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CLINICAL TRIAL

Functional electrical stimulation cycling-based muscular evaluation method in mechanically ventilated patients

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Abstract

Background: Intensive care acquired muscle weakness is a common feature in critically ill patients. Beyond the therapeutic uses, FES-cycling could represent a promising nonvolitional evaluation method for detecting acquired muscle weakness.

Objectives: To assess whether FES-cycling is able to identify muscle dysfunctions, and to evaluate the survival rate in patients with detected muscle dysfunction.

Methods: A prospective observational study was carried out, with 29 critically ill patients and 20 healthy subjects. Maximum torque and power achieved were recorded, in addition to the stimulation cost, and patients were followed up for six months.

Results: Torque (2.64 [1.53 to 4.81] vs 6.03 [4.56 to 6.73] Nm) and power (3.31 [2.33 to 6.37] vs 6.35 [5.22 to 10.70] watts) were lower and stimulation cost (22 915 [5069 to 37 750] vs 3411 [2080 to 4024] μC/W) was higher in patients compared to healthy people ($p < 0.05$). Surviving patients showed a nonsignificant difference in power and torque in relation to nonsurvivors ($p > 0.05$), but they had a lower stimulation cost (4462 [3598 to 11 788] vs 23 538 [10 164 to 39 836] μC/W) ($p < 0.05$). In total, 34% of all patients survived during the six months of follow-up. Furthermore, 62% of patients with a stimulation cost below 15 371 μC/W and 7% of patients with a stimulation cost above 15 371 μC/W survived.

Conclusions: FES-cycling has good sensitivity and specificity for detecting muscle disorders. Critical patients have low torque and power and a high stimulation cost. Stimulation cost is related to survival. A low stimulation cost was related to a 3 times greater chance of survival.

KEYWORDS

FES-cycling, intensive care unit, muscle, weakness

Registered in the Brazilian Clinical Trial Registration Platform: Number: RBR-10gyv7wn.

1 | INTRODUCTION

Acquired muscle weakness is a common feature in patients during an Intensive Care Unit (ICU) stay, affecting 67% of critically ill patients with sepsis.[1,2] This condition is labeled "acquired" due to the lack of a plausible etiology other than critical illness and its treatments.[1] Clinically detected weakness has a generalized symmetrical involvement, affecting limb (with proximal emphasis) and respiratory muscles, whilst sparing facial and eye muscles.[2,3] Muscle tone is almost invariably reduced and deep tendon reflexes may be reduced or normal.[1]

Pronounced loss of muscle mass, which can exceed 10% over the first week in the ICU, is associated with functional impairments.[8,9] This loss mainly affects the lower limbs[4] and determines short-term consequences, such as: prolonged mechanical ventilatory assistance[5,6]; enhanced extubation failure[7]; swallowing disorders[8]; reduced functional capacity[18]; and longer ICU and hospital length of stay and higher costs.[4,9,10] Therefore, this weakness is associated with worse short- term outcomes, contributing to hospital mortality.[11,12]

Several techniques are used to detect weakness. The maximal voluntary strength assessment is a voluntary assessment; however, it requires volitional effort from the patient, and as such is a disadvantage and limitation in the ICU. A reduced consciousness level (sedative uses, delirium, coma) impairs this assessment and weakness may be under or over diagnosed.[13] Non- volitional techniques to detect muscle dysfunction, such as evoked peak torque, electroneuromyography, and electrophysiological assessments,[14–16] can be used when the volitional method is not available. In addition, a variety of imaging techniques have been used for muscle strength substitution. Ultrasound is the most commonly performed technique for assessing muscle mass and quality; however, it is highly dependent on the evaluator.[17–19]

There is growing evidence of the therapeutic benefits of functional electrical stimulation (FES) cycling in several pathological models, including critically ill patients.[20,21] This technology aims to promote cycle ergometry exercise induced by functional electrical stimulation. The concept is to induce exercise and muscle contraction by depolarization of the motoneuron and, consequently, all the physiological stages of muscular contraction. It uses computer-driven electrical pulses delivered by transcutaneous electrodes, promoting muscle contractions,[22] even in situations of physiological pathway dysfunction, such as in intensive care unit acquired neuropathy.

Beyond the therapeutic uses, FES-cycling could be a promising nonvolitional evaluation method for detecting acquired muscle weakness. Objectively, the equipment provides an electrical stimulus and measures the muscle's mechanical response. The maximum torque and power output achieved[23] can be assessed, in addition to the stimulation cost (defined as the total electrical charge delivery rate per watt of output power [microcoulomb/watt - μC/W] for the stimulated muscle groups during exercise).[24] However, to date, the capacity of the FES-cycling evaluation method for detecting muscle dysfunction has never been assessed in critically ill patients undergoing mechanical ventilatory assistance. Thus, the primary objective of this study was to assess whether FES-cycling is able to identify muscle dysfunction in critically ill patients. The secondary objective was to assess the survival rate in patients with detected muscle dysfunction.

2 | MATERIALS AND METHODS

2.1 | Study design and participants

A prospective observational study was conducted in the ICU of a cardiology referral hospital in Brazil. Study participants underwent a single evaluation using FES-cycling equipment. After this single evaluation, the patients were followed up for a six-month period. The study period was from December 2021 to October 2022. The protocol was approved by the Real Hospital Português ethics committee in accordance with the Declaration of Helsinki (opinion number 5069827/21, CAAE: 50202821.1.0000.9030) and was registered in the Brazilian Clinical Trials Registry Platform (Number: RBR-10gyv7wn). The legal guardians of the patients signed a free and informed consent form before the evaluation. The study included consecutive individuals, over 18 years of age, of both sexes, admitted to the ICU, who were critically ill and mechanically ventilated. Patients with hemodynamic instability (mean arterial pressure <65 or >110 mm Hg) or patients with skin or musculoskeletal lesions which prevented FES-cycling were excluded.

In addition, a group of community recruited individuals who reported no cardiopulmonary and/or musculoskeletal morbidity were recruited to serve as the control group. The controls were paired by age, sex, and height to the ICU participants.

2.2 | Patient height measurement for pairing

The height of mechanically ventilated patients was measured using an inelastic tape, according to the equations previously described by Chumlea.[25] For women, height (cm) = 84.88 + [1.83 × knee height (cm)] − [0.24 × age (years)]. For men, height (cm) = 64.19 + [2.04 × knee

height (cm)] – [0.04 × age (years)]. Knee height was considered as the distance between the sole of the foot and the anterior surface of the left thigh (above the condyles of the femur and immediately proximal to the patella) with the ankle and knee flexed at a 90-degree angle.

2.3 | Muscle assessment protocol

The patients were attached to the FES-cycling equipment (Figure 1) (MOBITRONICS®, INBRAMED, Porto Alegre, Brazil). Equipment height and distance and leg support positions were individually adjusted, to prevent knee hyperextension and promote proper range of motion. The skin was cleaned and trichotomy was necessary in three patients, before the electrode placement. Self-adhesive electrodes, made of adhesive hydrogel and rubber (Arktus, Santa Tereza do Oeste, Brazil), were placed bilaterally on the belly of the quadriceps (vastus lateralis and vastus medialis) (5 × 9 cm electrode size), hamstrings (5 × 9 cm electrode size), and tibialis anterior muscles (5 × 5 cm electrode size), and then plugged into the electrical stimulation device cables.

Eight electrical stimulation channels were used (the stimulation device is part of the cycling system). The FES (biphasic, interval, rectangular shape pulse) was set with the same pulse width and intensity in all eight channels. As a large pulse width is usually needed in critically ill patients, the pulse width range was started with a minimum 500 μs. For the same reason, pulse amplitude intensity was started with a minimum of 50 mA. The following parameter sets were used: 500 μs pulse width for 50-100 mA intensity; 600 μs pulse width for 101-130 mA intensity; 700 μs pulse width for 131-160 mA intensity; 800 μs pulse width for 161-190 mA intensity; 900 μs pulse width for 191-220 mA intensity; and 1000 μs pulse width for 221-250 mA intensity. Prior to the evaluation, the right vastus lateralis channel was activated for one second to detect the quality of muscle contraction.

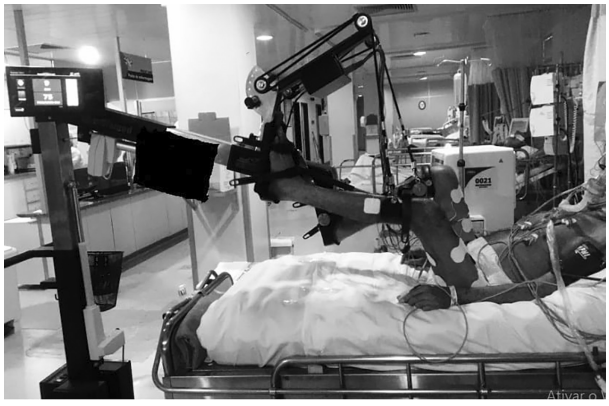

FIGURE 1 Patient attached to the FES-cycling equipment.

FES parameters of pulse width and intensity were set to promote the highest visible muscular contraction without pain. Pain was evaluated in conscious patients by self-report. The patients were asked to indicate "yes or no" by nodding or shaking their head in response to the question: "Does it hurt?". If the patient answered "yes", the parameters were reduced until a "no" answer was given. Pain in unconscious patients was evaluated by the Critical-Care Pain Observation Tool,[26] with a cutoff point ≥2 for pain.

The FES was triggered (ON) and stopped (OFF) by the crank position. The equipment has a sensor to detect the 360° crank position, and the FES trigger/stop was set according to physiological joint positions during the cycling movement. In one leg, quadriceps channels (vastus lateralis and vastus medialis) were triggered at around 90° of hip and knee flexion and stopped at around 10° hip flexion and 160° knee extension. In the opposite leg, hamstrings and tibialis anterior channels were triggered at around 30° of hip and knee flexion and stopped at around 75° of hip and knee flexion.

The equipment was set in the evaluation mode to perform an automatic preset combination (unchangeable) of different cycle ergometry cadences (rotations per minute - RPM) and electrical stimulation frequencies (1st = 10 RPM and 50 Hz, 2nd = 10 RPM and 75 Hz, 3rd = 10 RPM and 100 Hz, 4th = 15 RPM and 50 Hz, 5th = 15 RPM and 75 Hz, 6th = 15 RPM and 100 Hz, 7th = 20 RPM and 50 Hz, 8th = 20 RPM and 75 Hz, and 9th = 20 RPM and 100 Hz) maintaining the previously selected pulse width and intensity throughout the evaluation protocol (in all combinations). The patients performed 7 cycling movements in each combination (63 cycling movements in total). The patients did not undertake any voluntary effort. All the work was performed by the FES-cycling equipment.

The equipment recorded torque (newton meter, Nm) and power output (watts, W), in addition to the stimulation cost (microcoulomb/watt - μC/W), during the entire cycle ergometry cadences and electrical stimulation frequency combinations. The equipment software reported maximal torque and power output, as well as the minimal stimulation cost reached. Torque information is generated by the servo motor drive. The servo motor has an auto tuning which provides a specific electrical charge to maintain the programmed rotation. The torque calculation is based on the variance of electrical charge applied to maintain the rotation. The servo motor drive also provides the angular velocity. The power output values are achieved by mathematical calculation (torque times angular velocity). The stimulation cost is the total electrical charge (intensity times pulse width), delivered by the electrical stimulator, divided by the power output.

2.4 | Follow-up

Each patient included in this study was followed from the day of the assessment for the subsequent 6 months. While they were hospitalized, follow-up was performed through bedside visits. If the patient was discharged from the hospital, they were followed up monthly by phone contact with the legal guardians/family members.

2.5 | Statistical analysis

Data normality was verified using the Shapiro–Wilk test. Data are presented as means ± standard deviations (when data are normally distributed) or as medians and interquartile ranges (when data are non-normally distributed) and percentages. For basic group characteristics, differences were evaluated by the Mann–Whitney test or Unpaired *t* test (according to data normality). The categorical variables were analyzed with the Fisher exact test. For muscle dysfunction and survival analysis differences, the Mann–Whitney test and effect size were performed. The effect size convention adopted was: small > 0.2; medium > 0.5; and large > 0.8.[27] The sensitivity and specificity of the variables for determining muscle dysfunction and survival were observed by receiver operating characteristic (ROC) curve analysis. The optimal cutoff points were set as the values with greatest sensitivity and specificity. The Kaplan–Meier curve was also elaborated for survival analysis. A statistically significant value of $p < 0.05$ was set for all analyses. GraphPad Prism 7.0 and GPower 3.0.10 software programs were used.

3 | RESULTS

Of the 35 patients initially enrolled in the study, 6 were excluded due to hemodynamic instability. The control group was composed of 20 participants. The characteristics of the participants are presented in Table 1.

3.1 | Muscle dysfunction

Critically ill patients presented lower values of power output compared to control (3.31 [2.33 to 6.37] vs 6.35 [5.22 to 10.70] watts, $p < 0.05$, 95% CI = 1.24 to 5.13), with a large effect size (Figure 2). Torque was also lower in critically ill patients (2.64 [1.53 to 4.81] vs 6.03 [4.56 to 6.73] Nm, $p < 0.05$, 95% CI = 1.37 to 4.13) compared to control, with a large effect size (Figure 2). Total electrical charge was 70 200 μC (600 μs of pulse width and 117 mA of intensity) on average for critically ill patients, and 22 500 μC (500 μs of pulse width and 45 mA of intensity) for control. Critically ill patients presented a higher stimulation cost compared to control (22 915 [5069 to 37 750] vs 3411 [2080 to 4024] μC/W, $p < 0.05$, 95% CI = −35 406 to −13 553), with a large effect size (Figure 2). The ROC curve analysis is presented in Table 2. In total, 70% of the patients presented a power output and torque below the optimal cutoff point and a stimulation cost above the optimal cutoff point.

3.2 | Survival

Survivor patients presented no difference in power output compared to nonsurvivors (6.26 [3.27 to 7.91] vs 3.26 [2.42 to 5.97] watts, $p = 0.13$, 95% CI = −4.08 to 1.65), with a small effect size (power = 0.62, effect size = 0.39). Torque also presented no difference in survivor patients compared to nonsurvivors (3.90 [2.24 to 6.57] vs 2.28 [1.54 to 4.71] Nm, $p = 0.22$, 95% CI = −3.20 to 1.53), with a small effect size (power = 0.62, effect size = 0.39). The total electrical charge was 85 800 μC (660 μs of pulse width and 130 mA of intensity) on average for nonsurvivors, and 43 200 μC (540 μs of pulse width and 80 mA of intensity) for survivors. Survivor patients presented a significant lower stimulation cost compared to nonsurvivors (4462 [3598 to 11 788] vs 23 538 [10 164 to 39 836] μC/W, $p < 0.05$, 95% CI = 615 to 44 245), with a large effect size (power = 1.0, effect size = 0.97). The ROC curve analysis is presented in Table 2. In total, 34% of total patients survived during the six-month follow-up, made up of 62% of the patients with a stimulation cost below 15 371 μC/W and 7% of the patients with a stimulation cost above 15 371 μC/W (Figure 3). Patients with stimulation cost below and above 15 371 μC/W cutoff point characteristics are presented in Table 3.

4 | DISCUSSION

The main findings of this study were: (1) critically ill patients undergoing mechanical ventilation presented low values of torque and power output and a high stimulation cost when compared with healthy individuals; (2) the muscle assessment method based on the FES-cycling technology showed good sensitivity and specificity to detect muscle dysfunction; (3) 70% of the assessed patients presented muscle dysfunction; (4) survivor patients presented a lower stimulation cost (3 times more chance of survival); and (5) power output and torque were not different between survivors and nonsurvivors.

The muscle assessment method based on the FES-cycling technology showed good sensitivity and specificity for detecting muscle dysfunction. A total of 70% of the

TABLE 1 Characteristics of the participants.

Variables	Critically ill $n = 29$	Control $n = 20$	p value	CI 95%
Anthropometric data				
Age, years	65 (54.50–78.50)	64.50 (51.00–69.75)	0.28	−12.37 to 2.80
Gender, F/M%	20 (69%)/9 (31%)	11 (55%)/9 (45%)	0.37	–
Height, cm	161.70 ± 6.46	164.10 ± 8.54	0.32	−2.47 to 7.31
FES-CYCLING parameters				
Pulse width, μs	600 (500–725)	500 (500–500)	<0.05	−164.80 to −68.54
Intensity, mA	117 (60–145)	45 (40–50)	<0.05	−83.04 to −47.39
Clinical characteristics				
ICU stay, days	3.5 (2–8)	–		
Mechanical ventilation, days	4.5 (2.75–8)	–		
SAPS III	73.17 ± 9.43	–		
12 h Water balance, mL	756.20 ± 727.70	–		
24 h Water balance, mL	910.70 ± 1442			
Vasopressor support, n/%	18/62%	–		
Sedation use, n/%	20/69%	–		
Corticosteroid use, n/%	9/31%	–		
Corticosteroid use time, days	5.33 ± 4.03			
Lower limbs edema, n/%	13/45%	–		
Sepsis, n/%	27/93%	–		
Glucose, mg/dL	199 ± 102	–		
Clinical diagnosis				
Acute myocardial infarction, n/%	4/14%	–		
Heart failure, n/%	2/7%	–		
Shock, n/%	4/14%	–		
Arrhythmias, n/%	5/17.2%	–		
Post-CPA, n/%	11/37.93%	–		
Acute pulmonary edema, n/%	2/7%	–		
Acute respiratory failure (n/%)	1/3.44%	–		

Note: Data are presented as mean ± standard deviation or median (interquartile range).

Abbreviations: CI, confidence interval; cm, centimeters; F, female; ICU, intensive care unit; M, male; mA, milliamps; mL, milliliters; mg/d, milligrams per deciliter; Post-CPA, post cardiopulmonary arrest; SAPS 3, Simplified Acute Physiology Score III; μs, microseconds.

assessed patients presented muscle dysfunction. This rate is similar to those reported in previous studies using different evaluation methods.[1,2] As this is the first study to compare critically ill patients with healthy subjects using FES-cycling for muscle assessment, the optimal cutoff points (4.53 watts for power output, 4.04 Nm for torque and 7461 μC/W for stimulation cost) need to be confirmed in further studies.

While power output and torque failed to predict six-month survival, the stimulation cost showed good sensitivity and specificity. Patients below the 15 371 μC/W optimal cutoff point had 3 times more chance of survival. As the majority of the high stimulation cost patients died in the first month of follow-up, this variable can be used in the calculation of the risk of short-term mortality. However, the present data should be used with care and the optimal cutoff point needs to be confirmed in further studies.

Delving deeper into the participants' characteristics, the patients with a stimulation cost above 15 371 μC/W were a little older, had higher 12 h water balance, a little higher ICU length of stay and mechanical ventilation time compared to patients with a stimulation cost below 15 371 μC/W. They also had higher vasopressor use, sedation, limb edema, and corticosteroid use rates. Surprisingly, they had lower sepsis rate.

Considering the past few decades, various bedside strength evaluation methods have been used to detect intensive care acquired muscle weakness.[28] The Medical Research Council scale and hand grip dynamometry are probably the most widespread adopted methods

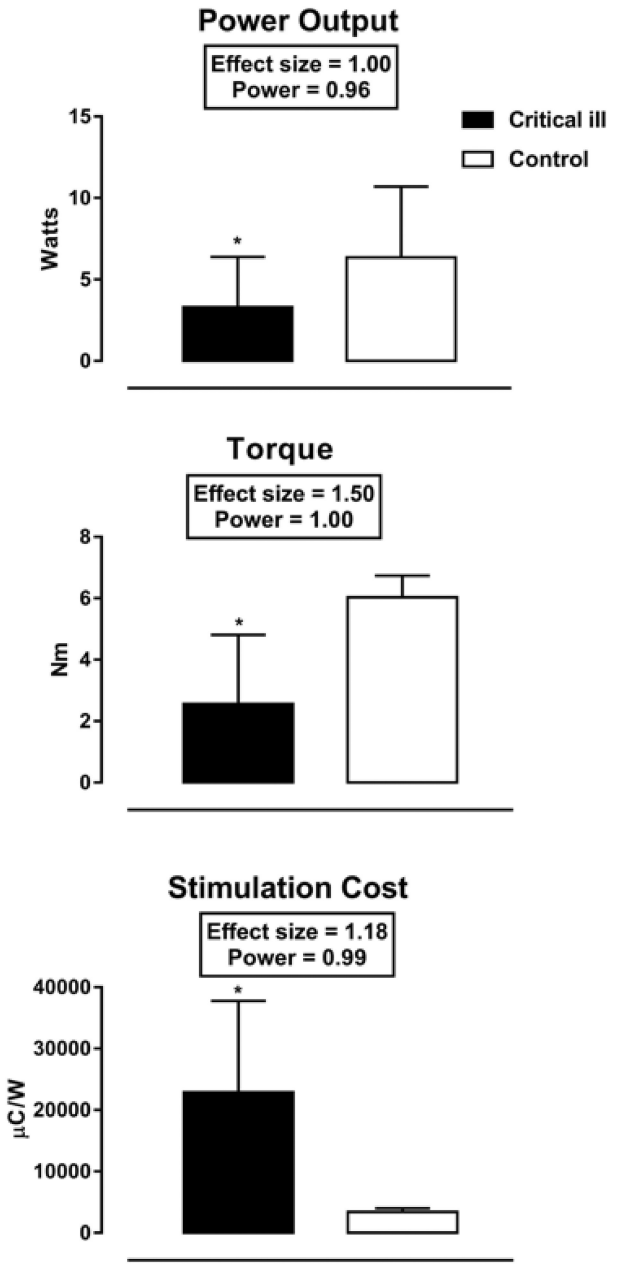

FIGURE 2 Power output, torque and stimulation cost assessment. * statistically significant difference, $p < 0.05$ compared to control. Median and interquartile range. Nm, newton meter; µC/W, microcoulombs per watt.

worldwide. They present good interrater reliability, are very simple to use (requires simple tasks), and low cost (needs basic or no equipment).[29] Despite these advantages, the methods have a crucial limitation for ICU use: they need a high consciousness level of the patient. Beyond consciousness, the patient needs to be cooperative to obey the voice command and perform the task. As a large number of patients are in a coma or sedated, the applicability of voluntary strength methods is limited in the ICU. The FES-cycling evaluation method overcomes this limitation, as it can be performed independently of the patient's consciousness level.

Evoked force evaluation methods have been developed to evaluate unconscious patients. In general, the patient's limb is placed on an device and an extrinsic method of muscle contraction is applied. The most commonly used techniques for muscle contraction production are muscle belly[30] or nerve electrical stimulation[31] and nerve magnetic stimulation.[32] The majority of these devices consist of an adjustable platform with a force transducer.[15,30–32] The force transducer attached to the device provides torque measurement during the isometric evaluation.

FES-cycling allows a functional movement evaluation performed isokinetically, providing power data beyond the torque. Another advantage is that the FES is a bilateral ergometer. The operator does not need to know the patient's dominant side for a precise evaluation or to change the ergometer from one limb to another. An additional advantage is the provision of multiple muscle stimulation. Multiple muscle stimulation is quite common in FES-cycling,[20,23] achieving higher mechanical power. Major power output is produced during knee extension (approximately 83% of total work); however, during knee/hip flexion, a considerable amount of power is also generated.[33] The FES-cycling evaluation method has advantages; however, FES-cycles are more expensive than the other equipment.

In the present study, critically ill patients presented lower values of torque and power output. We speculate that this is due to structural and biomechanical alterations. Biomechanics is influenced by several individual and clinical factors. Critically ill patients suffer from extensive muscle wasting and atrophy, which occurs rapidly at the onset of an intensive care unit stay.[34] Disuse-induced situations caused by prolonged immobility also promote other musculoskeletal structural alterations which impact biomechanics, such as a reduction in tissue stiffness and tendon thickness.[35] The use of corticosteroids contributes to structural muscle alterations.[36] Extracellular water/total body water is associated with muscle strength.[37] Limb edema also increases the distance between the electrical stimulation electrode and the muscle.

Electrodiagnostic testing is the gold standard method for neuropathy analysis in intensive care acquired weakness. However, performing an electrodiagnostic study in the ICU can be a daunting task. The environment is electrically unfriendly, and a 60 cycle artifact is routinely encountered, especially in sensory nerve conduction studies, F-wave testing, and needle electromyography. To reduce this interference, lights and unnecessary electrical equipment should be turned off, and the electromyography machine should be plugged into a separate outlet.[38] The evaluation also requires very specialized professionals.

TABLE 2 Receiver operating characteristics.

Variable	AUC (95% CI)	*p* value	Optimal cutoff	Sensitivity	Specificity
Muscle dysfunction					
Power	0.79 (0.66 to 0.92)	<0.05	<4.53 W	67%	100%
Torque	0.82 (0.70 to 0.94)	<0.05	<4.04 Nm	100%	70%
Stimulation cost	0.91 (0.83 to 0.99)	<0.05	>7461 μC/W	70%	100%
Survival					
Power	0.69 (0.47 to 0.90)	0.12	<3.49 W	63%	78%
Torque	0.65 (0.42 to 0.87)	0.21	<2.78 Nm	63%	78%
Stimulation cost	0.81 (0.63 to 0.99)	<0.05	>15 371 μC/W	74%	89%

Abbreviations: AUC, area under the curve; CI, confidence interval; Nm, Newton meter; W, Watts; μC/W, microcoulombs per watt.

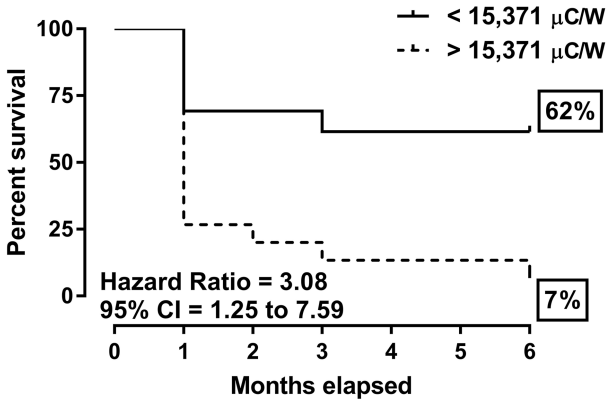

FIGURE 3 Kaplan–Meier survival curve for stimulation cost. CI, confidence interval; μC/W, microcoulombs per watt.

TABLE 3 Patients with stimulation cost below and above 15 371 μC/W cutoff point characteristics.

Variables	<15 371 μC/W	>15 371 μC/W
Mean age, years	61	71
Male/female, %	69/31	69/31
Mean 12 h water balance, mL	585	826
Mean 24 h water balance, mL	882	834
Mean ICU length of stay, days	5.2	6.6
Mean mechanical ventilation time, days	5.8	7.3
Sepsis, %	100	81
Mean SAPS III	71	75
Vasopressor use, %	54	69
Sedation, %	54	75
Limb edema, %	19	62
Mean glucose level, mg/dL	191	204
Corticosteroid use, %	15	43

Abbreviations: ICU, intensive care unit; SAPS III, Simplified Acute Physiology Score III; μC/W, microcoulombs per watt.

FES-cycling evaluation enables simultaneous force and neuromuscular analysis, does not require very specialized professionals, and does not suffer environment interferences. The stimulation cost measures the amount of electrical charge necessary to promote one watt of power output. Healthy/preserved neuromuscular electrophysiological pathways demand low amounts of electrical charge to promote one watt of power output. On the contrary, impaired neuromuscular electrophysiological pathways demand high amounts of electrical charge. At the present moment, the stimulation cost analysis could be used as an initial screening exam, and its results could provide a rational course of action for subsequent classic electrodiagnostic studies.

Analyzing the electrical stimulation parameters used in this study, critically ill patients required much higher (more than 3×) electrical stimulation levels than control to promote the highest visible muscular contraction without pain. These electrical stimulation levels were necessary due to neuromuscular impairment. Almost all patients were evaluated in the first week of mechanical ventilation (several patients started mechanical ventilation in the emergency room before being admitted to the ICU). It is known that a large number of patients develop an axonal sensorimotor polyneuropathy within 1–3 weeks.[38] Neuromuscular electrophysiological disorders alter the neuromuscular excitability threshold and critically ill patients often present chronaxie ≥1000 μs.[39]

The high electrical stimulation levels needed to obtain muscle contraction influenced the stimulation cost results. A high total electrical charge was necessary to generate the power output, demonstrating the patient's neuromuscular inefficiency. Several critical ill clinical conditions may have contributed to this increased stimulation cost. Sepsis and hyperglycemia are two major risk factors for polyneuropathy development.[38] Vasopressor support is another independent risk factor.[40] Muscle silencing induced by sedation also leads to dysfunction.[41] In

the present study, a large number of patients had sepsis, hyperglycemia, vasopressor support, and were sedated.

We speculate that torque and power output are related to myopathy (structural and biomechanical alterations), while stimulation cost is related to neuropathy (neural alterations) and that all variables are altered in the case of polyneuromyopathy. Our speculation is based on the hypothesis that stimulation cost, but not power output and torque, is related to survival. When comparing myopathy to neuropathy, myopathy is typically associated with better outcomes. Overall mortality is significantly higher for patients with neuropathy.[42] This reinforces the idea that these variables focus on different mechanisms, presynaptic (neuropathy) or postsynaptic (myopathy), of acquired weakness and could be useful for a precise diagnosis.

The current study has some limitations. (1) This is a single center study developed in a cardiac intensive care unit, so it is possible the results do not reflect other clinical conditions. (2) A detailed electrophysiological evaluation method was not available to confirm our speculations that torque and power output are related to myopathy, while stimulation cost is related to neuropathy.

5 | CONCLUSIONS

FES-cycling technology showed good sensitivity and specificity for detecting muscle dysfunction and may be a useful tool for muscle evaluation in mechanically ventilated patients. Critically ill patients produced low values of torque and power output and a high stimulation cost compared to healthy controls. Analysis showed that stimulation cost predicted survival in patients with a low stimulation cost being related to a 3 times higher chance of survival. Further research is required to determine the physiological origins of the differences in torque, power output and stimulation cost.

AUTHOR CONTRIBUTIONS

Thainá de Gomes Figueiredo involved in conceptualization, methodology, data curation, formal analysis, investigation, writing the original draft, review, and editing. Murillo Frazão involved in conceptualization, methodology, formal analysis, investigation, writing the original draft, review, and editing. Luís Augusto Werlang, Maikel Peltz involved in investigation, writing the original draft, review, and editing. Dário Celestino Sobral Filho involved in conceptualization, methodology, formal analysis, investigation, writing the original draft, review, and editing.

CONFLICT OF INTEREST STATEMENT

Luís A. Werlang and Maikel Peltz work at INBRAMED. They provided technical support for this research.

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