	0.089	-2.889	0.003

Table 5. Biological and clinical variables (mild vs. active physiotherapy).

The factorial analysis applied to the investigated data exhibit the contribution of three distinct factors (Figure 3).



Figure 3. Graphical representation of factor weights in the case of patients who performed mild and active physiotherapy.

The first factor represents 38% of the total variation of the data set and is represented by dry cough on discharge, dyspnea on discharge, and mild physiotherapy. This is supported by the data shown in Table 1, which points out that 66% of the patients had dyspnea on admission and 53% had a dry cough. Only 11% of the patients who performed one of the two forms of physiotherapy displayed persistent dry cough and dyspnea at discharge. These findings highlight physiotherapy as having a positive impact on several of the most disturbing symptoms in patients suffering from COVID-19.

The second factor represents 13.9% of the total variation of the data set and is represented by the parameter pulse at admission/at discharge. Pulse values at admission are one of the clinical parameters that show a statistical difference between patients diagnosed with COVID-19 who participated in mild/active therapy (p = 0.024). The third factor represents 12.5% of the total variation of the data set and is represented by the oxygen saturation values at admission/at discharge. The results of the Man-Whitney U test showed that the parameter oxygen saturation at hospitalization has a statistical difference between the groups of patients who participated in mild/active physiotherapy (p = 0.036). In fact, oxygen saturation values are a significant parameter in the diagnosis of patients with COVID-19, especially in establishing the severity of the disease.

4. Discussion

To the best of our knowledge, this is one of the few studies in the scientific literature that investigates the impact of different types of physiotherapeutic intervention on the symptoms and the effort capacity of COVID-19 patients.

The study results suggest that for the patients included in the present study, the combination of active physiotherapy with pharmacological treatment significantly reduce symptoms like dry cough, as well as dyspnea. Depending on the type of physiotherapy, a significant improvement in symptoms was observed.

Our data are in concordance with literature data, which emphasize the real effectiveness of physiotherapy in respiratory patients admitted to the ICU for reducing their oxygen need [37].

This study has several limitations, one of which is represented by the small number of participants. Also, we studied only the acute effects of the interventions, and thus, long-term effects could not be evaluated. The global assessment of the lung function during this study was not possible because this type of investigation was not allowed to be conducted on patients infected with SARS-CoV-2 [6].

A limitation of this study is the impact on the quality of life (QOL) of patients with COVID-19, regardless of the time of discharge after hospitalization and recovery. Healthcare providers need to focus on assessing patients' needs and implementing effective strategies to quantify the quality of life of post-COVID-19 patients who have or have not had PT. Nandasena et al., in 2022, published a study on the evaluation of QOL in post-COVID-19 patients, which shows that QOL has been severely affected, regardless of the time elapsed since discharge or recovery. They show that older patients with various disabilities, along with women, have experienced a considerable decrease in quality of life [38].

More studies are needed to investigate not only the impact that physiotherapy has on the clinical manifestation of the disease but also on effort capacity, muscle strength, and lung capacity.

We consider that the implementation of physiotherapy in the treatment of this category of patients can be considered an interesting therapeutic tool, which can be implemented after a thorough assessment of the abilities, needs, and comorbidities of each patient. Especially in countries with a high prevalence of SARS-CoV-2 and a subsequent number of patients with temporary pulmonary disability, physiotherapy may represent a cost-efficient option, able to diminish respiratory symptoms, preserve or improve lung function, and reduce both short- and long-term complications. Breathing exercises, along with other types of physiotherapies, conducted in the acute phase of this disease, can represent a promising therapeutic strategy for improving the physical competence of these patients and addressing the most disturbing COVID-19 symptoms (such as dry cough and dyspnea). Also, the findings of the present study could be exploited by researchers and clinicians, in order to better understand and address the impairments and rehabilitation needs of COVID-19 patients.

Author Contributions: Study design, I.O., D.M., R.G., O.P.-V., and I.B.; data collection, I.O., R.G., and D.M.; data analysis, G.D.M., M.-E.D., O.-D.H.-E., O.P.-V., D.E.C., and I.B.; drafting manuscript, I.O., M.-E.D., O.P.-V., D.-A.I., A.-G.D., I.L.S., and A.-I.G. All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas, and took part in drafting, revising, or critically reviewing the article. All authors have read and agreed to the published version of the manuscript.

Funding: The present manuscript's article publishing charges were paid by "Dunarea de Jos" University of Galati.

Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Institutional Review Board (Ethics Committee of Micromedica) no. 263/11 May 2020.

Informed Consent Statement: Informed consent was obtained from all subjects that were involved in the study at the hospital.

Data Availability Statement: Data are contained within the main text of the article.

Acknowledgments: All authors have equally contributed to this article as senior authors.

Conflicts of Interest: The authors declare no conflict of interest.

References

- 1. Mocanu, G.D.; Murariu, G.; Iordan, D.A.; Sandu, I.; Munteanu, M.O.A. The Perception of the Online Teaching Process during the COVID-19 Pandemic for the Students of the Physical Education and Sports Domain. *Appl. Sci.* **2021**, *11*, 5558. [CrossRef]
- Wiersinga, W.J.; Rhodes, A.; Cheng, A.C.; Peacock, S.J.; Prescott, H.C. Pathophysiology, Transmission, Diagnosis, and Treatment of Coronavirus Disease 2019 (COVID-19): A Review. *JAMA* 2020, *324*, 782–793. [CrossRef] [PubMed]
- Wu, J.T.; Leung, K.; Leung, G.M. Nowcasting and forecasting the potential domestic and international spread of the 2019-nCoV outbreak originating in Wuhan, China: A modelling study. *Lancet* 2020, 395, 689–697. [CrossRef]
- 4. Huang, C.; Wang, Y.; Li, X.; Ren, L.; Zhao, J.; Hu, Y.; Zhang, L.; Fan, G.; Xu, J.; Gu, X.; et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020, *395*, 497–506. [CrossRef]
- 5. Li, J. Rehabilitation management of patients with COVID-19: Lessons learned from the first experience in China. *Eur. J. Phys. Rehabil. Med.* **2020**, *56*, 335–338. [CrossRef]
- 6. Oltenacu, R.C.; Ciubara, A.B.; Nechifor, A.; Burlea, S.L.; Ciubara, A. The Evolution of Mental Health in Patients with Psoriasis during the COVID-19 Pandemic. *BRAIN Broad Res. Artif. Intell. Neurosci.* **2021**, *12*, 342–348. [CrossRef]
- Munteanu, C.; Păun, D.L.; Şuță, A.F.; Florescu, S.A.; Onose, G. Diabetes mellitus and COVID-19 in the post-acute phase patients—possible links with physical and rehabilitation medicine and balneotherapy. *Balneo Res. J.* 2020, *11*, 350–367. [CrossRef]
- 8. Elena, R.O.; Adrian, C.D.R.; Cristina, V.; Magdalena, Ț.A.; Carmen, T.A.; Ioana, B. Challenges in the diagnosis, treatment and management of asthma during COVID-19 pandemic. *Pneumologia* **2020**, *69*, 73–80. [CrossRef]
- 9. Oxley, T.J.; Mocco, J.; Majidi, S.; Kellner, C.P.; Shoirah, H.; Singh, I.P.; De Leacy, R.A.; Shigematsu, T.; Ladner, T.R.; Yaeger, K.A.; et al. Large-vessel stroke as a presenting feature of Covid-19 in the young. *N. Engl. J. Med.* **2020**, *382*, e60. [CrossRef] [PubMed]
- Williamson, E.; Walker, A.J.; Bhaskaran, K.; Bacon, S.; Bates, C.; Morton, C.E.; Curtis, H.J.; Mehrkar, A.; Evans, D.; Inglesby, P.; et al. OpenSAFELY: Factors associated with COVID-19-related hospital death in the linked electronic health records of 17 million adult NHS patients. *MedRxiv* 2020, 584, 430–436. [CrossRef]
- 11. World Health Organization. Coronavirus Disease (COVID-2019) Situation Reports. 2020. Available online: https://www.who. int/emergencies/diseases/novel-coronavirus-2019/situation-reports/ (accessed on 15 January 2022).
- 12. Sharma, A.; Ahmad Farouk, I.; Lal, S.K. COVID-19: A Review on the Novel Coronavirus Disease Evolution, Transmission, Detection, Control and Prevention. *Viruses* 2021, *13*, 202. [CrossRef]
- Yüce, M.; Filiztekin, E.; Özkaya, K.G. COVID-19 diagnosis—A review of current methods. *Biosens. Bioelectron.* 2021, 172, 112752. [CrossRef] [PubMed]
- 14. COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. National Institutes of Health. Available online: https://www.covid19treatmentguidelines.nih.gov/ (accessed on 21 April 2022).
- 15. Therapeutics and COVID-19: Living Guideline. Available online: https://www.who.int/publications/i/item/WHO-2019-nCoV-therapeutics-2022.3 (accessed on 15 January 2022).
- Bai, C.; Chotirmall, S.-H.; Rello, J.; Alba, G.-A.; Ginns, L.-C.; Krishnan, J.A.; Rogers, R.; Bendstrup, E.; Burgel, P.-R.; Chalmers, J.D.; et al. Updated guidance on the management of COVID-19: From an American Thoracic Society/European Respiratory Society coordinated International Task Force. *Eur. Respir. Rev.* 2020, *29*, 200287. [CrossRef]
- Yang, L.-L.; Yang, T. Pulmonary rehabilitation for patients with coronavirus disease 2019 (COVID-19). *Chronic Dis. Transl. Med.* 2020, *6*, 79–86. [CrossRef]
- Halpin, D.M.G.; Criner, G.J.; Papi, A.; Singh, D.; Anzueto, A.; Martinez, F.J.; Agusti, A.A.; Vogelmeier, C.F. Global Initiative for the Diagnosis, Management, and Prevention of Chronic Obstructive Lung Disease. The 2020 GOLD Science Committee Report on COVID-19 and Chronic Obstructive Pulmonary Disease. Am. J. Respir. Crit. Care Med. 2021, 203, 24–36. [CrossRef]
- Hsieh, M.J.; Lee, W.C.; Cho, H.Y.; Wu, M.-F.; Hu, H.-C.; Kao, K.-C.; Chen, N.-H.; Tsai, Y.-H.; Huang, C.-C. Recovery of pulmonary functions, exercise capacity, and quality of life after pulmonary rehabilitation in survivors of ARDS due to severe influenza A (H1N1) pneumonitis. *Influenza Other Respir. Viruses* 2018, 12, 643–648. [CrossRef]
- Rokach, A.; Romem, A.; Arish, N.; Azulai, H.; Chen, C.; Bertisch, M.; Izbicki, G. The effect of pulmonary rehabilitation on non-chronic obstructive pulmonary disease patients. *Isr. Med. Assoc. J.* 2009, *5*, 326–329.

- Lindenauer, P.K.; Stefan, M.S.; Pekow, P.S.; Mazor, K.M.; Priya, A.; Spitzer, K.A.; Lagu, T.C.; Pack, Q.R.; Pinto-Plata, V.M.; ZuWallack, R. Association between initiation of pulmonary rehabilitation after hospitalization for COPD and 1-year survival among Medicare beneficiaries. JAMA 2020, 232, 1813. [CrossRef] [PubMed]
- Sanz-Santiago, V.; Diez-Vega, I.; Santana-Sosa, E.; Lopez Nuevo, C.; Iturriaga Ramirez, T.; Vendrusculo, F.M.; Donadio, M.-V.F.; Villa Asensi, J.R.; Pérez-Ruiz, M. Effect of a combined exercise program on physical fitness, lung function, and quality of life in patients with controlled asthma and exercise symptoms: A randomized controlled trial. *Pediatr. Pulmonol.* 2020, 55, 1608–1616. [CrossRef]
- Yuetong, Z.; Wang, Z.; Zhou, Y.; Onoda, K.; Maruyama, H.; Hu, C.; Liu, Z. Summary of respiratory rehabilitation and physical therapy guidelines for patients with COVID-19 based on recommendations of World Confederation for Physical Therapy and National Association of Physical Therapy. *J. Phys. Ther. Sci.* 2020, *32*, 545–549. [CrossRef]
- Ohtake, P.J.; Lee, A.C.; Scott, J.C.; Hinman, R.S.; Ali, N.; Hinkson, C.R.; Needham, D.M.; Shutter, L.; Smith-Gabai, H.; Spires, M.C.; et al. Physical Impairments Associated with Post-Intensive Care Syndrome: Systematic Review Based on the World Health Organization's International Classification of Functioning, Disability and Health Framework. *Phys. Ther.* 2018, *98*, 631–645. [CrossRef]
- Popa-Velea, O.; Pristavu, C.; Ionescu, C.; Mihăilescu, A.; Diaconescu, L. Teaching Style, Coping Strategies, Stress and Social Support: Associations to the Medical Students' Perception of Learning during the SARS-CoV-2 Pandemic. *Educ. Sci.* 2021, 11, 414. [CrossRef]
- Cieloszczyk, A.; Lewko, A.; Śliwka, A.; Włoch, T.; Pyszora, A. Recommendations for physiotherapy of adult patients with COVID-19. Available online: https://world.physio/sites/default/files/2020-06/Polish-Respiratory-Physiotherapy-Expert-Group-adult-patients-English.pdf (accessed on 15 January 2022).
- Boldrini, P.; Bernetti, A.; Fiore, P. SIMFER Executive Committee and SIMFER Committee for international affairs. Impact of COVID-19 outbreak on rehabilitation services and Physical and Rehabilitation Medicine (PRM) physicians' activities in Italy. An official document of the Italian PRM Society (SIMFER). *Eur. J. Phys. Rehabil. Med.* 2020, 56, 316–318. [CrossRef]
- 28. Agostini, F.; Mangone, M.; Ruiu, P.; Paolucci, T.; Santilli, V.; Bernetti, A. Rehabilitation settings during and after covid-19: An overview of recommendations. *J. Rehabil. Med.* **2021**, *53*, jrm00141. [CrossRef]
- Liu, K.; Zhang, W.; Yang, Y.; Zhang, J.; Li, Y.; Chen, Y. Respiratory rehabilitation in elderly patients with COVID-19: A randomized controlled study. *Complement. Ther. Clin. Pract.* 2020, 39, 101166. [CrossRef]
- Battaglini, D.; Robba, C.; Caiffa, S.; Ball, L.; Brunetti, I.; Loconte, M.; Giacobbe, D.R.; Vena, A.; Patroniti, N.; Bassetti, M.; et al. Chest physiotherapy: An important adjuvant in critically ill mechanically ventilated patients with COVID-19. *Respir. Physiol. Neurobiol.* 2020, 282, 103529. [CrossRef] [PubMed]
- Hoffman, M.; Clerckx, B.; Janssen, K.; Segers, J.; Demeyere, I.; Frickx, B.; Merckx, E.; Hermans, G.; Van der Meulen, I.; Van Lancker, T.; et al. Early mobilization in clinical practice: The reliability and feasibility of the 'Start To Move' Protocol. *Physiother. Theory Pract.* 2022, *38*, 908–918. [CrossRef]
- 32. Tordjman, M.; Mekki, A.; Mali, R.D.; Monnier, H.; Neveu, S.; Chassagnon, G.; Mihoubi, F.; Carlier, N.; Marey, J.; Fournier, L.; et al. Determining extent of COVID-19 pneumonia on CT based on biological variables. *Respir. Med.* **2020**, 175, 106206. [CrossRef]
- Thakur, A.K.; Yerra, A.; Shaikh, F.; Dekate, P.; Sachane, K.; Chirla, D.; Desai, U.; Narayanan, K. Role of serum il-6 and ferritin levels as marker of severity and outcome predictor in children with multiorgan dysfunction syndrome. *Indian J. Crit. Care Medicin.* 2021, 25, S99–S100. [CrossRef]
- Sabaka, P.; Koščálová, A.; Straka, I.; Hodosy, J.; Lipták, R.; Kmotorková, B.; Kachlíková, M.; Kušnírová, A. Role of interleukin 6 as a predictive factor for a severe course of Covid-19: Retrospective data analysis of patients from a long-term care facility during Covid-19 outbreak. *BMC Infect. Dis.* 2021, 21, 308. [CrossRef]
- 35. Kaushal, K.; Kaur, H.; Sarma, P.; Bhattacharyya, A.; Sharma, D.J.; Prajapat, M.; Pathak, M.; Kothari, A.; Kumar, S.; Rana, S.; et al. Serum ferritin as a predictive biomarker in COVID-19. A systematic review, meta-analysis and meta-regression analysis. J. Crit. Care 2022, 67, 172–181. [CrossRef]
- World Medical Association. World Medical Association Declaration of Helsinki: Ethical principles for medical research involving human subjects. JAMA 2013, 310, 2191–2194. [CrossRef]
- Jiandani, M.P.; Salagre, S.B.; Kazi, S.; Iyer, S.; Patil, P.; Khot, W.Y.; Patil, E.; Sopariwala, M. 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. [PubMed]
- Nandasena, H.M.R.K.G.; Pathirathna, M.L.; Atapattu, A.M.M.P.; Prasanga, P.T.S. Quality of life of COVID 19 patients after discharge: Systematic review. PLoS ONE 2022, 17, e0263941. [CrossRef] [PubMed]