



# Effects of early passive cycling exercise on quadriceps femoris thickness in critically ill patients: a controlled randomized pilot study

*Efeitos do exercício passivo precoce em cicloergômetro na espessura muscular do quadríceps femoral de pacientes críticos: estudo-piloto randomizado controlado*

*Efectos del ejercicio pasivo precoz en cicloergómetro en el espesor muscular del cuádriceps femoral de pacientes críticos: un estudio piloto aleatorizado controlado*

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**ABSTRACT** | The objective of this study was to evaluate the effects of early passive cycling exercise on quadriceps femoris thickness (QFT) in critically ill patients admitted in the intensive care unit (ICU) of a tertiary care university hospital. A controlled randomized pilot study was conducted with a sample of 24 patients (51±18.11 years, 16 male), on mechanical ventilation (MV) from 24 to 48 hours, who were randomly divided into two groups: control group (n=12), receiving conventional physical therapy; and an intervention one (n=12), receiving passive cycle ergometer, once a day, throughout seven days of protocol, in addition to conventional physical therapy. The QFT was measured by ultrasonography. The first ultrasonographic measurement was performed within 48 hours after the start of MV, and the second at the end of the protocol. There were no significant differences in QFT of the left (27,29±5,86mm vs 25,95±10,89mm; p=0,558) and right (24,96±5,59mm vs 25,9±9,21mm; p=0,682) in the control group, and in QFT of the left (27,2±7,38mm vs 29,57±7,89mm; p=0,299) and right (26,67±8,16mm vs 28,65±8,04mm; p=0,381) in the intervention group. There were no significant between-groups differences for left QFT (3,61±1,07mm; p=0,248)

and right QFT (2,75±0,85mm; p=0,738). The results of this pilot study demonstrate that application of early passive cycle ergometer exercises has not significantly change the muscle layer thickness. However, our findings indicate that conventional physical therapy is able to preserve the quadriceps femoris thickness in critically ill patients admitted in ICU.

**Keywords** | Physical Therapy Modalities; Intensive Care Units; Ultrasonography; Exercise Therapy; Early Ambulation.

**RESUMO** | O objetivo deste estudo foi avaliar os efeitos do exercício passivo precoce em cicloergômetro na espessura muscular (EM) do quadríceps femoral (EMQ) de pacientes críticos admitidos em uma Unidade de Terapia Intensiva (UTI) de um hospital universitário terciário. O método utilizado foi um estudo-piloto randomizado controlado conduzido em uma amostra de 24 pacientes (51±18,11 anos, 16 do sexo masculino), com 24 a 48 horas de ventilação mecânica (VM), aleatoriamente divididos em dois grupos: grupo-controle (n=12), que recebeu a fisioterapia convencional; e grupo-intervenção (n=12), que

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recebeu o exercício passivo em cicloergômetro, uma vez ao dia, durante o período de sete dias do protocolo, em adição à fisioterapia convencional. A EMQ foi mensurada através da ultrassonografia. A primeira medida ultrassonográfica foi realizada entre as primeiras 48 horas de VM e a segunda ao término do protocolo. Não houve diferenças significativas na EMQ esquerda ( $27,29 \pm 5,86 \text{ mm}$  vs.  $25,95 \pm 10,89 \text{ mm}$ ;  $p=0,558$ ) e direita ( $24,96 \pm 5,59 \text{ mm}$  vs  $25,9 \pm 9,21 \text{ mm}$ ;  $p=0,682$ ) do grupo-controle e na EMQ esquerda ( $27,2 \pm 7,38 \text{ mm}$  vs  $29,57 \pm 7,89 \text{ mm}$ ;  $p=0,299$ ) e direita ( $26,67 \pm 8,16 \text{ mm}$  vs  $28,65 \pm 8,04 \text{ mm}$ ;  $p=0,381$ ) do grupo-intervenção. Na comparação entre os grupos, não houve alterações significativas em relação à EMQ esquerda ( $3,61 \pm 1,07 \text{ mm}$ ;  $p=0,248$ ) e a EMQ direita ( $2,75 \pm 0,85 \text{ mm}$ ;  $p=0,738$ ). Os resultados deste estudo-piloto demonstraram que a aplicação precoce do exercício passivo em cicloergômetro não promoveu mudanças significativas na espessura da camada muscular avaliada. No entanto, nossos achados sinalizam que a fisioterapia convencional foi capaz de preservar a EMQ de pacientes críticos admitidos em UTI.

**Descritores** | Modalidades de Fisioterapia; Unidades de Terapia Intensiva; Ultrassonografia; Terapia por Exercício; Deambulação Precoce.

**RESUMEN** | El presente estudio tuvo como objetivo evaluar los efectos del ejercicio pasivo precoz en cicloergómetro en el espesor muscular (EM) del cuádriceps femoral (EMC) de pacientes críticos ingresados en una Unidad de Cuidados

Intensivos (UCI) de un hospital universitario terciario. Se utilizó como método un estudio piloto aleatorizado controlado con una muestra de 24 pacientes ( $51 \pm 18,11$  años, 16 varones), con 24 a 48 horas de ventilación mecánica (VM), quienes fueron divididos aleatoriamente en dos grupos: grupo de control ( $n=12$ ), que recibió fisioterapia convencional; y grupo intervención ( $n=12$ ), que recibió el ejercicio pasivo en cicloergómetro una vez al día durante el período de protocolo de siete días, además de la fisioterapia convencional. El EMC se midió por ecografía. La primera medición ecográfica se realizó entre las primeras 48 horas de VM, y la segunda al final del protocolo. No hubo diferencias significativas en el EMC izquierdo ( $27,29 \pm 5,86 \text{ mm}$  vs.  $25,95 \pm 10,89 \text{ mm}$ ;  $p=0,558$ ) y derecho ( $24,96 \pm 5,59 \text{ mm}$  vs  $25,9 \pm 9,21 \text{ mm}$ ;  $p=0,682$ ) del grupo de control; y en el EMC izquierdo ( $27,2 \pm 7,38 \text{ mm}$  vs  $29,57 \pm 7,89 \text{ mm}$ ;  $p=0,299$ ) y derecho ( $26,67 \pm 8,16 \text{ mm}$  vs  $28,65 \pm 8,04 \text{ mm}$ ;  $p=0,381$ ) del grupo intervención. En la comparación entre grupos, no hubo cambios significativos en el EMC izquierdo ( $3,61 \pm 1,07 \text{ mm}$ ;  $p=0,248$ ) y en el EMC derecho ( $2,75 \pm 0,85 \text{ mm}$ ,  $p=0,738$ ). Los resultados de este estudio piloto demostraron que la aplicación precoz del ejercicio pasivo en cicloergómetro no promovió cambios significativos en el espesor de la capa muscular evaluada. Sin embargo, nuestros hallazgos indican que la fisioterapia convencional pudo preservar el EMC de pacientes críticos ingresados en la UCI.

**Palabras clave** | Modalidades de Fisioterapia; Unidades de Cuidados Intensivos; Ultrasonografía; Terapia por Ejercicio; Ambulación Precoz.

## INTRODUCTION

The rapid decay of the skeletal muscle mass is the main factor for common physical deficiency in critical patients of mechanical ventilation (MV)<sup>1</sup>. Early muscle dysfunction occurs in hours to days, specifically in the first 7 to 10 days of hospitalization in the intensive care unit (ICU), there is decay in quadriceps femoris thickness (QFT)<sup>2,3</sup>.

The quantification of peripheral muscle thickness (MT) may be performed by muscle ultrasound (US). This tool represents an attractive way for early application in critical patients, once it is a safe, non-invasive technique that can predict muscle volume and evaluate intervention effectiveness<sup>4-6</sup>.

Among the resources used in the prophylaxis for quadriceps femoris atrophy, lower limb cycling is

highlighted. This device is used passively, specially in the first ICU hospitalization days, allowing for patients with reduced level of consciousness to perform it<sup>7</sup>. Previous studies have shown that performing continuous passive cycling mobilization, besides being a feasible and safe activity, helps recovering peripheral muscle strength for critical ICU patients<sup>8,9</sup>.

Supposing that the first ICU hospitalization week is a decisive period regarding peripheral MT decay, specially for the quadriceps femoris, it is necessary to apply resources preventing muscle atrophy. The objective of this study was, thus, to investigate the effects of early passive cycling exercise associated to conventional physical therapy on QFT for ICU patients.

## METHODOLOGY

A clinical randomized pilot essay with blind outcome evaluators, carried out in the Adult ICU of the University Hospital of Santa Maria (HUSM) of the Universidade Federal de Santa Maria (UFSM), in Santa Maria, Rio Grande do Sul, Brazil, between June and October 2015. All participants or their family members have signed the Informed Consent Form before being included in the study, as established by the Resolution no. 466/2012 of the Brazilian National Health Council.

It was included in the study both male and female patients, who were older than 18 years-old, between 24 and 48 MV hours after being admitted into the ICU, with deep sedation level assessed by the Richmond Agitation Sedation Scale<sup>10</sup> (RASS=-4) and hemodynamically stable. It was excluded from the study patients receiving palliative care, amputees or with lower limb fracture, with neuromuscular or neurological diseases, motor sequelae, just as patients who were unable to use the cycle ergometer due to pre-existing articular and/or muscle-skeletal disfunctions.

### Randomization and intervention

The patients recruited for the study were evaluated by clinical records, demographic information, primary cause for ICU hospitalization, and the score on the acute physiology and chronic health evaluation II (APACHE II)<sup>11</sup>.

The subjects were allocated based on a random numbers table, computer-generated, with a randomization sequence designed by the software Random Number Generator (Pro v2.00, Segobit, Issaquah, WA, USA). All participants had the intervention applied by two physical therapists. Due to the intervention's nature, the physical therapists responsible for early cycling mobilization were not blind regarding the patients' randomization. However, outcome evaluators were blinded regarding the allocation, given that they did not participate in the study's interventions.

The patients who met inclusion criteria were allocated in the intervention group (IG) or control group (CG). The CG was submitted to conventional physical therapy, while the intervention group also received passive exercise sessions with the use of lower limb cycle ergometer (MOTOmed letto 2, RECK-Technik GmbH & Co.KG, Betzenweiler, Germany). Therefore, passive cycling

sessions were performed with the patient in decubitus position and head elevation at 30°, for 20 minutes, with a fixed cadence of 20 cycles/min. once a day, during the first ICU hospitalization week. Aiming to ensure the performance of passive exercise, the equipment's screen, which allows for the visualization/analysis of the practice and detects active movements, was constantly monitored during the protocol.

Conventional physical therapy (respiratory and motor therapy) was conducted by ICU physical therapists twice a day, for around 30 minutes for 7 days. The protocol included vibrocompression maneuvers, hyperinflation through mechanical ventilator and tracheal suctioning, if needed, besides motor exercises for upper and lower limbs, passive and active-assisted ones, according to the patient's clinical evolution.

During and after the protocol application, cardiovascular parameters were constantly monitored, such as: peripheral oxygen saturation (SpO<sub>2</sub>), heart rate (HR), mean blood pressure (MBP), systolic and diastolic blood pressure, in a non-invasive way by observing the multiparametric monitor DX 2022 (Dixtal Biomédica, Manaus, Brazil). The criteria for interrupting the protocol were: hemodynamic instability (MBP < 60 or > 125 mmHg), SPO<sub>2</sub> < 88%, HR > 130 bpm or < 40 bpm, and respiratory discomfort signs.

### Evaluating quadriceps femoris thickness

QFT was evaluated by high resolution US (Mindray Ultrasound, portable DP-2022), in B mode, with a micro-convex echocardiologic transducer (65C15EA 5, 0-9.0 MHz, 4W). The initial QFT evaluation was performed during the first 48 MV hours, and the second one 7 days after the mobilization (end of the protocol).

The protocol for US evaluation was based on the study by Fivez et al.<sup>12</sup>. The patient was positioned in decubitus, with outstretched lower limbs. After that, the transducer was positioned perpendicularly to the mean quadriceps femoris point, which was identified by a measuring tape. After detecting the ultrasound image in a resolution fit for muscle visualization (Figure 1), it was captured and the measures, expressed in millimeters, were taken. QFT was determined through transversal images measuring the distance between the external femoral edge and the upper aponeurosis of the rectus femoris muscle.

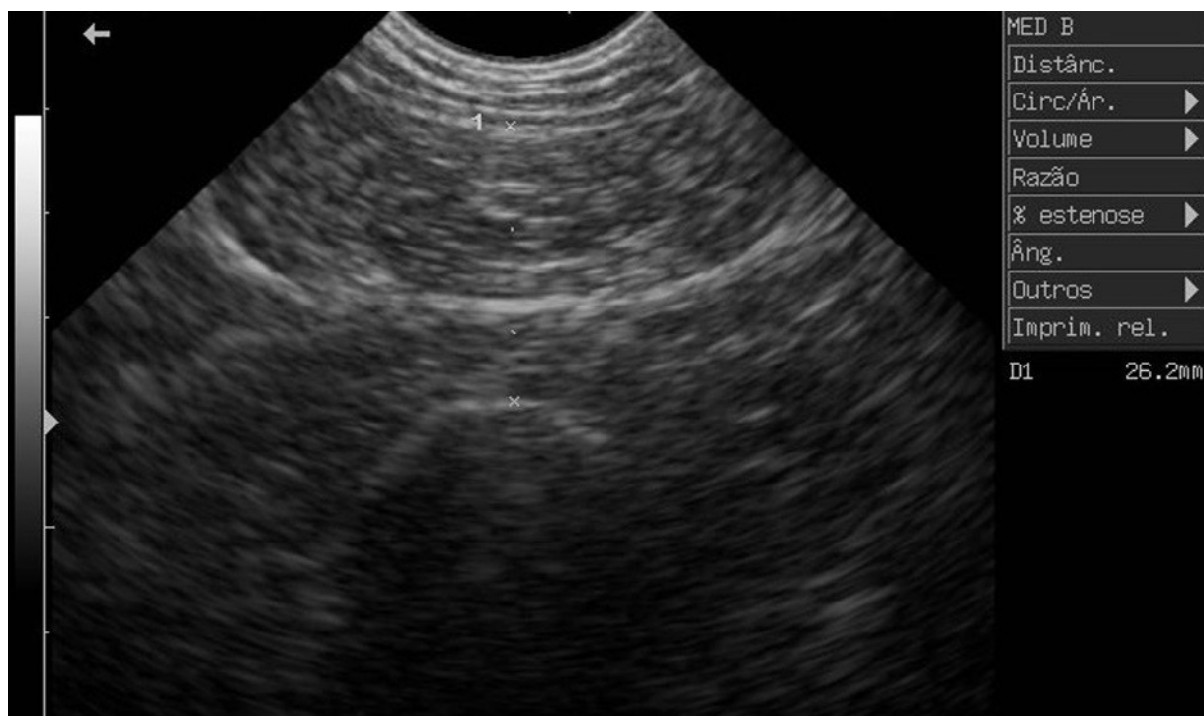


Figure 1. Quadriceps femoris thickness evaluated by ultrasound in an intervention group patient

### Sample size calculation

The sample for this pilot study was used for sample inference of the randomized clinical essay. It was estimated to obtain a 5% significance level ( $p < 0.05$ ), and 80% power (WinPepi program, version 10.5), considering a difference of 2.37mm in QFT and a sample of 64 patients for each group.

### Statistical analysis

The statistical analysis was performed with the use of the program IBM SPSS Statistics, version 2.0 (IBM Corporation, Armonk, NY, USA). Variable normality was evaluated by the Shapiro-Wilk test. Continuous variables were presented as mean  $\pm$  standard-deviation and confidence interval of 95% (CI 95%), while the categories were presented in absolute frequencies and percentages. To compare pre and post-intervention moments within the group, the paired Student's t-test was used. The comparison between groups was performed by a two-way ANOVA test followed by the Bonferroni post-hoc test. The effect size was determined by the Cohen to  $f^2$  compare the groups and classify them as great, moderate, and small<sup>13</sup>. For statistically significance, it was considered a value of  $p < 0.05$ .

### RESULTS

In the studied period, 76 patients were admitted in the institution's Adult ICU, 32 of them met the inclusion criteria, being randomized in CG ( $n=16$ ) and IG ( $n=16$ ). Later on, 4 patients in the CG deceased, as well as 4 patients in the IG. Therefore, the final sample was composed by 24 patients, with a total sum of 12 for each group (Figure 2).

Table 1 presents the sample's general characterization, which was homogeneous for most variables, except for the gender. The IG had more men when compared to the CG ( $p=0.009$ ). During the study, there was no need to interrupt the protocol nor was any adverse event observed during and after its application.

QFT remained unchanged in both groups after implementing the protocol. There were no significant differences in the left QFT ( $27.29 \pm 5.86$ mm vs.  $25.95 \pm 10.89$ mm;  $p=0.558$ ; CI 95%: -3.53 to 6.20) and right QFT ( $24.96 \pm 5.59$ mm vs.  $25.9 \pm 9.21$ mm;  $p=0.682$ ; CI 95%: -5.82 to 3.95) of the CG; and in the IG's left QFT ( $27.2 \pm 7.38$ mm vs.  $29.57 \pm 7.89$ mm;  $p=0.299$ ; CI 95%: -6.92 to 2.34) and right QFT ( $26.67 \pm 8.16$ mm vs.  $28.65 \pm 8.04$ mm;  $p=0.381$ ; CI 95%: -6.77 to 2.80). When comparing both groups, there were no significant changes regarding the left QFT ( $3.61 \pm 1.07$ mm;  $p=0.248$ ; CI 95%: -4.16 to 11.40) and the right one ( $2.75 \pm 0.85$ mm;  $p=0.738$ ; IC 95%: -4.69 to 10.21) with great effect size (Cohen  $f^2=0.634$ ) (Figure 3).

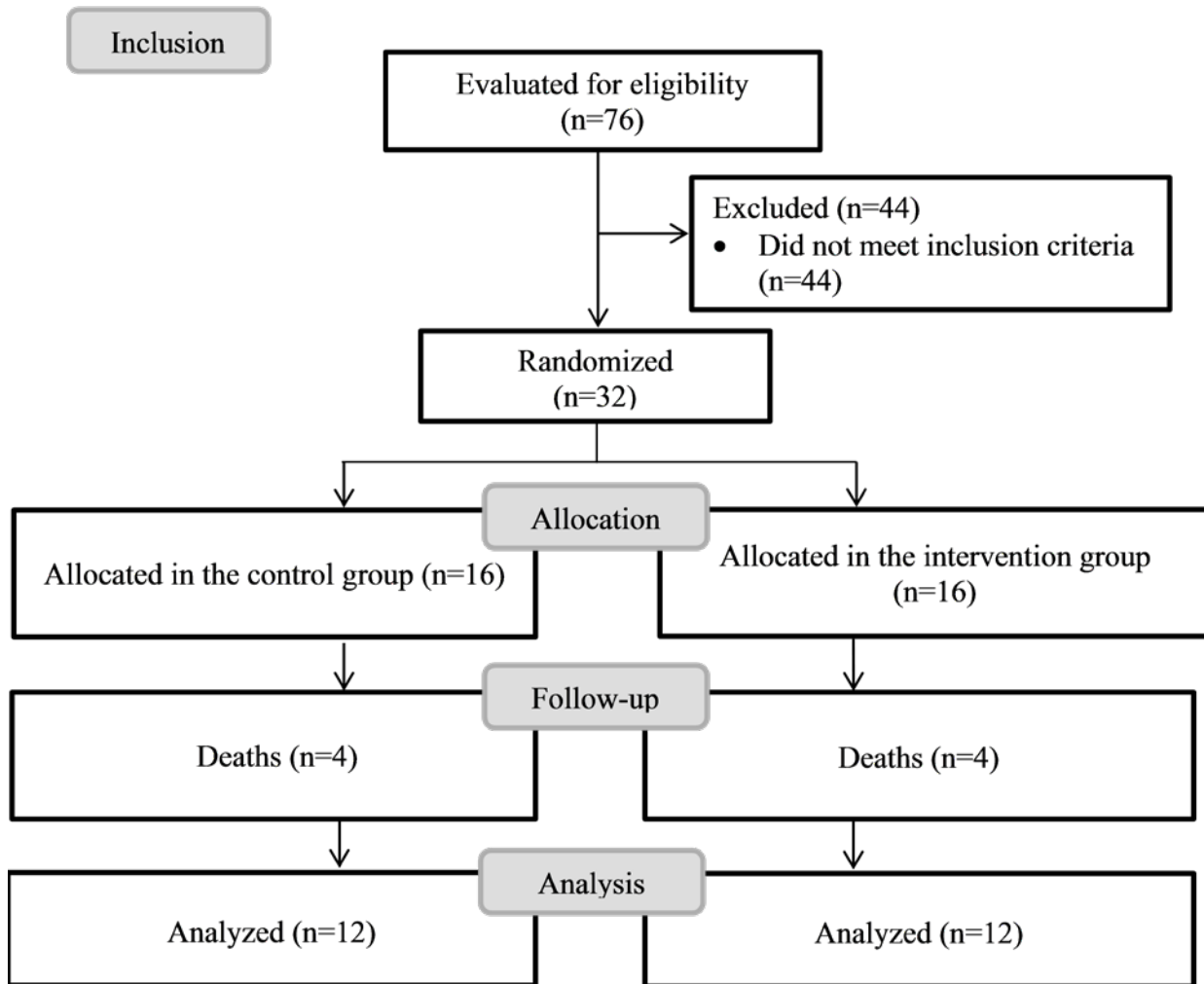


Figure 2. Study flowchart

Table 1. Clinical and demographical characteristics of the patients

Variables	Control group (n=12)	Intervention group (n=12)
Age (years)	54.17±16.71	47.83±19.61
Males, (n/%)*	5 (31.2)	11 (68.8)
BMI (kg/m <sup>2</sup> )	25.58±5.93	25.58±4.84
APACHE II score	16.00±5.84	14.42±6.25
Primary cause for admission into the ICU (n/%)*		
Cardiac	0 (0.0)	1 (8.33)
Abdominal	5 (41.66)	2 (16.66)
Neurologic	3(25)	5 (41.66)
Respiratory	2 (16.66)	0 (0.0)
Others	2 (16.66)	4 (33.33)
Medicines (n/%)*		
Neuromuscular blocking agents	0 (0)	0 (0)
Corticosteroids	5 (41.7)	3 (25.0)
Vasopressors	5 (41.7)	5 (41.7)

Apache II: acute physiology and chronic health evaluation II. All comparisons were performed by Student's t-test, except for the ones indicated by an asterisk (Mann-Whitney U test).

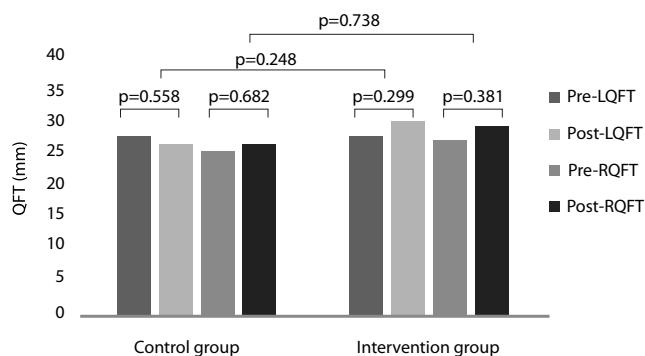


Figure 3. Evaluated left and right quadriceps femoris thickness (LQFT and RQFT)

Measures taken by ultrasound, before and after the implementation of the study protocol. Intragroup Student's t-test and two-way ANOVA test followed by an intragroup Bonferroni post-hoc test.

## DISCUSSION

To the best of our knowledge, this is the first randomized pilot study that investigate the effects of early passive cycling exercise associated to conventional physical therapy on critical patients' QFT. After implementing the protocol, there were no significant changes in the thickness of the muscle layer both for the CG and the IG, however, it was observed that conventional physical therapy, performed with both groups, has promoted QFT preservation.

Studies performed in ICUs have demonstrated that 17% to 30% of muscle mass may be lost in the 10 first hospitalization days for critical patients<sup>3,14</sup>. Considering the lack of evidence regarding the effects of early passive cycling exercise on QFT, it is important to mention the randomized pilot clinical essay carried out by Gruther et al.<sup>15</sup>, in which it was investigated, during the first week in the ICU, the efficacy of neuromuscular electrical stimulation on the prevention of peripheral muscle atrophy, however, a significant reduction in QFT was observed, demonstrating that the early intervention did not prevent the loss of muscle mass. In our study, the mobilization through cycle ergometer did not promote additional affects to the traditional physical therapy protocol, on the other hand, it was concluded that implementing this protocol has preserved QFT. A possible explanation for this finding is that, in this study, all patients received early physical therapy, during the first week in the ICU, specifically initiated in the first 48 hospitalization hours. Besides that, it is concluded that there probably was an attenuation of oxidative stress<sup>16</sup>, the maintenance of intrinsic muscle contractility properties<sup>17</sup> and the activation of anti-inflammatory cytokines that inhibit mechanisms responsible for peripheral muscle

deterioration<sup>18</sup>, however, these outcomes were not assessed in this study.

Studies developed in ICUs have demonstrated that implementing early rehabilitation promotes anabolic stimulation to peripheral muscle fibers<sup>19,20</sup>. In the study performed by Burtin et al.<sup>21</sup>, it was observed an increase in quadriceps strength after combining passive and active mobilization associated to early cycling exercise. In this study, all patients were in deep sedation (Richmond agitation and sedation scale=-4), a factor that made it impossible to measure muscle strength. In this context, as described by Puthuchery et al.<sup>22</sup>, ultrasound can replace other resources when evaluating peripheral muscle strength, such as the Medical Research Council, specially when patients are unable to follow verbal commands; besides that, this is a promising tool used for muscle-skeletal evaluation and its success owes to the reduction of bias created by conventional anthropometric measurements<sup>23-26</sup>.

In our sample, there was predominance of men, given that, male individuals physiologically present higher muscle mass when compared to females, however, it is highlighted that this aspect does not protect muscle thickness<sup>27</sup>. In the observational study conducted by Turton et al.<sup>1</sup>, in which there was also prevalence of men, the ultrasound evaluations performed in the 10 first ICU days have demonstrated a significant decay of QFT.

Our study has some limitations. Firstly, the outcome was restricted to the evaluation of QFT in the first ICU week, therefore, it is not possible to confirm if the QFT preservation would be maintained until medical discharge. Secondly, other parameters involved in muscle architecture, such as pennation angle, fascicle length and cross-sectional area, were not measured, considering that most studies in literature performed with critical patients use only the QFT parameter<sup>12,15,26,27</sup>. In third place, a share of the sample received corticosteroids, however, the casual relation between neuromuscular disfunctions and the use of corticosteroids is not well-established, probably since these dysfunction are related to more complex mechanisms, such as: dose, time, and concomitant glycemic control<sup>28</sup>.

## CONCLUSION

The results of this pilot study have demonstrated that early application of passive cycling exercise associated to conventional physical therapy did not promote changes in quadriceps femoris thickness. However, our findings indicate that conventional therapy helped preserving muscle

thickness for critical patients in the first ICU week. It is hoped that increasing the sample size may indicate significant results regarding the increase of muscle thickness with the use of passive cycle ergometer, given that there was a great effect size along with this intervention.

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