



3

4

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

26

27

28

29

30

31

33

34

35

36

37

38

39

40

41

42

43

44

45

47

48

Proceedings

# The Effect of Post-ICU Physiotherapy on Respiratory and Physical Functioning Status in Patients with COVID-19: A Pilot Study †

Eirini Grammatopoulou <sup>1</sup>, Dimitra Sdravou <sup>2</sup>, Foteini Gkiliri <sup>2</sup>, Aikaterini Bourtzi <sup>2</sup>, Artemisia Polymerou <sup>2</sup>, Simeon Metallidis <sup>3</sup>, Eleni Geka <sup>3</sup>, George A. Koumantakis <sup>4,\*</sup>, Anna Christakou <sup>4</sup> and Afrodite Evangelodimou <sup>4</sup>

- Laboratory of Advanced Physiotherapy (LAdPhys), Physiotherapy Department, University of West Attica (UNIWA), Ag. Spyridonos 28, Aigaleo, 122 43, Athens, Greece; <a href="mailto:igrammat@uniwa.gr">igrammat@uniwa.gr</a>
- AHEPA University Hospital, Health Sciences Faculty, Physiotherapy Department, Aristotle University of Thessaloniki, Stilponos Kiriakidi 1, 54621, Thessaloniki, Greece; <u>dsdravou@gmail.com</u> (D.S.); <u>fotinig2012@gmail.com</u> (F.G.); <u>bourtzi.kat@gmail.com</u> (A.B.); <u>polymerou.artemis@gmail.com</u> (A.P.)
- <sup>3</sup> AHEPA University Hospital, School of Medicine, Health Sciences Faculty, Aristotle University of Thessaloniki, Stilponos Kiriakidi 1, 54621, Thessaloniki, Greece; <a href="metallidissimeon@yahoo.gr">metallidissimeon@yahoo.gr</a> (S.M.); <a href="metallidissimeon@yahoo.gr">gekhel@gmail.com</a> (E.G.)
- Laboratory of Advanced Physiotherapy (LAdPhys), Physiotherapy Department, University of West Attica (UNIWA), Ag. Spyridonos 28, Aigaleo, 122 43, Athens, Greece; <u>achristakou@phed.uoa.gr</u> (A.C.); <u>aevangelodimou@uniwa.gr</u> (A.E.)
- \* Correspondence: gkoumantakis@uniwa.gr
- † Presented at the 1st International Electronic Conference on Medicine, 20-30 June 2021; Available online: https://iecmd2021.sciforum.net/.

Abstract: Background and Objectives: According to the recent physiotherapy recommendations (WHO, WCPT, 2020) for patients with COVID-19, after discharge from ICU, they are expected to experience respiratory, physical, cognitive, and psychological problems due to the duration and nature of the immobilization and sedation, ventilation duration, and underlying morbidity. Moreover, only patients with a limitation in physical capacity and/or physical activity have an indication for physiotherapy. However, little is known about the effect of physiotherapy treatment on the functional capacity of patients with COVID-19. Purpose: The aim of the present study was to provide information for the effectiveness of physiotherapy intervention on the respiratory and physical functional status of patients with COVID-19, since there will be a great demand for physiotherapy treatment for these people soon. Materials and Methods: The Ethics Committee of the AHEPA University Hospital, School of Medicine, Health Sciences Faculty, Aristotle University of Thessaloniki, Greece granted approval for this study. This pilot clinical study was conducted from March to June 2020. The sample consisted of 11 patients with COVID-19, discharged form ICU and hospitalized in the COVID-19 clinic of AHEPA University Hospital. All participants had indication for physiotherapy, according to the recommendations, and medical referral as well. The duration of their hospitalization ranged from two to six weeks. Among participants, there were seven males and four females, aged from 44-75 yrs, five smokers and six nonsmokers, four obese and seven nonobese. According to the recommendations, physiotherapy intervention was tailored to the patients' needs and goals. Breathing exercises, early mobilization and self-management for daily living were performed once a day, for five days a week, as tolerated. Measurement tools: Pulse Oximeter (SpO2), Respiratory Rate (RR), Borg scale (intensity of dyspnea), Medical Research Council scale for disability (MRCd), clinical evaluation for dysfunctional breathing (DB), Medical Research Council scale for muscle strength (MRCms), Berg balance scale, Sit to Stand test (leg strength and endurance), Time Up and Go test (TUG) (general mobility), 1 min walk test (1MWT) (aerobic capacity) and Barthel Index (BI) (performance in daily activities). For the purposes of the study, two measurements were conducted: at admission and at discharge from the COVID-19 clinic. Results: Dependent samples tests showed a significant effect (p < 0.001) for the recommended physiotherapy treatment on respiratory variables: 6.9 (1.4)% for SpO2, 3.4 (0.9) breaths for Respiratory Rate, 5.0 (1.3) for Borg

Citation: Grammatopoulou, E.; Sdravou, D.; Gkiliri, F.; Bourtzi, A; Polymerou, A; Metallidis, S; Geka, E.; Koumantakis, G.A.; Christakou, A.; Evangelodimou, A. The effect of post-ICU physiotherapy on respiratory and physical functioning status in patients with COVID-19: a pilot study. *Proceedings* **2021**, *68*, x. https://doi.org/10.3390/xxxxx

Published: date

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



Copyright: © 2021 by the authors. Submitted for possible open access publication under the terms and conditions of the Creative Commons Attribution (CC BY) licenses (http://creativecommons.org/licenses/by/4.0/).

scale score. Significant improvements (p < 0.001) were additionally noted for physical functioning: 25.3 (13.0) for Berg balance scale, 18.5 (11.2) for MRCms score, 3 (1.3) s for Sit to Stand and 40.4 (40.6) s for TUG efforts, 44.1 (25.5) s for 1MWT and 65.9 (20.2) for BI. All patients displayed DB at admission to the COVID-19 clinic, while nine of them adopted a diaphragmatic breathing pattern at discharge. At admission to the COVID-19 clinic, all patients were at level 5 disability (MRCd), whereas at discharge 10 out of 11 patients improved (three at level 4, four at level 3 and three at level 2). *Conclusion:* The present pilot study provided a first evidence for the effectiveness of the WHO and WCPT physiotherapy recommendations on the respiratory and physical functioning status of patients with COVID-19. Further studies are needed to support these early findings.

Keywords: physiotherapy; respiratory; physical functioning; COVID-19

1. Introduction

Recent physiotherapy recommendations for patients with COVID-19 after discharge from ICU declare that they are expected to experience respiratory, physical, cognitive, and psychological problems due to the duration and nature of the immobilization and sedation, ventilation duration, and underlying morbidity [1–4]. Additionally, some patients with COVID-19, after discharge from ICU, might be at risk of long-term impairment and disability of unknown extent [5].

A holistic rehabilitation approach is needed in every stage of COVID-19 [4]. Physiotherapists are frontline healthcare professionals and potentially involved in the management of patients with COVID-19, as members of the multidisciplinary rehabilitation team [5]. They are engaged with the transition from the acute phase to the post-acute phase of COVID-19. After discharge from ICU, among patients with COVID-19, indication for physiotherapy have only those with a limitation in physical capacity and/or physical activity [3,4]. Physiotherapy is suggested for the assessment and management of ongoing respiratory and mobility impairments [5]. As recommended, physiotherapists should evaluate mobility (physical activity, balance), symptoms (dyspnea, impact of dyspnea), peripheral muscle strength, fatigue, quality of life and oxygen saturation levels. In addition, physiotherapy should be tailored to the individual patients' needs and goals including breathing exercises, early mobilization and self-management for daily living were performed once a day, for five days a week, as tolerated [3–5]. Nonetheless, the effect of physiotherapy treatment on the respiratory and functional capacity of patients with COVID-19 remains unproven as well as benefits of early physical rehabilitation following ICU discharge on quality of life and mortality are unclear [6].

#### 2. Materials and Methods

#### 2.1. Participants

This pilot clinical study was conducted from March to June 2020. The sample consisted of 11 patients with COVID-19, discharged form ICU and hospitalized in the COVID-19 clinic of AHEPA University Hospital. All participants had indication for physiotherapy, according to the recommendations, and medical referral as well. The duration of their hospitalization ranged from two to six weeks. Among participants, there were seven males and four females, aged from 44–75 yrs, five smokers and six nonsmokers, four obese and seven nonobese, seven participants had drop-foot and all of them had dysfunctional breathing. SpO<sub>2</sub> ranged from 88–93% and suffered from severe and above dyspnea, according to the Borg scale.

#### 2.2. Measurement Tools

## 2.2.1. Respiratory Measures

Pulse Oximeter (SpO<sub>2</sub>), Respiratory Rate (RR), Borg scale (intensity of dyspnea), Medical Research Council scale for disability (MRCd), and clinical evaluation of dysfunctional breathing (D.B.) were used.

Borg scale: The Borg scale measures the intensity of dyspnea (maximal intensity at 10). Subjects are asked to score breathlessness by selecting a number or words that most appropriately described their sensation of breathlessness [7].

Medical Research Council scale for disability (MRCd): The MRCd measures the extent to which their breathlessness affects their mobility (maximal intensity at 5) [8].

Clinical evaluation of dysfunctional breathing (D.B.): A physiotherapist-member of the research team assessed this outcome. Criteria for the D.B. evaluation were upper chest dominant breathing and thoraco-abdominal asynchrony [9].

# 2.2.2. Physical Function Measures

Medical Research Council scale for muscle strength (MRCms), Berg Balance Scale, 30 Second Sit to Stand test (30CST), Time Up and Go test (TUG), 1 minute walk test (1MWDT), and Barthel Index (BI) were used.

Medical Research Council scale for muscle strength (MRCms): The MRCms is a commonly used scale for assessing muscle strength from Grade 5 (normal) to Grade 0 (no visible contraction). Six muscle groups are examined bilaterally (shoulder abductors, elbow flexors, wrist extensors, hip flexors, knee extensors, and foot dorsiflexors). An MRCms total score below 48/60 refers to significant weakness [10].

Berg balance scale: It measures a patient's ability to balance during a series of predetermined tasks through 14 items. A cutoff score of 56 indicates functional balance, as well a cutoff score of <45 a greater risk of falling [11].

30 Second Sit to Stand test (30CST): The 30CST measures leg strength and endurance by counting the number of times a patient can stand to a fully erect position from a seated position with arms folded across their chest in 30 seconds time (floor effect five to ten repetitions) [12].

Time Up and Go test (TUG): TUG measures general mobility (balance, sit to stand and walking) and determines fall risk. The patient starts from a seated position, walks three meters, turns around, walks back to the chair, and sits down. The time stops when the patient is seated. Cut of scores indicating risk of falls for the community dwelling adults is 13.5 s [13].

1 minute walk test (1MWDT): The 1MWDT obtained during the first minute of a 6MWD is a valid measure for assessing functional ability and has shown a strong correlation to total 6MWDT [14].

Barthel Index (BI): The Barthel Index (BI) measures the patient's level of dependency through its capacity to perform 10 basic activities of daily living, divided to self-care and mobility components. The score ranges from 0 (totally dependent) to 100 (totally independent). BI classifies patients as having minimal or no disability (BI score, >90), moderate disability (BI score, 55–90) or severe disability (BI score < 55) [15].

For the purposes of the study, measurements were conducted at two time-points: at admission and at discharge from the COVID-19 clinic.

### 2.3. Intervention

Although consensus on type of physiotherapy intervention and timing is still missing, we followed the current recommendations and developed and applied a program tailored to the patients' priorities, needs and goals. Individualized breathing exercises, early mobilization and self-management for daily living were performed one to one, once a day, for five days a week, as tolerated for intensity, duration, and frequency.

Individualized breathing exercises comprised airway clearance methods for patients with secretions (usually active cycle of the breathing technique), breathing retraining to reduce dysfunctional breathing, diaphragmatic breathing, pursed-lip breathing for dyspnea relief, rib cage mobilization, slow and deep breathing, use of incentive spirometer, and alveoli recruitment for lung segments expansion, patient's oxygenation, and prevention of atelectasis [5].

Early mobilization (Figure 1) was an individualized program that consisted of passive-active exercises, actively moving or rolling in bed, sitting on the edge of the bed, stretching, progressive strength training, balance exercises, mobility training and gait retraining.

Self-management for daily living involved individualized education on breathlessness and fatigue management, energy conservation to promote independence with activities of daily living, participation in physical activity, when to stop exercising, and how to advise Borg scale (up to 4) and Pulse Oximeter (>90%).

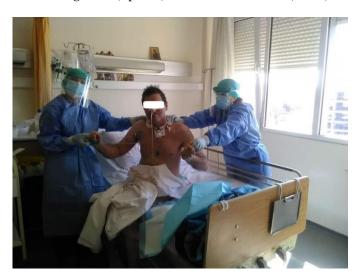


Figure 1. Early mobilization at the COVID-19 Clinic, AHEPA University Hospital.

# 3. Results

Dependent samples tests showed a significant effect (p < 0.001) for the recommended physiotherapy treatment on respiratory variables (SpO<sub>2</sub>, Respiratory Rate, Borg scale score) (Table 1) and physical functioning (Berg balance scale, MRCms score, Sit to Stand and TUG efforts, 1MWDT, BI) (Table 2). All patients displayed DB at post-ICU discharge, while nine of them adopted a diaphragmatic breathing pattern at post hospital discharge. At post ICU discharge, all patients were at level five disability (MRCd), whereas at post hospital discharge 10 patients improved (three at level four, four at level three and three at level two).

**Table 1.** Mean (SD) values of respiratory parameters after ICU discharge vs hospital discharge (n = 11).

	SpO <sub>2</sub>	RR	Borg Scale
ICU discharge	90.3 (1.7)	21.0 (1.5)	7.5 (1.7)
Hospital discharge	97.2 (1.1)	17.6 (1.2)	2.5 (1.1)
x difference	6.9 (1.4) **	3.4 (0.9) **	5.0 (1.3) **

<sup>\*\*</sup> *p* < 0.001.

**Table 2.** Mean (SD) values of physical function parameters after ICU discharge vs hospital discharge (n = 11).

	Berg Balance Scale	MRCms	30CST	TUG	1MWDT	BI
ICU discharge	9.4 (4.9)	30.2 (15.6)	0 (0)	0 (0)	0 (0)	0 (0)
Hospital discharge	34.6 (14.4)	48.7 (8.4)	3 (1.3)	40.4 (40.6)	44.1 (25.5)	65.9 (20.2)
<i>x</i> difference	25.3 (13.0) **	18.5 (11.2) **	3 (1.3) **	40.4 (40.6) **	44.1 (25.5) **	65.9 (20.2) **

\*\* *p* < 0.001.

4. Discussion

The present study was an attempt to provide evidence for the respiratory and physical functional impact of a physiotherapy intervention in a specific sample of patients with COVID-19. This is the first survey to demonstrate respiratory and physical functioning benefits through a physiotherapy program tailored to the COVID-19 patients' priorities, needs and goals, after discharge form ICU and hospitalization in a COVID-19 clinic.

This pilot study showed significant improvements on all respiratory outcome measures, with normative values achieved for the oxygen saturation (SpO<sub>2</sub>) and respiratory rate. The intensity of dyspnea (Borg Scale score), dysfunctional breathing, and level of disability (MRCd) were also significantly reduced for the specific sample of patients with COVID-19. This might be due to (a) the airway clearance methods that clear secretions and re-expand the atelectatic lung [16], (b) the diaphragmatic breathing that reduces respiratory rate, improves chest wall motion and distribution of ventilation, decreases dyspnea and energy cost of breathing and improves exercise performance [17], (c) the pursed-lips breathing that increases lung volumes and reduces breathing frequency [17,18], improves oxygen saturation and reduces arterial partial pressure of carbon dioxide (PCO2) [17], (d) the deep breathing exercises that reverse atelectasis, increase oxygenation, alveolar recruitment, functional residual capacity, and tidal volumes and potentially remove secretions [19], (e) the incentive spirometry that increases lung volumes and re-recruits atelectatic or collapsed areas of the lung [19] and (f) the breathing retraining that reduces dysfunctional breathing which results dyspnea [9,20].

Additionally, a significant improvement in the muscular strength and endurance, balance, general mobility, functional ability and level of dependency was achieved for the specific sample of patients with COVID-19. This might be due to early mobilization that increases joint mobility and reduces skeletal muscle atrophy, via provocation of physiological effects such as blood flow increase in patients' limbs and internal organs of the body [21]. Furthermore, mobilization limits the myosin loss and muscle wasting [22], while performing progressive resistance exercises leads to muscle strength increases and higher mobility status of ICU survivors [23]. Early mobilization improves functional capacity [24,25], muscle strength [26], walking distance [25], patients' independency after ICU discharge and discharge to home rate [24]. Balance training and gait training increase the distance the patient is able to walk unassisted at hospital discharge [24]. Finally, selfmanagement for daily living education as a part of the applied program in the present study aimed to the facilitation of the performance of activities of daily living (ADL) for the patients with COVID-19. The results showed significant improvement for the participant's level of dependency (Barthel index), ranging from 'totally dependent' to 'moderate disability'. The importance of this specific outcome lies on the association of Barthel Index with ICU readmission [27].

A limitation of the study was the absence of a control group, due to the small sample and its inhomogeneity. Further research is needed to demonstrate that physiotherapists are vital to the rehabilitation effort for the patients with COVID-19.

5. Conclusion

The present pilot study provided a first evidence for the effectiveness of the WHO and WCPT physiotherapy recommendations on the respiratory and physical functioning status of patients with COVID-19. The findings of the present study signify the need for early post-ICU physiotherapy provision within a holistic management framework of patients with COVID-19. Further studies are needed to support these early findings.

**Author Contributions:** For research articles with several authors, a short paragraph specifying their individual contributions must be provided. The following statements should be used "Conceptualization, E.G., S.M., E.G., G.A.K., A.C. and A.E.; methodology, E.G., G.A.K., A.C. and A.E.; formal analysis, E.G., G.A.K., A.C. and A.E.; investigation, E.G., D.S., F.G., A.B., A.P., S.M. and E.G.; resources, D.S., F.G., A.B., A.P. and G.A.K.; writing—original draft preparation, E.G., G.A.K., A.C. and A.E.; writing—review and editing, E.G., G.A.K., A.C. and A.E.; visualization, E.G., G.A.K., A.C. and A.E.; supervision, E.G.; project administration, E.G. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

**Institutional Review Board Statement:** The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Institutional Review Board of the AHEPA University Hospital, School of Medicine, Health Sciences Faculty, Aristotle University of Thessaloniki, Greece (457/6-3-2020).

**Informed Consent Statement:** Informed consent was obtained from all subjects involved in the study.

**Data Availability Statement:** The data presented in this study are available on request from the corresponding author. The data are not publicly available due to privacy reasons.

**Acknowledgments:** We thank the participants of the present study and the medical staff of the COVID-19 clinic of AHEPA University Hospital at Thessaloniki, Greece.

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

References

1. British Thoracic Society. Delivering rehabilitation to patients surviving COVID-19 using an adapted pulmonary rehabilitation approach – BTS guidance. London, 2020. Available online: <a href="https://www.brit-thoracic.org.uk/document-library/quality-improve-ment/covid-19/pulmonary-rehabilitation-for-covid-19-patients/">www.brit-thoracic.org.uk/document-library/quality-improve-ment/covid-19/pulmonary-rehabilitation-for-covid-19-patients/</a> (Accessed on 5 June 2020).

2. Royal Dutch Society for Physiotherapy. KNGF position statement: Physiotherapy recommendations in patients with COVID-19. Amersfoort, Netherlands: KNGF, 2020. Available online: <a href="www.kngf.nl/kennisplatform/guidelines">www.kngf.nl/kennisplatform/guidelines</a> (Accessed on 5 June 2020).

- 3. WHO. COVID-19 exposes the critical importance of patient rehabilitation. In: World Health Organization Regional Office for Europe, 2020. Available online: <a href="https://www.euro.who.int/en/health-topics/health-emergencies/coronavirus-covid-19/news/2020/4/covid-19-exposes-the-critical-importance-of-patient-rehabilitation">www.euro.who.int/en/health-topics/health-emergencies/coronavirus-covid-19/news/news/2020/4/covid-19-exposes-the-critical-importance-of-patient-rehabilitation</a> (Accessed on 28 April 2020).
- 4. World Confederation for Physical Therapy (WCPT). WCPT response to COVID-19 Briefing paper 2. Rehabilitation and the vital role of Physiotherapy. 2020. Available online: world.physio/sites/default/files/2020-07/COVID19-Briefing-Paper-2-Rehabilitation.pdf (Accessed on 5 June 2020).
- 5. Pan American Health Organization. Rehabilitation considerations during the COVID-19 outbreak. Washington DC, USA: PAHO, 2020. Available online: <a href="mailto:iris.paho.org/handle/10665.2/52035">iris.paho.org/handle/10665.2/52035</a> (Accessed on 5 June 2020).
- 6. Taito, S.; Yamauchi, K.; Tsujimoto, Y.; Banno, M.; Tsujimoto, H.; Kataoka, Y. Does enhanced physical rehabilitation following intensive care unit discharge improve outcomes in patients who received mechanical ventilation? A systematic review and meta-analysis. *BMJ Open* **2019**, *9*, e026075.
- 7. Crisafulli, E.; Clini, E.M. Measures of dyspnea in pulmonary rehabilitation. Multidiscip. Respir. Med 2010, 5, 202–210.
- 8. Stenton, C. The MRC breathlessness scale. Occup. Med. (Lond) 2008, 58, 226–227.
- 9. Boulding, R.; Stacey, R.; Niven, R.; Fowler, S.J. Dysfunctional breathing: a review of the literature and proposal for classification. *Eur Respir Rev* **2016**, *25*, 287–294.
- 10. Hermans, G.; Clerckx, B.; Vanhullebusch, T.; Segers, J.; Vanpee, G.; Robbeets, C.; Casaer, M.P.; Wouters, P.; Gosselink, R.; Van Den Berghe, G. Interobserver agreement of Medical Research Council sum-score and handgrip strength in the intensive care unit. *Muscle Nerve* 2012, 45, 18–25.
- 11. Berg, K.O.; Wood-Dauphinee, S.L.; Williams, J.I.; Maki, B. Measuring balance in the elderly: validation of an instrument. *Can. J. Pub. Health* **1992**, *83*, S7–S11.

20 21

- 12. Hameed, F.; Palatulan, E.; Jaywant, A.; Said, R.; Lau, C.; Sood, V.; Layton, A.; Gellhorn, A. Outcomes of a COVID-19 recovery program for patients hospitalized with SARS-CoV-2 infection in New York City: A prospective cohort study. *PM R.* **2021**, *13*, 609–617.
- 13. Shumway-Cook, A.; Brauer, S.; Woollacott, M. Predicting the probability for falls in community-dwelling older adults using the Timed Up & Go Test. *Phys. Ther.* **2000**, *80*, 896–903.
- 14. Nunes, F.S.; Pastre, J.; Brown, A.W.; Shlobin, O.A.; King, C.; Weir, N.A.; Nathan, S.D. Does 1-minute walk test predict results of 6-minute walk test in patients with idiopathic pulmonary fibrosis? *Sarcoidosis Vasc. Diffuse Lung Dis* **2021**, *38*, e2021005.
- 15. Mahoney, F.I.; Barthel, D.W. Functional evaluation: The Barthel Index. Md. State Med. J. 1965, 14, 61–65.
- 16. Jelic, S.; Cunningham, J.A.; Factor, P. Clinical review: airway hygiene in the intensive care unit. Crit. Care 2008, 12, 209.
- 17. Gosselink, R. Controlled breathing and dyspnea in patients with chronic obstructive pulmonary disease (COPD). *J. Rehabil. Res. Dev.* **2003**; *40*, 25–33.
- 18. Mendes, L.P.; Moraes, K.S.; Hoffman, M.; Vieira, D.S.; Ribeiro-Samora, G.A.; Lage, S.M.; Britto, R.R.; Parreira, V.F. Effects of Diaphragmatic Breathing With and Without Pursed-Lips Breathing in Subjects With COPD. *Respir. Care* **2019**, *64*, 136–144.
- 19. Pathmanathan, N.; Beaumont, N.; Gratrix, A. Respiratory physiotherapy in the critical care unit. BJA Educ. 2015, 15, 20–25.
- 20. Davido, B.; Seang, S.; Barizien, N.; Tubiana, R.; de Truchis, P. 'Post-COVID-19 chronic symptoms' Author's reply. *Clin. Microbiol. Infect.* **2021**, 27, 495–496.
- 21. Gosselink, R.; Bott, J.; Johnson, M.; Dean, E.; Nava, S.; Norrenberg, M.; Schönhofer, B.; Stiller, K.; van de Leur, H.; Vincent, J.L. Physiotherapy for adult patients with critical illness: recommendations of the European Respiratory Society and European Society of Intensive Care Medicine Task Force on Physiotherapy for Critically Ill Patients. *Intensive Care Med* 2008, 34, 1188–1199.
- 22. Llano-Diez, M.; Gustafson, A.M.; Olsson, C.; Goransson, H.; Larsson, L. Muscle wasting and the temporal gene expression pattern in a novel rat intensive care unit model. *BMC Genomics* **2011**, *12*, 602.
- 23. Hodgson, C.L.; Tipping, C.J. Physiotherapy management of intensive care unit-acquired weakness. J. Physiother. 2017; 63, 4–10.
- 24. Zhang, L.; Hu, W.; Cai, Z.; Liu, J.; Wu, J.; Deng, Y.; Yu, K.; Chen, X.; Zhu, L.; Ma, J.; Qin, Y. Early mobilization of critically ill patients in the intensive care unit: A systematic review and meta-analysis. *PLoS One* **2019**, *14*, e0223185.
- 25. Schweickert, W.D.; Pohlman, M.C.; Pohlman, A.S.; Nigos, C.; Pawlik, A.J.; Esbrook, C.L.; Spears, L.; Miller, M.; Franczyk, M.; Deprizio, D.; et al. Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial. *Lancet* 2009, 373, 1874–1882.
- 26. Dantas, C.M.; Silva, P.F.; Siqueira, F.H.; Pinto, R.M.; Matias, S.; Maciel, C.; Oliveira, M.C.; Albuquerque, C.G.; Andrade, F.M.; Ramos, F.F.; et al. Influence of early mobilization on respiratory and peripheral muscle strength in critically ill patients. *Rev. Bras. Ter. Intensiva* **2012**, 24, 173–178.
- 27. Silveira, L.; Silva, J.M.D.; Tanaka, C.; Fu, C. Decline in functional status after intensive care unit discharge is associated with ICU readmission: a prospective cohort study. *Physiotherapy* **2019**, *105*, 321–327.