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Factors associated with functional decline in an intensive care unit: a prospective study on the level of physical activity and clinical factors

Fatores associados com o declínio funcional em uma unidade de terapia intensiva: estudo prospectivo sobre o nível de atividade física e os fatores clínicos

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ABSTRACT

Objective: To identify the factors associated with functional status decline in intensive care unit patients.

Methods: In this prospective study, patients in an intensive care unit aged 18 years or older without neurological disease or contraindications to mobilization were included. The exclusion criteria were patients who spent fewer than 4 days in the intensive care unit or died during the study period. Accelerometry was used to assess the physical activity level of patients. We recorded age, SAPS 3, days on mechanical ventilation, drugs used, comorbidities, and functional status after intensive care unit discharge. After intensive care unit discharge, the patients were assigned to a dependent group or an independent group according to their Barthel index. Logistic regression and the odds ratio were used in the analyses.

Results: Sixty-three out of 112 included patients were assigned to the dependent group. The median Charlson comorbidity index was 3 (2 - 4). The mean SAPS 3 score was 53 ± 11. The patients spent 94 ± 4% of the time spent in inactivity and 4.8 ± 3.7% in light activities. The odds ratio showed that age (OR = 1.08; 95%CI 1.04 - 1.13) and time spent in inactivity (OR = 1.38; 95%CI 1.14 - 1.67) were factors associated with functional status decline. Time spent in light activity was associated with a better functional status (OR = 0.73; 95%CI 0.60 - 0.89).

Conclusions: Age and time spent in inactivity during intensive care unit stay are associated with functional status decline. On the other hand, performing light activities seems to preserve the functional status of patients.

Keywords: Exercise; Physical functional performance; Intensive care units

INTRODUCTION

Studies have shown that patients frequently present physical function impairment after intensive care unit (ICU) stays.[1,2] This renders patients partially or completely dependent,[3,4] impairing their quality of life.[5,6] These consequences may persist for up to five years after ICU discharge, keeping the patients dependent on their activities of daily living and affecting their ability to return to work.[7-10]

During an ICU stay, critically ill patients are exposed to factors that could lead to functional loss; one such factor is inactivity.[11] Inactivity is characterized by low mobility and the absence of physical activity.[12] A period of inactivity has been described as a common yet undesirable situation during hospital stays, and it can be caused by many factors present in the ICU.[13,14] Physical activity and exercises performed during an ICU stay may counteract the state of inactivity and prevent the complications associated with it, such as functional status decline.[15] Although early mobility and exercise for ICU patients seem to be feasible and safe and potentially decrease immobility-related complications,[16-18] studies on mobilization in the ICU have shown that ICU patients are still inadequately stimulated.[13,19] Studies have also shown the benefits of performing exercises in the ICU, but little is known about specific factors, such as the activity level and its association with different levels of functionality.

The recognition of the association between clinical factors, such as illness severity, age, comorbidities, specific therapeutics, and the level of activity during an ICU stay, with functional status after ICU discharge may aid in the planning of future therapeutic interventions. We hypothesized that low activity levels during an ICU stay would be highly associated with functional status decline after ICU discharge, with a stronger correlation than other variables. Therefore, the objective of this study was to determine the association between clinical factors and physical activity with functional status after ICU discharge.

METHODS

Design and participants

This was a prospective observational study performed at a general ICU in a tertiary care university hospital. Patients admitted to the ICU were assessed daily for eligibility criteria. The inclusion criteria were as follows: patients admitted directly to the ICU, aged greater than or equal to 18 years, without neurological disease or medical contraindication for mobilization and with a Barthel Index (BI)[20] greater than or equal to 85. The exclusion criteria were an ICU stay less than four days and death during the study. This study met was approved by the local Ethics Committee (CAAE 21453514.9.0000.0068).

After inclusion in the study, an accelerometer was placed on each patient's dominant ankle until ICU discharge.

Patients were followed daily and were reassessed on the first day after ICU discharge for handgrip muscle strength and functional status.

Patients underwent routine physical therapy twice daily, every day during their ICU stay. Routine physical therapy included patients mobility and both sitting in an armchair and sitting on the bedside. There was no protocol for early mobility.

Demographic and clinical information

Age, sex, weight, and height were recorded on the patients' first day in the ICU. The presence of comorbid conditions was scored using the Charlson comorbidity index,[21] and the severity of disease was evaluated using the Simplified Acute Physiology Score 3 (SAPS 3).[22] Other clinical data, such as ICU admission diagnosis, length of ICU stay, use of vasopressors and corticosteroids, use and duration of mechanical ventilation, dialysis, and other therapies, were collected until ICU discharge.

Level of physical activity

The ActiGraph GT3X (Actigraph, U.S.A.) is an activity monitor with a triaxial accelerometer; it was used to assess the level of physical activity. This is an instrument with which to objectively measure a patient's level of activity. [23,24] It can detect changes in acceleration while maintaining a continuous record of minimal movements. In addition, it provides specific information such as the percentage of time that the patient spent at different levels of physical activity (inactivity, light activity and moderate activity) during hospitalization.

The monitor was inspected daily to ensure proper positioning and recording of data. The multidisciplinary team was advised not to remove the instrument. The activity data were analyzed using ActiLife 6 software using a validated algorithm for healthy elderly patients.[25] Analyzed data corresponded to the period between 7 a.m. until 7 p.m., every day, from ICU admission until ICU discharge. The activity data were analyzed using the percentage of time spent at each level of physical activity.

Muscle strength

Handgrip strength was measured after ICU discharge using a Jamar dynamometer. The assessments were performed on each patient's dominant hand within 24 hours after ICU discharge. Patients were positioned as close to the upright position as possible, with the shoulder in neutral rotation and the elbow flexed at 90 degrees.

Patients were provided verbal encouragement to squeeze the dynamometer tightly for 2 or 3 seconds. Three trials were performed, and the highest value was registered.[26]

Functional status

Functional status before hospitalization was assessed using the BI, based on interviews with the patient or patient's family, evaluating the patient's functional status two weeks before admission to the ICU. The BI analyzes a patient's functional status via a questionnaire on pre-established daily living activities.[20] A higher score indicates functional independence. The BI has been used in several studies of critically ill patients after ICU hospitalization and has been proven to be an effective tool for assessing this population.[1,16] Functional status after ICU discharge was assessed within 24 hours. According to a cutoff score described in the literature, patients were considered functionally dependent if their BI was lower than 85.[27]
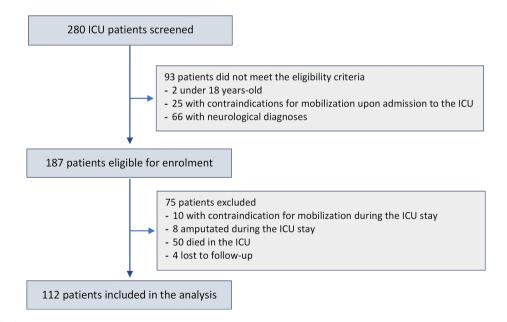
Statistical analysis

Statistical analysis was performed using SigmaStat (version 3.0). The Kolmogorov-Smirnov test was used to verify data normality. Data that conformed to a normal distribution are presented as the mean ± standard deviation (SD), and data that conformed to a nonnormal distribution are presented as the median and interquartile range. The absolute number and percentage were used to describe qualitative data. Statistical significance was set at a 5% or 95% confidence interval (CI).

For the analysis, patients were divided into two groups according to their functional status after ICU discharge based on the BI: the Functionally Independent Group (IG), with a BI equal to or greater than 85; and the Functionally Dependent Group (DG), with a BI less than 85. For comparing characteristics between the IG and the DG, the independent *t* test was used for data that conformed to a normal distribution, and the Mann-Whitney U test was applied for data that conformed to a nonnormal distribution. The chi-square test was used for frequencies.

For the final analysis on functional status, logistic regression was performed. The variables age, use of mechanical ventilation, sedatives, vasoactive drugs, corticosteroids, percentage of time at different levels of activity, days spent in the ICU and muscle strength after discharge were tested for the final model. Age, the percentage of time spent in inactivity and time spent in light activity were included in the logistic regression as independent variables. The dependent variable was functional status (BI) after ICU discharge. Bonferroni correction was applied after multiple correlations (0.05/variables tested +1) were determined.

RESULTS

Out of the 187 patients screened for inclusion in this study, 75 were excluded; therefore, 112 patients completed the study (Figure 1). The included patients were aged 57 ± 15 years, and 52% were male. The median Charlson comorbidity index was 3 (2 - 4), and the mean SAPS 3 was 53 ± 11. All patients were functionally independent before ICU admission. The characteristics of the study population are listed in table 1.

Figure 1 - Patients' selection.
ICU - intensive care unit.

Table 1 - Characteristics of the intensive care unit population

Variables	
Female	52 (46)
Age (years)	57 ± 15
SAPS 3	53 ± 11
Charlson comorbidity index	3 (2 - 4)
Surgical patients	19 (16)
Use of sedative drugs	13 (21)
Duration of sedation (days)	3 (2 - 5)
Use of mechanical ventilation	41 (36)
Duration of mechanical ventilation (days)	2.5 (1 - 4)
Use of vasopressors	52 (46)
Duration of vasopressors (days)	2 (1-3)
Use of corticoids	36 (32)
ICU length of stay (days)	7 (5 - 11)
Medical conditions	
Respiratory	56 (51)
Others	55 (49)
Handgrip force after ICU discharge (kgf)	18 (12-25)
Barthel Index before hospital admission	100 (100 - 100)
Barthel Index after ICU discharge	80 (60 - 100)

SAPS - Simplified Acute Physiology Score; ICU - intensive care unit. Results expressed as the n (%), mean ± standard deviation or median (1st - 3rd quartiles).

Table 2 - Comparison of demographic and hospitalization characteristics between the functionally dependent and functionally independent groups

Variables	IG (n=49)	DG (n=63)	p value
Age (years)	48 ± 14	64 ± 11	< 0.001
Sex (male/female)	14/12	19/17	0.86
SAPS 3	49 ± 10	56 ± 10	< 0.001
Charlson comorbidity index	2 (2 - 3)	4 (3 - 5)	< 0.001
Surgical patients	8	11	0.9
Corticoid use	14	22	0.6
Sedation use	5	8	0.9
Sedation duration (days)	2.2 ± 0.4	4.1 ± 2.5	0.12
Mechanical ventilation (yes/no)	8/18	15/21	0.5
Ventilator (days)	2 (1 - 4)	3 (1 - 5.5)	0.6
Vasopressor use	9	13	0.88
Vasopressors (days)	2 (1 - 2.2)	2.5 (1 - 4)	0.59
ICU stay (days)	7 (5 - 8)	9 (5 - 11)	0.13
Hospital stay (days)	14 (9 - 26)	14 (8 - 24)	0.87
Handgrip force upon discharge (kgf)	24 (18 - 36)	17 (12 - 20)	< 0.001
Barthel Index at admission	100 (100 - 100)	100 (100 - 100)	0.9
Barthel Index after discharge	100 (95 - 100)	60 (45 - 75)	0.01

IG - functionally independent group; GD - functionally dependent group; SAPS - Simplified Acute Physiology Score; ICU - intensive care unit. Results expressed as the n (%), mean ± standard deviation or median (1st - 3rd quartiles).

Patients in the DG were older and had more comorbidities and a higher SAPS 3 (Table 2). In contrast, patients in the IG performed higher levels of physical activity during their ICU stays and presented greater handgrip muscle strength after ICU discharge. This group spent a higher percentage of the time in light and moderate activities, whereas the DG spent more time in inactivity (96 ± 2% *versus* 92 ± 4%; p < 0.001) (Table 3).

Factors associated with functional status decline

The results of the regression analysis showed that the variables independently associated with a poor functional status after ICU discharge were the percentage of time spent in inactivity, percentage of time spent in light activity and older age.

Level of physical activity

Activity was measured between 7 a.m. and 7 p.m. Patients spent 94.6 ± 4% of their ICU stay in inactivity. Patients performed some level of physical activity only 5.4% of the entire duration of their ICU stay: 4.85 ± 3.7% of their time was spent in light activity, and 0.55 ± 0.2% of their time was spent in moderate activity.

Functional status

After ICU discharge, 56% of the participants showed some level of functional dependence. The median BI for the IG was 100, whereas that for the DG was 60 (Table 2).

Table 3 - Comparison of physical strength, functional status, and level of activity between the functionally dependent and independent groups

Variables	IG (n = 49)	DG (n = 63)	p value	95%CI
Handgrip force after ICU discharge (kgf)	24 (18 - 36)	17 (12 - 20)	< 0.001	-11,540 - -4,206
Barthel Index before hospital admission	100 (100 - 100)	100 (100 - 100)	0.9	-0,516 - 0,198
Barthel Index after ICU discharge	100 (95 - 100)	60 (45 - 75)	0.01	-40,643 - -30,672
Level of activity				
Inactivity (%)	90 ± 4	96 ± 2	< 0.001	2,169 - 4,555
Light activity (%)	8 ± 3	3 ± 2	< 0.001	-3,931 - -1,812
Moderate activity (%)	0.76 ± 0,36	0.16 ± 0,09	< 0.001	-0,666 - -0,269

IG - functionally independent group; GD - functionally dependent group; 95%CI - 95% confidence interval; ICU - intensive care unit. Results expressed as the n (%), mean ± standard deviation or median (1st - 3rd quartiles).

Older age resulted in an 8% increase in the odds of presenting functional dependence after ICU discharge (odds ratio - OR = 1.08; 95%CI 1.04 - 1.13). The percentage of time spent in inactivity increased this chance by 38% (OR = 1.38; 95%CI 1.14 - 1.67) (Table 4). The results showed that time spent in light activity was a protective factor for functional status (OR = 0.73; 95%CI 0.60 - 0.89).

Table 4 - Factors associated with functional decline after intensive care unit discharge

Characteristics	Odds ratio	CI (5% - 95%)
Older age	1.08	(1.04 - 1.13)
Time in inactivity (%)	1.38	(1.14 - 1.67)
Time in light level of activity (%)	0.73	(0.60 - 0.89)

CI - Confidence interval. Odds ratio from logistic regression analysis.

DISCUSSION

In this study, clinical and therapeutic factors of ICU patients were evaluated to identify the factors associated with functional status after ICU discharge. Thus, the level of inactivity was a factor more closely associated with a poorer functional status after discharge from the ICU than the other clinical and therapeutic variables addressed. Similarly, a light level of physical activity was associated with patients who were functionally independent after discharge.

Age was the only clinical and therapeutic variable associated with functional loss after discharge from the ICU. Studies have observed an association between functional status decline and age, demonstrating that elderly patients are the most affected after hospitalization.[28,29] Brown et al. showed that age and low mobility during hospitalization were associated with functional status decline, and low mobility was classified as an iatrogenic factor in older patients.[30] These data, in addition to our own, emphasize the importance of greater attention to the elderly population, since age is a nonmodifiable risk factor and the only associated clinical factor we identified On the other hand, the largest associated risk factor was the duration of inactivity, already described in the literature as associated with muscle weakness acquired in the ICU, which can lead to functional loss.[31] Low levels of activity on admission have already been associated with low levels of mobility after ICU discharge,[32] which in elderly patients was associated with an inability to return home. Other potential factors that could be associated with functional decline after an ICU stay, such as strength, corticosteroid use, sedation use, and mechanical ventilation,[11] did not show significance in our regression analysis.

We believe that inactivity was a factor associated with functional decline because it increased the patients' predisposition to the negative effects of immobility on the body systems, including those systems essential for maintaining functionality.[33-35]

On the other hand, studies have shown that an increase in the level of physical activity during an ICU through exercise programs favors greater independence after discharge from the ICU.[36] Studies have indicated that early mobility is a positive strategy for better outcomes after discharge.[16,36,37] Our data showed the time spent at a light level of activity as a protective factor for functional loss. We believe that although our patients were under specific ICU conditions, they also benefitted from undergoing physical activity. Although the percentage of time that our patients spent in physical activity was small, our data show that taking these patients out of bed, even just to engage them in light activity, was sufficient for them to experience smaller functional declines. Studies have shown the benefits of early mobilization in the ICU,[16,36,37] and our data suggest that not only should mobilization be early, but it should also augment the time and the level of activity. It is important to emphasize that keeping these patients engaged in higher levels of activity is important, but always with a focus on individualization and following the principles of exercise, such as frequency, repetition and quality of exercises.

We evaluated several factors to which patients in the ICU are subject to determine each variable's contribution to functional decline. To analyze the physical activity level, we measured the activity during the entire ICU stay. Previous studies that analyzed mobility in hospitalized patients were performed using restricted time frames.[19,30] The data derived in the current study quantitatively contribute to research on the physical activity of patients in the ICU based on a technology that allows objective and quantitative information to be collected. The use of these methods has been encouraged, and ActiGraph GT3X has proven to be a promising and efficient instrument for evaluating critical patients.[24]

Because our data were obtained from only one hospital, we consider this a limitation to our study. The BI was assessed at only two specific times, rendering it impossible to detect the specific moment of functional decline. There is no specific algorithm for using the ActiGraph GT3X to analyze the level of physical activity in the ICU. With our data, it is possible to analyze the level of physical activity; however, we do not know the level of activity provided by specific exercises.

A recent review of the literature has suggested the need for research to determine the optimal dose and intensity of different levels of exercise under specific conditions.[38] The results of our study offer the first evidence that different levels of physical activity during an ICU stay are related to different functional levels after ICU discharge.

CONCLUSION

We conclude that older age and time spent in inactivity during intensive care unit stays were factors associated with the loss of functional independence. In addition, performing light activity during an intensive care unit stay was associated with a better functional status in intensive care unit patients. Therefore, the only modifiable factor associated with the maintenance of functionality in our study was physical activity, even when performed at a low level.

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RESUMO

Objetivo: Identificar os fatores associados com o declínio do estado funcional em pacientes na unidade de terapia intensiva.

Métodos: Foram incluídos neste estudo prospectivo pacientes com idade de 18 anos ou mais, sem doença neurológica ou contraindicações para mobilização, internados em uma unidade de terapia intensiva. Os critérios para exclusão foram pacientes com permanência na unidade de terapia intensiva inferior a 4 dias, ou com óbito durante o período do estudo. A avaliação do nível de atividade física dos pacientes foi realizada com acelerometria. Registraram-se idade, escore segundo o SAPS 3, dias de ventilação mecânica, fármacos utilizados, comorbidades e estado funcional por ocasião da alta da unidade de terapia intensiva. Segundo seu estado funcional na alta da unidade de terapia intensiva, os pacientes foram designados para os grupos "dependentes" ou "independentes", segundo seu índice na escala de Barthel. As análises foram realizadas com regressão logística e cálculo da razão de chance.

Resultados: Dos 112 pacientes incluídos, 63 foram atribuídos ao grupo "dependentes". O índice de comorbidade de Charlson mediano foi de 3 (2 - 4). O SAPS 3 médio foi de 53 ± 11. Os pacientes permaneceram 94 ± 4% do tempo na unidade de terapia intensiva em condições de inatividade e 4,8 ± 3,7% em atividades leves. As análises de razão de chance mostraram que idade (RC = 1,08; IC95% 1,04 - 1,13) e tempo de inatividade (RC = 1,38; IC95% 1,14 – 1,67) foram fatores associados ao declínio funcional. O tempo em atividades leves se associou com melhor estado funcional (RC = 0,73; IC95% 0,60 - 0,89).

Conclusão: Idade e tempo em inatividade durante a internação na unidade de terapia intensiva se associaram com declínio do estado funcional. Por outro lado, a realização de atividades leves parece preservar a condição funcional dos pacientes.

Descritores: Exercício físico; Desempenho físico funcional; Unidades de terapia intensiva

REFERENCES

1. Silveira LT, Silva JM, Soler JM, Sun CY, Tanaka C, Fu C. Assessing functional status after intensive care unit stay: the Barthel Index and the Katz Index. Int J Qual Health Care. 2018;30(4):265-70.

2. Bryant SE, McNabb K. Postintensive care syndrome. Crit Care Nurs Clin North Am. 2019;31(4):507-16.

3. Borges RC, Carvalho CR, Colombo AS, da Silva Borges MP, Soriano FG. Physical activity, muscle strength, and exercise capacity 3 months after severe sepsis and septic shock. Intensive Care Med. 2015;41(8):1433-44.

4. Dietrich C, Leães CG, Veiga GM, Rodrigues CS, Cunha LS, Santos LJ. Funcionalidade e qualidade de vida de pacientes internados na unidade de terapia intensiva. ASSOBRAFIR Ciência. 2014;5(1):41-51.

5. Hodgson CL, Udy AA, Bailey M, Barrett J, Bellomo R, Bucknall T, et al. The impact of disability in survivors of critical illness. Intensive Care Med. 2017;43(7):992-1001. Erratum in Intensive Care Med. 2017;43(12):1938.

6. van der Schaaf M, Beelen A, Dongelmans DA, Vroom MB, Nollet F. Poor functional recovery after a critical illness: a longitudinal study. J Rehabil Med. 2009;41(13):1041-8.

7. Hermans G, Van Mechelen H, Clerckx B, Vanhullebusch T, Mesotten D, Wilmer A, et al. Acute outcomes and 1-year mortality of intensive care unit-acquired weakness. A cohort study and propensity-matched analysis. Am J Respir Crit Care Med. 2014;190(4):410-20.

8. Herridge MS, Cheung AM, Tansey CM, Matte-Martyn A, Diaz-Granados N, Al-Saidi F, Cooper AB, Guest CB, Mazer CD, Mehta S, Stewart TE, Barr A, Cook D, Slutsky AS; Canadian Critical Care Trials Group. One-year outcomes in survivors of the acute respiratory distress syndrome. N Engl J Med. 2003;348(8):683-93.

9. Herridge MS, Tansey CM, Matté A, Tomlinson G, Diaz-Granados N, Cooper A, Guest CB, Mazer CD, Mehta S, Stewart TE, Kudlow P, Cook D, Slutsky AS, Cheung AM; Canadian Critical Care Trials Group. Functional disability 5 years after acute respiratory distress syndrome. N Engl J Med. 2011;364(14):1293-304.

10. Dowdy DW, Eid MP, Dennison CR, Mendez-Tellez PA, Herridge MS, Guallar E, et al. Quality of life after acute respiratory distress syndrome: a meta-analysis. Intensive Care Med. 2006;32(8):1115-24.

11. Vanhorebeek I, Latronico N, Van Den Berghe G. ICU-acquired weakness. Intensive Care Med. 2020;46(4):637-53.

12. Vollman KM. Introduction to progressive mobility. Crit Care Nurse. 2010;30(2):S3-5.

13. Jolley SE, Moss M, Needham DM, Caldwell E, Morris PE, Miller RR, Ringwood N, Anders M, Koo KK, Gundel SE, Parry SM, Hough CL; Acute Respiratory Distress Syndrome Network Investigators. Point prevalence study of mobilization practices for acute respiratory failure patients in the United States. Crit Care Med. 2017;45(2):205-15.

14. Parry SM, Remedios L, Denehy L, Knight LD, Beach L, Rollinson TC, et al. What factors affect implementation of early rehabilitation into intensive care unit practice? A qualitative study with clinicians. J Crit Care. 2017;38:137-43.

15. Anekwe DE, Biswas S, Bussières A, Spahija J. Early rehabilitation reduces the likelihood of developing intensive care unit-acquired weakness: a systematic review and meta-analysis. Physiotherapy. 2020;107:1-10.

16. Schweickert WD, Pohlman MC, Pohlman AS, Nigos C, Pawlik AJ, Esbrook CL, et al. Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial. Lancet. 2009;373(9678):1874-82.

17. Nydahl P, Sricharoenchai T, Chandra S, Kundt FS, Huang M, Fischill M, et al. Safety of patient mobilization and rehabilitation in the intensive care unit. Systematic review with meta-analysis. Ann Am Thorac Soc. 2017;14(5):766-77.

18. Tipping CJ, Harrold M, Holland A, Romero L, Nisbet T, Hodgson CL. The effects of active mobilisation and rehabilitation in ICU on mortality and function: a systematic review. Intensive Care Med. 2017;43(2):171-83.

19. Berney SC, Rose JW, Bernhardt J, Denehy L. Prospective observation of physical activity in critically ill patients who were intubated for more than 48 hours. J Crit Care. 2015;30(4):658-63.

20. Mahoney FI, Barthel DW. Functional evaluation: the Barthel Index. Md State Med J. 1965;14:61-5.

21. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987;40(5):373-83.

22. Moreno RP, Metnitz PG, Almeida E, Jordan B, Bauer P, Campos RA, Iapichino G, Edbrooke D, Capuzzo M, Le Gall JR; SAPS 3 Investigators. SAPS 3--From evaluation of the patient to evaluation of the intensive care unit. Part 2: Development of a prognostic model for hospital mortality at ICU admission. Intensive Care Med. 2005;31(10):1345-55.

23. Troiano RP, McClain JJ, Brychta RJ, Chen KY. Evolution of accelerometer methods for physical activity research. Br J Sports Med. 2014;48(13):1019-23.

24. Kamdar BB, Kadden DJ, Vangala S, Elashoff DA, Ong MK, Martin JL, et al. Feasibility of continuous actigraphy in patients in a medical intensive care unit. Am J Crit Care. 2017;26(4):329-35.

25. Freedson PS, Melanson E, Sirard J. Calibration of the computer science and applications, Inc. accelerometer. Med Sci Sports Exerc. 1998;30(5):777-81.

26. Richards LG, Olson B, Palmiter-Thomas P. How forearm position affects grip strength. Am J Occup Ther. 1996;50(2):133-8.

27. Cincura C, Pontes-Neto OM, Neville IS, Mendes HF, Menezes DF, Mariano DC, et al. Validation of the National Institutes of Health Stroke Scale, modified Rankin Scale and Barthel Index in Brazil: the role of cultural adaptation and structured interviewing. Cerebrovasc Dis. 2009;27(2):119-22.

28. Ferrante LE, Pisani MA, Murphy TE, Gahbauer EA, Leo-Summers LS, Gill TM. Functional trajectories among older persons before and after critical illness. JAMA Intern Med. 2015;175(4):523-9.

29. Mattocks C, Deere K, Leary S, Ness A, Tilling K, Blair SN, et al. Early life determinants of physical activity in 11 to 12 year olds: cohort study. Br J Sports Med. 2008;4(9):721-4.

30. Brown CJ, Friedkin RJ, Inouye SK. Prevalence and outcomes of low mobility in hospitalized older patients. J Am Geriatr Soc. 2004;52(8):1263-70.

31. Eggmann S, Luder G, Verra ML, Irincheeva I, Bastiaenen CH, Jakob SM. Functional ability and quality of life in critical illness survivors with intensive care unit acquired weakness: a secondary analysis of a randomised controlled trial. Plos One. 2020;15(3):e0229725.

32. Beach LJ, Fetterplace K, Edbrooke L, Parry SM, Curtis R, Rechnitzer T, et al. Measurement of physical activity levels in the intensive care unit and functional outcomes: an observational study. J Crit Care. 2017;40:189-96.

33. Morris PE, Herridge MS. Early intensive care unit mobility: future directions. Crit Care Clin. 2007;23(1):97-110.

34. Berry MJ, Morris PE. Early exercise rehabilitation of muscle weakness in acute respiratory failure patients. Exerc Sport Sci Rev. 2013;41(4):208-15.

35. Bernhardt J, Dewey H, Thrift A, Donnan G. Inactive and alone: physical activity within the first 14 days of acute stroke unit care. Stroke. 2004;35(4):1005-9.

36. Schujmann DS, Teixeira Gomes T, Lunardi AC, Zoccoler Lamano M, Fragoso A, Pimentel M, et al. Impact of a progressive mobility program on the functional status, respiratory, and muscular systems of ICU patients: a randomized and controlled trial. Crit Care Med. 2020;48(4):491-7.

37. Burtin C, Clerckx B, Robbeets C, Ferdinande P, Langer D, Troosters T, et al. Early exercise in critically ill patients enhances short-term functional recovery. Crit Care Med. 2009;37(9):2499-505.

38. Connolly B, Denehy L. Hindsight and moving the needle forwards on rehabilitation trial design. Thorax. 2018;73(3):203-5.