Short-term effect of active lower limb cycle ergometry on mobility and muscle strength in critically ill patients: a randomized blinded clinical trial

Efeito a curto prazo da ergometria ativa do membro inferior sobre a mobilidade e a força muscular em pacientes criticamente doentes: um ensaio clínico randomizado e cego

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Nayanne Paula de Andrade
Master in Health Science
Institution: Universidade Federal de Uberlândia, Faculdade de Medicina, Fisioterapeuta no Centro de Reabilitação Especializado em Uberlândia
Address: R. do Cedro, 283, Jaraguá, Uberlândia – MG, Brazil, CEP: 38413-006
E-mail: nayanne_paula@hotmail.com

Ricardo Kenji Nawa
PhD in Science
Institution: Universidade de São Paulo, Faculdade de Medicina de Ribeirão Preto, Fisioterapeuta da Unidade de Assistência Intensiva a Adultos do Hospital Israelita
Address: Albert Einstein, São Paulo, SP - Brazil
E-mail: rkenji@hotmail.com

Eliane Maria de Carvalho
PhD in Experimental Pathophysiology by Universidade de São Paulo
Institution: Faculdade de Educação Física e Fisioterapia da Universidade Federal de Uberlândia
Address: R. Benjamin Constant, 1286, Nossa Senhora Aparecida, Uberlândia – MG, CEP: 38400-678
E-mail: elianemc@ufu.br

Valdeci Carlos Dionísio
PhD in Functional and Molecular Biology
Institution: Universidade Federal de Uberlândia, Faculdade de Educação Física e Fisioterapia
Address: R. Benjamin Constant, 1286, Nossa Senhora Aparecida, Uberlândia – MG, CEP: 38400-678
E-mail: vcdionisio@gmail.com
ABSTRACT
Background: The effects of in-bed cycling on mobility and muscle strength is not well established, in parts due to the difficulty of measuring mobility. Objective: Investigate the effect of active lower limb cycle ergometry on mobility and muscle strength in critically ill patients evaluated by the Perme Intensive Care Unit Mobility Score and Medical Research Council, respectively. Methods: Critically ill patients dependent on mechanical ventilation were randomized, determining the control group and the experimental group. A intervention was applied for eight consecutive days and a blind physiotherapists assessed mobility before and after interventions. The experimental group (EG) was an active lower limb in-bed cycle ergometry by 15 minutes (once a day), associated with routine physiotherapy intervention (twice a day). The control group (CG) had routine physiotherapy intervention. The two-factor mixed ANOVA with Bonferroni correction tested the mobility status and muscle strength, evaluated by Perme Intensive Care Unit Mobility Score and Medical Research Council, respectively. Results: Thirty-seven patients were eligible, but 24 completed the study (12 each group). There was an interaction between interventions (before and after) and groups for mobility (F=59.513, p=0.006). But there was no interaction for muscle strength (F=4.097 p=0.055). The groups were similar before intervention for mobility [(p=0.343); confidence interval: (CG: 8.239 to 10.761) and (EG: 7.405 to 9.928)], but only the experimental group demonstrated improvement in mobility post-intervention [(p=0.017); confidence interval: (15.807 to 21.193)]. Conclusion: Compared to routine physiotherapy, in-bed cycling improved the mobility level, but not in muscle strength. Perme score was sensible to measure the mobility evolution in critical patients.

Keywords: mechanical ventilation, rehabilitation exercises, critical care, treatment outcome.

RESUMO
Fundo: Os efeitos do ciclismo no leito sobre a mobilidade e a força muscular não estão bem estabelecidos, em partes devido à dificuldade de medir a mobilidade. Objetivo: Investigar o efeito da ergometria ativa do membro inferior sobre a mobilidade e a força muscular em pacientes criticamente doentes avaliados pelo Perme Intensive Care Unit Mobility Score e Medical Research Council, respectivamente. Métodos: Pacientes criticamente doentes dependentes de ventilação mecânica foram randomizados, determinando o grupo controle e o grupo experimental. Uma intervenção foi aplicada por oito dias consecutivos e um fisioterapeuta cego avaliou a mobilidade antes e depois das intervenções. O grupo experimental (EG) foi uma ergometria ativa do ciclo de membros inferiores no leito por 15 minutos (uma vez por dia), associada à intervenção de fisioterapia de rotina (duas vezes por dia). O grupo controle (GC) teve intervenção de fisioterapia de rotina. A ANOVA mista de dois fatores com correção de Bonferroni testou o estado de mobilidade e a força muscular, avaliada pela Pontuação de Mobilidade da Unidade de Terapia Intensiva de Perme e pelo Conselho de Pesquisa Médica, respectivamente. Resultados: Trinta e sete pacientes foram elegíveis, mas 24 concluíram o estudo (12 cada grupo). Houve interação entre intervenções (antes e depois) e grupos de mobilidade (F=59.513, p=0.006). Mas não houve interação para força muscular.
(F=4,097 p=0,055). Os grupos foram semelhantes antes da intervenção para mobilidade [(p=0,343); intervalo de confiança: (CG: 8,239 a 10,761) e (EG: 7,405 a 9,928)], mas apenas o grupo experimental demonstrou melhora na mobilidade após a intervenção [(p=0,017); intervalo de confiança: (15,807 a 21,193)]. Conclusão: Comparado à fisioterapia de rotina, o ciclismo em cama melhorou o nível de mobilidade, mas não a força muscular. O escore de Perme foi sensato para medir a evolução da mobilidade em pacientes críticos.

Palavras-chave: ventilação mecânica, exercícios de reabilitação, atendimento crítico, resultado do tratamento.

1 INTRODUCTION

The intensive medicine advances increased the proportion of patients that survive severe diseases; however, they usually end up with a functional burden. Survivals at the intensive care unit (ICU) are exposed to post-hospital morbidity problems, related mainly to mobility deficits.1,2

The mobility and rehabilitation of critically ill patients are strongly related to better outcomes.3 Although some studies documented the safety of in-bed cycle ergometry, few randomized clinical trials were conducted.3,4,5 A recent systematic review analyzing the effects of active critical patients’ mobilization excluded studies that had cycle ergometer intervention in-bed due to its complexity in standardizing the results.3 Some trials used the cycle ergometer passively,4,6 and some associated it with other therapies.7,8 Previous studies demonstrated that active exercise demands more metabolic income in critically ill patients. Still, the patients submitted to active in-bed cycle ergometry have no shown better mobility and/or muscle strength when compared to those offered only to routine physiotherapy intervention.5,9

The mobility evaluation is challenging once it contemplates various aspects as mental status, functional strength, mobility barriers, milestones progression, among others. Difficulty in standardizing the results is also related to the heterogeneity of mobility measurements,3,10 and could explain the difference between the studies. Several studies showed the value of the physiotherapeutic intervention, but some of them have not established the evolution of the patients' mobility status through a score.5,11,12 Other studies
used non-specific scales for functional evaluation of patients’ mobility.$^{13,14}$ Thus, the effect of physiotherapy intervention on mobility remains uncertain. In recent years, the Perme Intensive Care Unit Mobility Score (Perme Score) was developed to evaluate the mobility status in ICU patients$^{15,16}$ and could be solving that problem. Nevertheless, although the applicability and reliability already tested, up to date, there is no studies that objectively measure the critically ill patients submitted to physiotherapy intervention with the Perme Score.

Therefore, this study aimed to investigate the effect of in-bed cycling on mobility and muscle strength in critically ill patients evaluated by Perme Intensive Care Unit Mobility Score and Medical Research Council, respectively. We hypothesized that patients submitted to active cycle ergometry would present better mobility and muscle strength than the control group.

2 METHODS

This study followed the recommendations of the Consolidated Standards for Reporting Trials, and ethical approval was obtained from the local Research Ethics Board (CAAE: 82259317.9.0000.5152) and was registered in the in the Brazilian Clinical Trials Registry (U1111-1215-1362)

2.1 TRIAL DESIGN AND PARTICIPANTS

A randomized blinded clinical trial, performed in an ICU at the University Hospital. After the pilot trial, the main physiotherapeutic conducts were risen in the ICU, as the average length of stay in the Unit (eight days).

The patients were recruited while admitted to an ICU of a University Hospital between July 2018 and February 2019. An experienced and trained physiotherapist performed the sorting of all patients admitted daily in the ICU. At the sorting, the patients’ muscle strength was evaluated based on the Medical Research Council (MRC).$^{17}$ We included in the study patients older than 18 years old; with no distinction of gender or ICU admission; but who presented lower limb MRC results equal to 3, were able to perform lower limb active cycle ergometer; were previously depended on mechanical ventilation...
for more than 48 hours; could follow simple commands, and were hemodynamic stable. We respected the hemodynamic stability criteria and the active safety mobilization proposed earlier.

2.2 RANDOMIZATION AND BLINDING METHOD

An unlinked professional to study randomized the patients from a random number table created using the spreadsheet editor Microsoft® Office Excel, determining the control group (CG) and the experimental group (EG). The physiotherapist who assessed mobility before and after the intervention not aware of the treatment assignments. The statistician also was not involved in the randomization process either.

2.3 INTERVENTIONS

During all interventions, we kept the patients monitored and hemodynamic stable. The criteria for protocol interruption was the safety criteria for active mobilization.

We standardized the CG intervention (routine physiotherapy) after surveying the main conducts related to physiotherapy in the ICU and a pilot study. Four physiotherapists from ICU with an average experience of 10 years of intensive care conducted the routine physiotherapy twice a day for eight consecutive days. The intervention was compound by active-assisted or active upper and lower limb exercises in bed (including sitting and mobilizing), but we have not used the cycle ergometer.

We submitted the EG to routine physiotherapy twice a day. An independent and trained physiotherapist conducted in-bed cycling (Minibike to exercises Acte Sports®) once a day in the supine position, and headboard elevated at 45 degrees. The patients actively cycled the cycle ergometer by 15 minutes and a progressive load increase was performed, according to the patients’ tolerance. We respected the 6 hours gap between the routine and cycle ergometer intervention.

2.4 OUTCOME MEASURES

The primary outcomes were mobility status and muscle strength, which we obtained by MRC and Perme Score, respectively. An experienced and trained
physiotherapist collected the data before and after eight consecutive days of stay.

The MRC consists of muscle strength through six bilateral tested movements. The muscle scale grades muscle power of every movement from 0 (total paralyses) to 5 (normal muscle strength). The total scale goes from 0 (complete tetraparesis) to 60 (normal muscle strength).\(^{17}\)

The Perme Score evaluates through fifteen items the critical patient mobility status, and its divided into seven categories: mental status, potential mobility barriers, functional strength, bed mobility, transfers, gait, and endurance. The score varies from 0 to 32, where a lower score means lower mobility and more assistance need.\(^{15}\)

As secondary outcomes, we obtained data from age, ICU stays, mechanical ventilation length, and Simplified Acute Physiology Score 3 (SAPS 3). The SAPS 3 is a predictive system utilized in the patients' admission to the ICU, where we performed this study. It comprises of 20 parameters, representing an acute physiologic score and establishes a predictive mortality rate for patients admitted to ICUs.\(^{19}\)

2.5 STATISTICAL ANALYSIS

We calculated the sample size with the G* Power 3.1.2.9 software to determine the sample size a large effect size (0.40), standard significance level (\(\alpha = 0.05\)), statistical power (0.95) - (with family F tests - ANOVA measurement of repeated measures, in-between interaction). The minimum total sample was of 24 participants.

We performed the statistical analysis using the IBM SPSS Statistics software, version 22.0 (IBM Corporation, Armonk, NY, USA). We tested and confirmed data normality with the Shapiro-Wilk test. To test the statistical significance for the variables age, length of stay, SAPS 3, and MV length, we used the t-test for independent samples. To test the hypothesis that the EG was more effective than CG, we used the two-factor mixed ANOVA with Bonferroni correction separately for mobility (Perme Score) and muscle strength (MRC). We tested the presence of outliers in residual values and homogeneity of variance with the Levene test. As the criteria for no outliers and no heterogeneity of the residues were met, and having the effect of interaction, the univariate analysis of variance test was applied to verify the significance at each moment separately (before and
after intervention). The effect size (r) was calculated according to Cohen’s criteria, where 0.1, 0.3, and 0.5 indicated small, medium, and large effects, respectively. For all tests, the significance level was p <0.05.

3 RESULTS

For this study, 37 patients were eligible, but three patients were excluded as they become unconscious or incapable of answering for themselves, and their legal responsible did not authorize their participation. The other ten patients were excluded during the intervention for not completing the proposed intervention time. There was no death during the research (Figure 1). We allowed patients with the distinguished physiologic conditions to participate, and their distribution between the groups had a similar percentage. (Table 1).

Figure 1. Flow Chart CONSORT: Provides the flow of participants throughout the study, showing the interested participants assessed for eligibility, the randomization process, and those who were included in the analysis.
Table 1. Sample characterization according to phatophysiological condition.

<table>
<thead>
<tr>
<th>Causes</th>
<th>EG n (%)</th>
<th>CG n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgical</td>
<td>4 (33%)</td>
<td>3 (25%)</td>
</tr>
<tr>
<td>Neurological</td>
<td>3 (25%)</td>
<td>2 (16,6%)</td>
</tr>
<tr>
<td>Trauma</td>
<td>2 (16,6%)</td>
<td>2 (16,6%)</td>
</tr>
<tr>
<td>Pulmonary Disease</td>
<td>1 (8,3%)</td>
<td>1 (8,3%)</td>
</tr>
<tr>
<td>Sepsis</td>
<td>1 (8,3%)</td>
<td>2 (16,6%)</td>
</tr>
<tr>
<td>Others</td>
<td>1 (8,3%)</td>
<td>2 (16,6%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>12</strong></td>
<td><strong>12</strong></td>
</tr>
</tbody>
</table>

EG: Experimental Group; CG: Control Group; n: number; %: percentage.

Source: Author

The t-test for independent samples revealed that there was no statistically significant difference for age, length of stay, SAPS 3, and time of MV (p>0.341) (Table 2).

Table 2. Participants characterization.

<table>
<thead>
<tr>
<th>Variable</th>
<th>EG Average ± SD</th>
<th>CG Average ± SD</th>
<th>Test t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>56,16 ± 22,92</td>
<td>47,8 ±18,85</td>
<td>-0,973</td>
<td>0,341</td>
</tr>
<tr>
<td>SAPS 3</td>
<td>63,9 ± 19,9</td>
<td>67,5 ± 18,4</td>
<td>0,496</td>
<td>0,624</td>
</tr>
<tr>
<td>Length of stay in ICU</td>
<td>23,6 ± 10,72</td>
<td>24,4 ± 15,28</td>
<td>0,139</td>
<td>0,890</td>
</tr>
<tr>
<td>Time of MV (days)</td>
<td>16,3 ± 11,54</td>
<td>14,2 ± 10,80</td>
<td>-0,456</td>
<td>0,652</td>
</tr>
</tbody>
</table>

±SD: standard deviation; SAPS 3: Simplified Acute Physiology Score III; ICU: Intensive Care Unit; MV: Mechanical Ventilation; p: p value

Source: Author

The two-factor mixed ANOVA showed an interaction between the interventions (before and after) and groups for mobility (F=59.513, p=0.006), but there was no interaction for muscle strength (F=4.097 p=0.055). The univariate analysis of variance test for mobility revealed that there was no effect on the before-intervention group [(F = 0.939, p=0.343); confidence interval: (CG: 8.239 to 10.761) and (EG: 7.405 to 9.928)], but the mobility after the intervention was higher in EG [(F = 6.689, p = 0.017); confidence interval: (15.807 to 21.193); (d = 4.96)], as observed in Figure 2.
Figure 2. This figure shows the (A) Medical Research Council (MRC) and (B) Perme Mobility Score mobility (Perme) scores pre and post intervention in Intensive Care Unit for control group (CG) and experimental group (EG); *: p<0.05

Source: Author

4 DISCUSSION

This blinded randomized clinical trial proposed investigating the effect of in-bed cycling on the mobility of critical patients using the mobility scale (Perme Score) in an ICU. We hypothesized that the patients submitted to active in-bed cycle ergometry would present improvements in mobility and muscle strength compared to a control group. Our results showed the EG mobility improved significantly, but not muscle strength, although it has conducted a tendency to improve.

Although there was a tendency to improve muscle strength (MRC), there were no significant results for both groups. Randomized clinical trial submitted patients to in-bed cycle ergometry, and electric muscle neurostimulation did not reveal muscle strength improvement; Nevertheless, other studies demonstrated peripheral muscle strength gain in patients submitted to a rehabilitation protocol.\textsuperscript{20,21} The progression of difficulty levels and the use of electric stimulation could explain the discrepancy between our results with other studies.\textsuperscript{20,21} Muscle strength gain is related to high muscular effort and progressive and individualized load,\textsuperscript{22} but, in our study, there was no load increase protocol to the cycle ergometer and, therefore, not enough stimulation to increase muscle strength
significantly. A recent clinical trial using in-bed cycling (including resistive exercise) was unable to reduced muscle wasting in critically ill.\textsuperscript{5} How to avoid muscle wasting and improve muscle strength still a challenge.

A systematic review demonstrated that patients submitted to active exercises in the ICU as part of their rehabilitation gained better mobility at discharge.\textsuperscript{3} Our results confirmed those observations and suggested that patients submitted to lower limb active cycle ergometry improved mobility in the ICU. The pathophysiological mechanism through which the intervention may work is complex and still not clearly understood.\textsuperscript{23} The improvement is related to higher metabolic demanded by active cycling, which could enhance oxygen consumption;\textsuperscript{9} however, this aspect was not controlled in this study. Another factor that needs to be considered is muscle stimulation during the active exercise, reducing muscle injured induced by immobility in bed\textsuperscript{24} and favoring the preservation of muscular architecture.\textsuperscript{25}

While de peripheral muscle strength improvement was not significant, the mobility of patients submitted to cycle ergometry increased. That means muscle strength and mobility are not affected in a resembling way by the physiotherapeutic intervention.\textsuperscript{22} Our results suggest that the patient’s weakness does not exclusively influence mobility. Other factors could be related to mobility improvement, as a level of awareness, pain, mobility barriers, different assistance need, among others.\textsuperscript{15,26} Precisely, for this reason, we believed Perme Score showed to be a useful tool to measure the functional status of critical patients since these factors are considered in the Perme Score.

Previous studies evaluated the mobility in ICU by objective measures, but there were some limitations.\textsuperscript{12,27,28} For instance, the Short Physical Performance Battery was initially developed for the geriatric population.\textsuperscript{29} The Barthel Index score can be more appropriated as a post-ICU and post-hospital discharge measurement.\textsuperscript{30} The Physical Function in ICU Test\textsuperscript{31} and the Functional Status Score for the ICU,\textsuperscript{32} no-take accounts of the external conditions of the patients that interfere with their mobility.\textsuperscript{16,30}

Evaluation tools enable standardized outcome measurements\textsuperscript{33,12} strongly contributing to ICU exercise prescription,\textsuperscript{30} improving care quality for critically ill patients, and favoring scientific standardization.\textsuperscript{34} The use of the Perme Intensive Care Unit Mobility...

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\textsuperscript{5} The interference of muscle wasting.
\textsuperscript{6} The use of the Perme Intensive Care Unit Mobility.

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Score could diminish the methodological challenges in a randomized rehabilitation clinical trial conduction with critical patients and allow a reproducibility in scientific studies. In this study, we identify the mobility difference between the groups. Since waking up in the ICU until discharge, there was mobility improvement, showed by Perme Score. However, the patients still demonstrated substantial mobility deficits at ICU discharge. For example, the patients obtained an average score of 18.5 at the last evaluation, showing a mild mobility level, but without marching potential. Although there are no normative values to critical patients’ mobility, those who had marching potential at the ICU discharge present better prognostics. The critical patients’ mobility at discharge is related to better long-term quality of life.

Our results reflect a typical scenario of critical patients’ deficit mobilization. Studies from other countries have also demonstrated low mobility in critical patients, especially those on mechanical ventilation where the presence of the endotracheal tube is strongly correlated with the non-mobilization out of bed. It is estimated that the number of patients older than 60 years requiring MV will increase by 105% until 2026, representing a larger population of survivors that will have low mobility due to post-ICU incapacities. Thus, it is essential to improve the approach of rehabilitation in ICU. In addition, the absence of a consensual definition of what constitutes early mobilization in mechanically ventilated patients makes better analyzes difficult.

This study has no follow-up and no evaluation of mobility at long-term hospital discharge and could be considered a study limitation. Although a previous study showed that individuals under the active mobilization program showed better mobility after discharge, further research is necessary to verify the long-term effect of active lower limb cycle ergometry on mobility and muscle strength.

5 CONCLUSION

Compared to routine physiotherapy, in-bed cycling improved the mobility level, but not in muscle strength. Perme score was sensible to measure the mobility evolution in critical patients and can be an excellent tool to evaluate mobility.
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