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Functional electrical stimulation with cycling in the critically ill: A pilot case-matched control study

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ABSTRACT

Purpose: The purpose was to determine (*a*) safety and feasibility of functional electrical stimulation (FES)-cycling and (*b*) compare FES-cycling to case-matched controls in terms of functional recovery and delirium outcomes.
Materials and methods: Sixteen adult intensive care unit patients with sepsis ventilated for more than 48 hours and in the intensive care unit for at least 4 days were included. Eight subjects underwent FES-cycling in addition to usual care and were compared to 8 case-matched control individuals. Primary outcomes were safety and feasibility of FES-cycling. Secondary outcomes were Physical Function in Intensive Care Test scored on awakening, time to reach functional milestones, and incidence and duration of delirium.
Results: One minor adverse event was recorded. Sixty-nine out of total possible 95 FES sessions (73%) were completed. A visible or palpable contraction was present 80% of the time. There was an improvement in Physical Function in Intensive Care Test score of 3.9/10 points in the intervention cohort with faster recovery of functional milestones. There was also a shorter duration of delirium in the intervention cohort.
Conclusions: The delivery of FES-cycling is both safe and feasible. The preliminary findings suggest that FES-cycling may improve function and reduce delirium. Further research is required to confirm the findings of this study and evaluate the efficacy of FES-cycling.

1. Introduction

The initial insult of a critical illness has lingering repercussions for patients admitted to the intensive care unit (ICU) resulting in skeletal muscle wasting and weakness. This is particularly so for individuals with sepsis who experience high rates of intensive care unit-acquired weakness (ICU-AW) [1] and prolonged diminution of their physical capabilities and cognitive functioning [2,3]. Importantly, an improvement in survival rates and increasing awareness of post–intensive care syndrome [4] have resulted in a paradigm shift from mortality-based outcomes to include patient-centered outcomes around activity limitation, disability, participation, and quality of life [5].

Early mobility is shown to lead to improvements in physical function and delirium [6–9]. However, there is often a delay in commencement of therapy due to the inability of patients to participate as a result of sedation or delirium. There is increased interest in the use of assistive technology to aid early rehabilitation, without the need for volitional patient engagement [10]. A recent systematic review evaluating electrical muscle stimulation (EMS) in critically ill patients concluded that the outcomes of using EMS in this cohort were inconclusive because of the heterogeneity of the studies and outcome measures but that EMS may have a beneficial role in the ICU [11]. The studies to date have examined EMS in nonfunctional resting positions using isolated muscle groups, such as the quadriceps muscles [12–14]. Functional electrical stimulation (FES) is different to EMS, as it recruits several muscles concurrently in functional patterns that mimic voluntary muscle activation. Use of FES-cycling compared with EMS enables cyclical muscle contraction of large lower limb muscle groups including quadriceps, hamstrings, gluteals, and calf muscles. It is hypothesized that coordinated muscle contraction increases the muscle workload, facilitating increased training of strength and force while minimizing muscle fatigue [15]. Electrical stimulation using FES-cycling can translate to improvements in other functional tasks such as walking in other patient populations [16].

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This is the first study to investigate the use of FES-cycling in critically ill patients. The primary aims of this study were to determine the safety and feasibility of FES-cycling; secondary aims were to assess its effects on physical function, ICU length of stay (LOS), and delirium compared to a matched-case control cohort.

2. Materials and methods

2.1. Study design

This was a single-center interventional observational study of critically ill patients with case-matched control comparisons at a quaternary ICU in Melbourne, Australia. Individuals were recruited into the intervention (FES-cycling) over a 4-month period (January, March, May-June, July-August 2012). Institutional ethical approval was obtained for the pilot evaluation of FES-cycling. Written informed consent was obtained from the patient's proxy in the first instance followed by continuation of consent from the patient once he or she was able to provide consent. Retrospective case matching to identify control comparisons took place between January and December 2012. The institutional ethics committee approved a waiver of consent for case-matched controls.

2.2. Screening and eligibility

Subjects were initially included if they were adults at least 18 years of age; were admitted with a diagnosis of *sepsis* or *severe sepsis* as defined by the American College of Chest Physicians Consensus Conference Guidelines [17]; and were predicted, by the senior ICU physician on admission, to be mechanically ventilated (MV) for more than 48 hours and remain in the ICU for at least 4 days. The senior ICU physician made the prediction independent from the research team. Additionally, those screened to have the intervention were excluded if there were physical reasons for the intervention not to be applied such as the presence of an external fixator, pacemaker or defibrillator, open wound or skin abrasions, or obesity (body mass index >40 [weight too high for cycle machine]), or if the treating senior ICU physician deemed the patient to be approaching imminent death.

A control was identified for each of the 8 subjects who underwent the interventional program (FES-cycling). Matching was performed according to 3 a priori–identified matching criteria. The order of matching priority and subcategories for matching were as follows: (1) Acute Physiology and Chronic Health Evaluation II score—4 categories (a: <18 mild, b: 18-22 moderate, c: 23-27 severe, d: ≥28 very severe); (2) MV hours—3 categories (a: <72 hours, b: 72 hours-7 days, and c: >7 days); and (3) age ± 15 years. If more than one matched participant was identified, the matched case control was randomly selected using computer-generated random numbers. Severity of illness, mechanical ventilation time, and age have been associated with increased risk of intensive care acquired weakness; and thus, to minimize confounding, individuals were matched on these 3 criteria.

2.3. Study procedures

2.3.1. Protocols of care

Patients were managed in the unit according to institutional protocols for resuscitation and sepsis management including antibiotic treatment, sedation, delirium, and nutritional support. All care was under the direct supervision of senior ICU physicians and critical care qualified nursing staff with a nurse to patient ratio of 1:1.

2.3.1.1. Usual care. Physiotherapists routinely screened daily for awakening and presence of delirium using the De Jonghe 5-point criteria (*awake* defined as a score of greater than 3 out of 5) [18] and the cognitive assessment method for ICU [19], respectively. Once awake, patients commenced rehabilitation involving early mobility activities such as sitting on the edge of bed, sitting out of bed, standing, marching in place, and walking (if able) for up to a maximum of 15 minutes in duration per day.

2.3.1.2. Intervention. In addition to the usual care described above, 8 subjects received FES-cycling, which aimed to commence within 96 hours of admission and continue daily until ICU discharge. The FES-cycling intervention involved a supine motorized cycle ergometer attached to a current-controlled stimulator (RT-300 supine model and SAGE stimulator; Restorative Therapies, Ltd, Baltimore, MD) (Fig. 1).

Disposable adhesive gel electrodes were placed over the major muscles of the lower limb bilaterally including quadriceps, hamstrings, gluteals, and calf muscles. The FES-cycling was conducted for a minimum of 20 to a maximum of 60 minutes daily 5 times a week. Muscles were stimulated at specific stages throughout the cycling

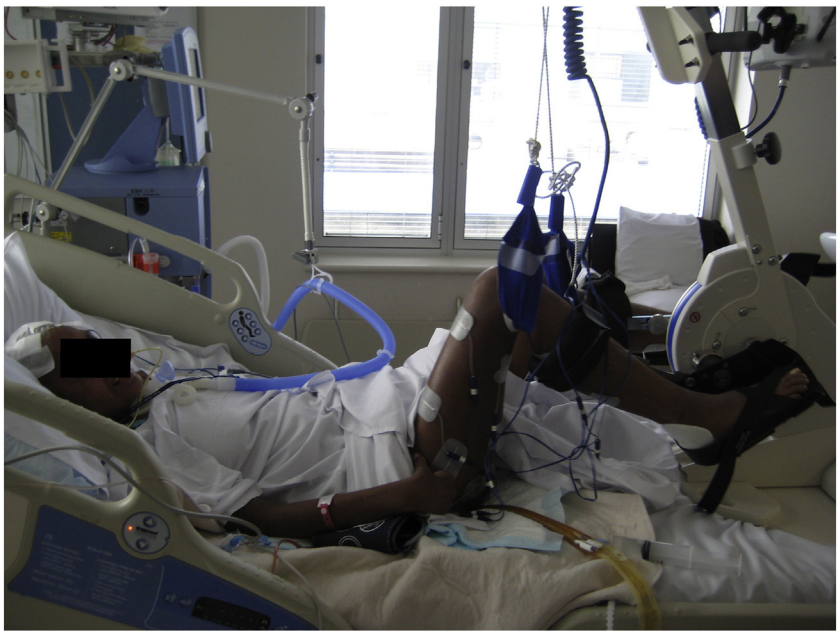

Fig. 1. FES-cycling machine (RT-300 supine model and SAGE stimulator; Restorative Therapies, Ltd, Baltimore, MD).

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phase based on normal muscular activation patterns regulated by the bicycle software. FES-cycling continued until ICU discharge.

2.3.2. Stimulation parameters

Stimulation involved an alternating monophasic rectangular waveform current. The stimulation was applied at intensities to cause visible contraction in all muscle groups. The presence of a muscle contraction was specifically monitored in the quadriceps muscle using a 4-point scoring system developed for the purpose of this study—(1) visible, (2) palpable, (3) flickers, and (4) no contraction observed—and were assessed at 5-minute intervals if difficult to establish the presence of contraction.

Other stimulation parameters were predetermined including pulse duration of 300 to 400 microseconds and frequency of 30 to 50 Hz, with intensity increased to a maximum milliamplitude of 140 mA [11]. Once the patient was awake and able to participate, he or she was provided with standardized encouragement to participate in training; and workload resistance was increased incrementally [20].

2.4. Outcome measures

2.4.1. Feasibility and safety

To determine the feasibility of the FES-cycling intervention, we examined (1) length of time from ICU admission to first training session, (2) total number of sessions conducted during the intervention period, (3) percentage of total potential sessions completed and reasons not completed, and (4) number of sessions where muscle contractions were observed. The authors, in conjunction with senior intensive care physicians in the ICU, developed criteria to determine when exercise training was unsafe to commence or should be ceased (Box 1).

In a subgroup of patients receiving the intervention (n = 5), the safety of FES-cycling was examined by recording the variability in cardiovascular and respiratory bedside parameters. Major and minor adverse events were decided a priori and are outlined in the online Supplementary Table E1. Patients were continuously monitored throughout the intervention session and 30 minutes after by the intervention physiotherapist and bedside critical care nurses. Pain levels were also monitored using a behavioral pain score while intubated and then a visual analogue scale to quantify any discomfort once the patient was able to communicate.

Box 1
Safety guidelines for exercise [20].

Safety guidelines: Exercise should not be delivered or should be ceased when:
HR <-50 or >-140 beats/min or new arrhythmia develops (including ventricular ectopic or new-onset atrial fibrillation)
MAP <-65 or below target pressure
>-30 ug/min of noradrenaline/min or comparable inotropic or vasopressor support required New-onset chest pain
Patient becomes pale or sweaty and/or specifically requests to stop due to feeling acutely unwell
Presence of ECMO or IABP
F_{IO_2} >-0.8
PEEP >-15 cmH_2O
RR >-35 breaths/per minute sustained for >-60 seconds
Spo_2 falls >-10% below resting level or <-85% for >-60 seconds
Pain levels >-7 out of 10 on the Visual Analogue Scale for five
5 minutes despite adjusting stimulation intensity
Abbreviations: ECMO, extracorporeal membrane oxygenation; F_{IO_2}, fraction of inspired oxygen; , heart rate; IABP, intra-aortic balloon pump; MAP, mean arterial pressure; PEEP, positive end expiratory pressure; RR, respiratory rate; $Spoo_2$, saturation of peripheral oxygen.

2.4.2. Trends in outcomes between FES-cycling and control cohort

In our center, the Physical Function in Intensive Care Test score (PFIT-s) is routinely assessed on awakening. The PFIT-s is scored out of 10, with the minimum clinically important difference (MCID) previously established by Denehy and colleagues [21] as greater than 1.5 points. Patient performance on initial PFIT-s has been shown to be predictive of ICU LOS and morbidity [21]. The treating physiotherapist also recorded the subject's highest level of function on a daily basis using an 11-point hierarchical scoring system [22]. The time to reach a priori–defined functional milestones (ie, standing, first ambulation) and highest functional level was recorded at 3 time points: (1) awakening, (2) intensive care, and (3) acute hospital discharge. Delirium was assessed using the cognitive assessment method for ICU tool at the time of physiotherapy assessments by routine care physiotherapists and extracted from the medical records for this study. Physiotherapists assessing physical function and delirium were unaware of the study being conducted.

Baseline demographics included age, sex, admission diagnosis, and severity of illness scoring. Additionally, number of sedation days and use of glucocorticoids were recorded. Intensive care LOS, MV hours, tracheostomy requirement, acute hospital LOS, discharge destination, and mortality were recorded.

2.5. Statistical analyses

Descriptive statistics were reported as mean (standard deviation) or median (interquartile range) for parametric and nonparametric data, respectively. Matched statistical analysis was performed using paired *t* test or nonparametric equivalent for continuous data with mean difference and 95% confidence intervals calculated, and Fisher exact statistical analyses for categorical variables were used. The level of statistical significance was set at α of .05. Box-plot graphical analyses for differences in awakening PFIT-s were plotted between groups. All data were analyzed using SPSS for MacIntosh statistical software package (version 21; SPSS, Chicago, IL).

3. Results

Seventy individuals were ventilated for more than 48 hours with a diagnosis of sepsis and expected to remain in the unit for at least 4 days over a 4-month recruitment time frame (January, March, May-June, July-August 2012). The control cohort was selected from a pool of 55 participants who were admitted to the ICU over the same period of time as the intervention cohort (Fig. 2). Within the case-matching process, no individuals who declined participation in the intervention were included. All participants in the intervention group were matched using the preset criteria from this pool.

Demographic data for patients in both groups are shown in Table 1. There were no significant differences in any of the matched variables. There were no significant differences between groups in terms of premorbid function (Table 1). Individuals included in this study were independent and high functioning in the community prior to admission with a small number of comorbidities (Table 1). The mean (SD) time to awakening and commencement of usual care rehabilitation was comparable between groups (control: 11.1 [5.9] vs intervention: 10.3 [8.1] days, $P = .685$) (Table 1). Sedation duration and average daily propofol dosages were also comparable across both groups (Table 2).

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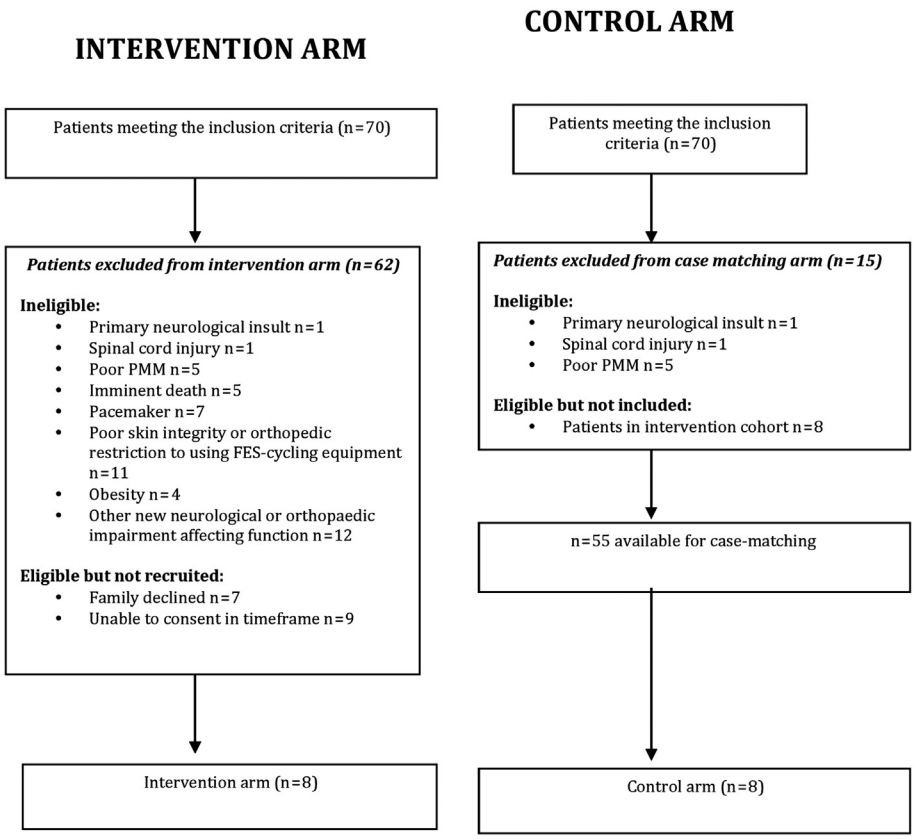

Fig. 2. Flow of participants diagram. n indicates number; PMM, premorbid mobility; SCI, spinal cord injury.

3.1. Feasibility and safety of FES-cycling

Seventy patients were screened, and 8 patients were recruited (11.5%). Time from recruitment to first intervention session was (median [interquartile range]) 15.3 (12.0-31.5) hours. The mean (SD) number of cycling sessions conducted was 8.6 (2.5) during the intervention period, with a total of 69 (73%) sessions out of a possible 95 sessions provided.

The reasons for the remaining sessions not being delivered are given in Table 3.

Table 1
Baseline demographics of cohort

	Control mean ± SD(n = 8)	Intervention mean ± SD(n = 8)
Age, y	60.5 ± 18.6	62.5 ± 17.7
Sex, male, n (%)	4 (50%)	4 (50%)
Independent ambulation (no gait aid), n (%)	8 (100%)	6 (75%)
BMI, kg/m^2	19.6 (4.5)	25.0 (4.3)
Functional Comorbidity Index [23], median [IQR]	3.0 [0.5-4.7]	2.5 [0.2-6]
MV, h, median [IQR]	190.0 [55.4-427.5]	197.8 [81.6-628.6]
Tracheostomy inserted, n (%)	3 (37%)	4 (50%)
Time to awakening and commencement of conventional rehab, d	11.1 ± 5.9	10.3 ± 8.1
Source of sepsis, n (%)		
Respiratory	5 (62%)	4 (50%)
Abdominal	2 (25%)	3 (37%)
Urological	0 (0%)	1 (12%)
Neurological	1 (12%)	0 (0%)
APACHE II score	20.3 ± 7.5	20.3 ± 7.9

Data are presented as mean ± SD or n (%) unless specifically stated in the table.
APACHE II indicates Acute Physiology and Chronic Health Evaluation II score; BMI, body mass index; n, number; SD, standard deviation; %, percentage.

Table 2
Sedation, delirium, and general outcomes comparing intervention and controls

	Control median (IQR) (n = 8)	Intervention median (IQR) (n = 8)
Sedation and other medications		
Duration of sedation, d	7.0 (4.5-10.5)	5.0 (3.3-15.0)
Average daily propofol dose (mg/h)	95.5 (54.8-133.2)	81.4 (68.5-156.6)
GC, n (%)	3 (37%)	5 (62%)
Duration of GC, d[*]	10 (8-11)	5 (4-12.5)
Highest level of vasopressor (noradrenaline) support on day 1, μg/h in mean ± SD	12.3 ± 7.6	24.5 ± 20.3
Delirium		
Delirium incidence, n (%)	7 (87%)	2 (25%)
Duration of delirium, d[†]	6.0 (3.3-13.3)	0.0 (0.0-3.0)
Discharge destination and LOS		
DC dest[‡]		
Rehab	6 (86%)	3 (43%)
Home	1 (14%)	4 (57%)
Mortality, n (%)	1 (12%)	1 (12%)
ICU LOS, d	13.5 (10.5-31.0)	12.0 (5.5-21.5)
Hospital LOS, d	31.0 (21.5-62.3)	24.0 (19.5-40.8)

Data are presented as median (25th-75th IQR) unless specifically stated otherwise in table.
DC dest indicates discharge destination; GC, glucocorticoids; mg/h, milligrams per hour; μg/h, micrograms per hour.
[*] Reported only for those who received any glucocorticoids during their hospital stay
[†] *P* value calculated on matched pairs to determine presence of statistical significance between groups ($P = .042$)
[‡] Reported on n = 7 in each arm secondary to n = 2 deceased across 2 groups.

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Table 3
Reasons for noncommencement of exercise sessions in the intervention cohort

Subject	Actual sessions commenced/out of total possible (%)	Reasons for noncommencement	Number of sessions not conducted
1	23/35 (65.7%)	Surgical or investigational medical procedure	2
		High RR > 35 breaths/min	2
		Febrile and heart rhythm irregularities	1
		Actively bleeding and worsening sepsis leading to death	7
2	9/16 (56.3%)	Febrile and heart rhythm irregularities	4
		High RR > 35 breaths/min	1
		Investigational medical procedure	2
3	5/5 (100%)		
4	3/4 (75%)	Severe agitation	1
5	4/4 (100%)		
6	10/12 (83.3%)	Heart rhythm irregularities	1
		Patient declined	1
7	13/17 (76.5%)	High F_{IO_2} (1.0) and inotropic support (40 μg of noradrenaline/min)*	1
		Heart rhythm irregularities	2
		Investigational medical procedure	1
8	2/2 (100%)		

FiO_2 indicates fraction of inspired oxygen; RR, respiratory rate; μg, micrograms; %, percentage.
* Safety criterion for exercise set at < 0.6 F_{IO_2} and inotropic support < 30 μg of noradrenaline/min—above the safety criterion for commencement of exercise.

No major adverse events were recorded. One minor adverse event occurred in the 30-minute posttraining period, whereby one subject had a transient desaturation to 86% for greater than 1 minute requiring a temporary increase in fraction of inspired oxygen (F_{IO_2}) from 0.4 to 0.6 for 1 hour.

The trends for cardiovascular and respiratory parameters are shown within each training session and for each of the 5 participants in Figure E1. The greatest difference between minimum and maximum values recorded was observed with heart rate with a variation of 20-40 beats per minute (Fig. E1). Although there was a variation during the exercise session for respiratory rate and heart rate as shown by maximum to minimum variation, the values recorded at the start (5 minutes prior to commencing exercise) and 30 minutes post–exercise training were similar for these parameters (Fig. E1, Table E2).

3.2. Trends in outcomes between FES-cycling and case-matched control cohort

At awakening, there was a clinically significant difference between groups for PFIT-s compared with the reported MCID [21] and a trend toward statistical significance ($P = .060$) (Table 4, Fig. E2). There was a trend towards earlier and faster recovery of functional milestones in the intervention group, which may have contributed to earlier discharge (Table 4). Fewer individuals required inpatient rehabilitation in the intervention group (n = 3/7, 43%) compared to the control group (n = 6/7, 86%) ($P = .5$). There was a lower frequency of delirium in the intervention vs control (25:87%), although this was not significant. Duration of delirium was significantly shortened in the intervention group (intervention: median 0.0 [0.0-3.0] days vs control: median 6.0 [3.3-13.3] days, $P = .042$).

4. Discussion

This is the first study to examine the safety and feasibility of FES-cycling in critically ill patients with sepsis. Based on our findings, FES-cycling is safe and feasible as a therapeutic intervention. FES-cycling showed promising trends for functional outcomes. This study is nonrandomized and involves a small sample size; therefore, inferences on efficacy are limited.

Safety limitations such as presence of a pacemaker or the weight limit of the cycle affected recruitment to the FES-cycling intervention (Fig. 2). This is important to take into consideration when considering the feasibility of this intervention.

Despite liberal safety criteria for exercise training compared to previous criteria used in rehabilitation studies in the ICU setting [24], there were no serious adverse events and only one minor transient event (desaturation). Bedside monitoring of cardiorespiratory parameters also demonstrated that individuals with marginalized cardiac and respiratory reserve were still able to be exercised in bed. Several participants were exercised during periods of marginal physiological reserve as indicated by high Sequential Organ Failure Assessment scores, high noradrenaline requirements, and respiratory support without deterioration in physiological signs. However, given that this study involved a small sample size, future studies should continue close monitoring of subjects while undertaking this form of exercise training in the ICU.

Table 4
Comparison between intervention and controls for time to reach functional milestones and awakening PFIT-s

Functional activity	Control mean (SD)	Intervention mean (SD)	Mean diff (95% CI)
a-PFIT-s	2.9 ± 1.8	5.3 ± 1.9	3.9‡ (−2.8 to 10.6)
Time to stand, d	14.6 ± 6.3	10.75 ± 8.8	−3.9 (−10.6 to 2.8)
Time to marching in place, d*	16.0 ± 7.8	12.28 ± 11.6	−3.7† (−14.4 to 7.0)
Time to 1st amb, d*	16.6 ± 7.9	13.1 ± 11.9	−3.4 (−13.8 to 6.9)
Time to indep amb, d*	39.0 ± 18.7	27.0 ± 22.5	−12.0 (−38.0 to 14.0)
Time from stand to indep amb, d*	24.8 ± 14.2	17.7 ± 17.3	−7.2 (−28.2 to 13.9)

The *P* value for statistical significance was calculated on matched pairs to determine the presence of statistical significance between groups. The data are on 8 matched pairs unless otherwise indicated.
Independent ambulation referred to patient being able to walk without needing hands on assistance from the therapist with/without a gait aid.
Amb indicates ambulation; a-PFIT-s, awakening Physical Function in Intensive Care Test score; indep amb, independent ambulation; mean diff, mean difference; SOEOB, sitting on the edge of the bed; CI, confidence interval.
* Mean difference (95% CI) calculated on 6 matched pairs, with 2 pairs not included secondary to deceased prior to time point of measurement.
† Significant result.
‡ Mean difference > MCID of 1.5 points between control and intervention groups on awakening.

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The application of FES-cycling was feasible, with greater than 70% of possible sessions completed in the majority of subjects and a visible or palpable contraction present in 80 % of subjects, which is similar to a previous study involving EMS in septic critically ill participants that reported a perceptible contraction 77% of time [25]. Our study was similar with regards to stimulation parameters (frequency, pulse duration) and treatment duration to previous studies examining EMS in the critically ill [11]. The inability to elicit a contraction on 20% of occasions in this study was consistent with previous research [25,26]. This may be explained by increased tissue impedance related to edema and/or changes in muscle membrane excitability [14,27,28]. Further, factors such as sex, age, and severity of edema have been related to increased difficulty of obtaining an adequate quadriceps contraction [26]. If obtaining a visible or palpable contraction is found to be an important factor influencing efficacy, other outcomes need to be explored that can sensitively and accurately quantify muscle contraction such as ultrasonography.

Another important consideration in terms of feasibility is the time to set up equipment and staffing required. The setup of FES-cycling can take up to 15 minutes in a routine patient and up to 30 minutes in a patient in whom a visible or palpable contraction is difficult or unable to be elucidated. The therapy can be delivered by 1 trained FES-cycling therapist in conjunction with assistance from the bedside nurse. This is often less staffing than might be required to initially mobilize and rehabilitate patients on awakening, which can take 2 or more therapists.

There is growing evidence to suggest that timing of rehabilitation may be important to achieve the greatest gains in functional recovery. Muscle wasting has been shown to occur early and rapidly, with significant reductions in rectus femoris cross-sectional area observed within the first 10 days [29]. In our study, FES-cycling was commenced at a median of 15.3 hours from recruitment. This is similar to Schweickert et al [7], who provided early conventional rehabilitation within a median of 1.5 days, despite the different inclusion criteria and patient demographics. Both studies examined individuals who were moderately unwell; however, our study specifically examined individuals with sepsis. Our findings are promising and in line with Schweickert et al [7], demonstrating trends toward improvement in functional independence and shorter delirium duration in individuals receiving early rehabilitation.

Consistent trends toward improvement were observed in the functional milestones in the intervention group, resulting in higher levels of function on awakening and earlier return to functional independence in this group compared with the controls. Given the positive and consistent direction of findings in functional outcomes, we believe that FES-cycling provides a promising early intervention in the critically ill.

4.1. Limitations and future directions

The major limitation of this study is the small sample size and case-control design. The study was not designed to be powered to detect a meaningful difference between groups. Therefore, it is important to caution readers as to the statistical findings and ability to draw meaningful comparisons between the 2 groups in terms of functional outcomes and frequency and duration of delirium. However the trends in results were all in a positive direction and thus promising. To minimize bias, selection and assessment occurred independent of the research team; and both groups were comparable in terms of baseline demographics including premorbid functioning and comorbidities (which were not matched). A further limitation for using FES-cycling is that the inclusion criteria are restrictive, which impact screening-recruitment ratios.

Further research is needed to determine the efficacy of FES-cycling in the critically ill population including longer-term effects of this treatment on function, delirium, and cognitive function in larger patient cohorts.

5. Conclusions

In conclusion, this study demonstrated that FES-cycling in a moderately unwell septic cohort was safe and feasible. It also suggests that FES-cycling may facilitate earlier and faster functional recovery and reduce the incidence and duration of delirium.

Conflicts of interest and source of funding

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References

[1] De Jonghe B, et al. Acquired neuromuscular disorders in critically ill patients: a systematic review. Intensive Care Med 1998;24:1242–50.
[2] Angus DC. The lingering consequences of sepsis: a hidden public health disaster? JAMA 2010;304(16):1833–4.
[3] Iwashyna TJ, et al. Long-term cognitive impairment and functional disability among survivors of severe sepsis. JAMA 2010;304(16):1787–94.
[4] Needham DM, et al. Improving long-term outcomes after discharge from intensive care unit: report from a stakeholders' conference. Crit Care Med 2012;40:502–9.
[5] Iwashyna TJ, Netzer G. The burdens of survivorship: an approach to thinking about long-term outcomes after critical illness. Semin Respir Crit Care Med 2012;33:327–38.
[6] Morris PE, et al. Early intensive care unit mobility therapy in the treatment of acute respiratory failure. Crit Care Med 2008;36(8):2238–43.
[7] Schweickert WD, et al. Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial. Lancet 2009;373 (9678):1874–82.
[8] Needham DM, et al. Early physical medicine and rehabilitation for patients with acute respiratory failure: a quality improvement project. Arch Phys Med Rehabil 2010;91(4):536–42.
[9] Vasilevskis EE, et al. Reducing iatrogenic risks: ICU-acquired delirium and weakness—crossing the quality chasm. Chest 2010;138(5):1224–33.
[10] Needham DM, Truong AD, Fan E. Technology to enhance physical rehabilitation of critically ill patients. Crit Care Med 2009;37(Suppl.):S436–41.
[11] Parry SM, et al. Electrical muscle stimulation in the intensive care setting: a systematic review. Crit Care Med 2013;41(10):2406–18.
[12] Gruther W, et al. Effects of neuromuscular electrical stimulation on muscle layer thickness of knee extensor muscles in intensive care unit patients: a pilot study. J Rehabil Med 2010;42:593–7.
[13] Meesen RLJ, et al. Neuromuscular electrical stimulation as a possible means to prevent muscle tissue wasting in artificially ventilated and sedated patients in the intensive care unit: a pilot study. Neuromodulation: Technology at the Neural Interface 2010;13:315–21.
[14] Poulsen JB, et al. Effect of transcutaneous electrical muscle stimulation on muscle volume in patients with septic shock. Crit Care Med 2011;39:456–61.
[15] Decker MJ, et al. Alternating stimulation of synergistic muscles during functional electrical stimulation cycling improves endurance in persons with spinal cord injury. J Electromyogr Kinesiol 2010:1163–9.

[16] Ambrosini E, et al. Cycling induced by electrical stimulation improves motor recovery in postacute hemiparetic patients - a randomized controlled trial. Stroke 2011;42:1068–73.
[17] Levy MM. SCCM/ESICM/ACCP/ATS/SIS international sepsis *definitions conference*. Crit Care Med 2003;31:1250–6.
[18] De Jonghe B, et al. Paresis acquired in the intensive care unit: a prospective multicenter study. JAMA 2002;288(9):2859–67.
[19] Ely EW, et al. Evaluation of delirium in critically ill patients: validation of the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU). Crit Care Med 2001;29:1370–9.
[20] Parry SM, et al. Early rehabilitation in critical care (eRiCC): functional electrical stimulation with cycling protocol for a randomised controlled trial. BMJ Open 2012;2(5).
[21] Denehy L, et al. A physical function test for use in the intensive care unit: validity, responsiveness and predictive utility of the Physical Function in Intensive Care Test (Scored). Phys Ther 2013;93(12):1636–45.
[22] Hodgson C, et al. Feasibility and inter-rater reliability of the ICU mobility scale. J Clin Epidemiol 2014;43:19–24.
[23] Groll DL, et al. The development of a comorbidity index with physical function as the outcome. J Clin Epidemiol 2005;58(5):595–602.
[24] Adler J, Malone D. Early mobilization in the intensive care unit: a systematic review. Cardiopulm Phys Ther J 2012;23(1):5–13.
[25] Rodriguez PO, et al. Muscle weakness in septic patients requiring mechanical ventilation: protective effects of transcutaneous neuromuscular electrical stimulation. J Crit Care 2012;27(319):1–8.
[26] Gosselink R, et al. Neuromuscular electrical stimulation in patients admitted to the intensive care unit: a feasibility study. Am J Respir Crit Care Med 2013;187: A3627.
[27] Weber-Carstens S, et al. Nonexcitable muscle membrane predicts intensive care unit-acquired paresis in mechanically ventilated, sedated patients. Crit Care Med 2009;37:2632–7.
[28] Allen DC, Arunachalam R, Mills JR. Critical illness myopathy: further eivdence from muscle-fiber excitability studies of an acquired channelopathy. Muscle Nerve 2008;37:14–22.
[29] Puthucheary ZA, et al. Acute skeletal muscle wasting in critical illness. JAMA 2013. http://dx.doi.org/10.1001/jama.2013.278481.

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