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ORIGINAL ARTICLE

THE EFFECT OF IN-BED LEG CYCLING EXERCISES ON MUSCLE STRENGTH IN PATIENTS WITH INTENSIVE CARE UNIT-ACQUIRED WEAKNESS: A SINGLE-CENTER RETROSPECTIVE STUDY

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***Objective*: To examine the effect of in-bed leg cycling exercise on patients with intensive care unit-acquired weakness (ICU-AW).**
***Design*: Single-center retrospective study.**
***Subjects/Patients*: Patients admitted to the ICU between January 2019 and March 2023 were enrolled in the ergometer group, and those admitted to the ICU between August 2017 and December 2018 were enrolled in the control group.**
***Methods*: The ergometer group performed in-bed leg cycling exercises 5 times per week for 20 min from the day of ICU-AW diagnosis. Furthermore, the ergometer group received 1 early mobilization session per day according to the early mobilization protocol, whereas the control group received 1 or 2 sessions per day. The number of patients with recovery from ICU-AW at ICU discharge and improvement in physical functions were compared.**
***Results*: Significantly more patients in the ergometer group recovered from ICU-AW than in the control group (87.0% vs 60.6%, $p=0.039$). Regarding physical function, the ergometer group showed significantly higher improvement efficiency in Medical Research Council sum score (1.0 [0.7–2.1] vs 0.1 [0.0–0.2], $p<0.001$).**
***Conclusion*: In-bed leg cycling exercise, in addition to the early mobilization protocol, reduced the number of patients with ICU-AW at ICU discharge.**

Key words: early mobilization; exercise; intensive care unit; muscle strength; muscle weakness; rehabilitation exercise.

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LAY ABSTRACT

Recent developments in intensive care have dramatically improved the short-term prognosis of critically ill patients; however, intensive care unit-acquired weakness (ICU-AW) is a specific systemic muscle weakness that occurs in these patients. ICU-AW has been demonstrated to reduce health-related quality of life, as well as contribute to cognitive impairment and functional disability, in survivors of critical illnesses for months to years. Therefore, the development of effective interventions to prevent and improve ICU-AW is required. The study showed that in-bed leg cycling exercises 5 times per week for 20 min in addition to usual care improved muscle strength in patients with ICU-AW. In-bed leg cycling exercises may be a potentially useful exercise therapy for patients with ICU-AW.

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Recent developments in intensive care have dramatically improved the short-term prognosis of critically ill patients (1); however, ICU-AW is a specific systemic muscle weakness that occurs in these patients (2, 3).

ICU-AW is characterized by acute and symmetrical limb weakness that occurs after ICU admission in critically ill patients (4). It is associated with worse short-term outcomes, including increased mortality, duration of mechanical ventilation, and lengths of ICU and hospital stay (5, 6). Furthermore, ICU-AW has been established to reduce health-related quality of life (HRQOL) (7), as well as contribute to cognitive impairment (8) and functional disability (9), in survivors of critical illnesses for months to years. Therefore, ICU-AW is important in critically ill patients. The prevalence of ICU-AW has been reported to be 24–47% of patients on mechanical ventilation for more than 7 days (3, 10). Another systematic review showed that ICU-AW occurred in 40% of critically ill adult patients (11). Therefore, the development of effective interventions to prevent and improve ICU-AW is required.

Currently, there is no effective intervention for ICU-AW, and the reduction of risk factors and avoidance of deep sedation (12) are the first choices of management in clinical settings. Early mobilization, such as cycling, is a well-established intervention for critically ill patients. Cycling exercises are expected to improve proprioceptive sensitivity, muscle coordination, lower limb circulation, and range of motion through continuous repetitive motion. In addition, they can be safely performed in bed by critically ill patients without hemodynamic changes (13), making them one of the most versatile tools at a therapist's disposal (13–15). A study examining the effects of in-bed cycling in critically ill patients who stayed in the ICU for more than 7 days showed that 20 min of cycling per day improved quadriceps muscle strength, 6-min walk distance (6 MWD), and HRQOL (15). In contrast, Nickels et al. (16) showed that in-bed cycling exercise for 30 min per day had no effect on the prevention of muscle atrophy, improvement of physical function, or HRQOL. Thus, the effects of in-bed cycling exercises in critically ill patients remain controversial.

We hypothesized that in-bed leg cycling exercises are effective for improving ICU-AW. The aim of this study was to retrospectively examine the effect of in-bed leg cycling exercise on ICU-AW in critically ill patients.

METHODS

Study design and setting

This was a single-center retrospective study conducted in the ICU of Fujita Health University Hospital. This is a closed ICU with 18 beds and is used as a general ICU for all departments and all ages. It is staffed by 3 intensivists and has a nurse-to-patient ratio of 1:2. In addition, 2 physical therapists (PTs) are on staff, and early mobilization is performed based on a standard protocol. Furthermore, a protocol to perform in-bed cycle exercises for ICU-AW patients was introduced in January 2019. This study was approved by the Medical Research Ethics Review Committee of the Fujita Health University (No. HM23-073, approved on 07 June 2023) and has been reported in accordance with STrengthening the Reporting of OBservational Studies in Epidemiology (STROBE) guidelines. The requirement for informed consent was waived due to the retrospective study design, and individuals who did not opt out were included.

Participants

Consecutive patients admitted to the ICU between August 2017 and March 2023 and diagnosed with ICU-AW were retrospectively enrolled. Patients admitted to the ICU between January 2019 and March 2023 after the introduction of in-bed cycling exercises were included in the ergometer group, and those admitted to the ICU between August 2017 and December 2018 were included in the control group. The exclusion criteria for both groups were as follows: (*i*) motor paralysis due to stroke or neuromuscular disease, (*ii*) lower limb amputation, (*iii*) death in the ICU, (*iv*) age less than 18 years, (*v*) inability to exercise due to rest restriction, (*vi*) not independent in daily activities prior to ICU admission, (*vii*) ICU-AW was diagnosed 1 day prior to ICU discharge, and (*viii*) missing data. In addition, the ergometer group excluded patients who (*i*) performed in-bed cycling exercises prior to the diagnosis of ICU-AW, (*ii*) had a diagnosis of deep vein thrombosis, and (*iii*) were deemed inappropriate to use an ergometer by the therapists.

In-bed leg cycling exercise and ICU early mobilization protocol

The patients in the ergometer group performed one session of in-bed leg cycling exercises per day at least 5 times per week for a maximum of 20 min from the day of ICU-AW diagnosis. We used 2 types of equipment: Terasu Ergo III PLUS-20 (Showa Denki, Osaka, Japan) and Escargo electric cycle machine (Wellup, Yokohama, Japan). In-bed cycling exercises were performed according to an in-bed leg cycling exercise protocol described in a previous study by Kimawi et al. (17) (Fig. 1). The in-bed leg cycling exercise protocol was characterized by a step-by-step approach involving four 5-min cycling sessions. In the first session, the intensity level was started at 3 watt, and on the next day, the intensity level was started at 1 level lower than the intensity level at the end of the previous day. The intensity level was increased incrementally in 1 step if 5 min of active cycling was possible at each interval. The intensity level was lowered by 1 level for the next interval if 5 min of active cycling was difficult due to fatigue or other reasons. If active cycling was difficult even at 3 watt, passive cycling was performed using the electric cycle machine Escargo. The PT constantly encouraged the patient to actively cycle. The PT could stop the session before the 20-min protocol was completed at their discretion if further exercise was difficult owing to fatigue or other reasons. In-bed cycling exercises were performed during the stay in the ICU.

In addition to the cycling exercises, the ergometer group underwent 1 mobilization session per day according to the ICU early mobilization protocol (Fig. 2), whereas the control group underwent 1 or 2 sessions per day. The ICU early mobilization protocol was developed based on a previous report by Morris et al. (18–20). The protocol begins with chest physiotherapy and passive range of motion in step 0 and progresses step-by-step to ambulation in step 5.

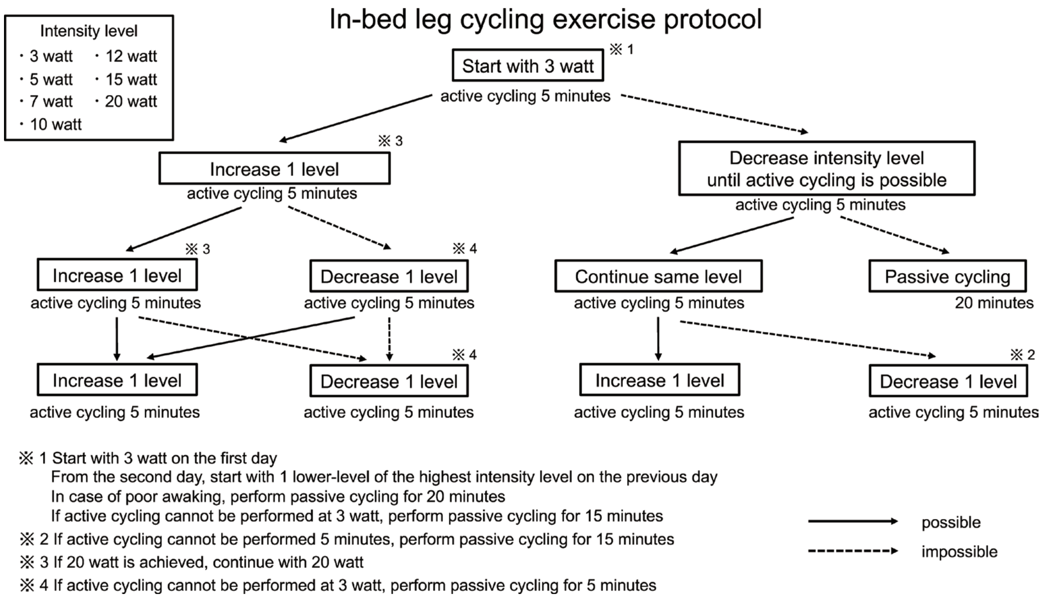

Fig. 1. In-bed leg cycling exercise protocol.

We proceeded with a step if the criteria for not proceeding with a step did not apply. In contrast, if the discontinuation criteria established during the implementation of rehabilitation were met, rehabilitation was discontinued.

After discharge from the ICU, both groups underwent conventional physical therapy programs, including muscle strength exercises, sitting at the edge of the bed, standing, endurance training, and activities of daily living until hospital discharge.

Data collection

Patient data were retrieved retrospectively from electronic medical records. Data characteristics of all enrolled patients were collected, including age, sex, height, body weight, body mass index (BMI), acute physiology and chronic health disease classification system II score (APACHE II score) (21), sequential organ failure assessment score (SOFA score) (22), ICU admission diagnosis, reason for ICU admission, length of ICU stay, duration from ICU admission to first rehabilitation, duration from ICU admission to diagnosis ICU-AW, duration from diagnosis of ICU-AW to ICU discharge, need for mechanical ventilation, duration of mechanical ventilation in the ICU, duration of hospitalization, destination of patient after hospital discharge, Medical Research Council sum score (MRC sum score) (23) at diagnosis of ICU-AW and ICU discharge, grip strength, functional status score for the ICU (FSS-ICU) (24), and functional independence

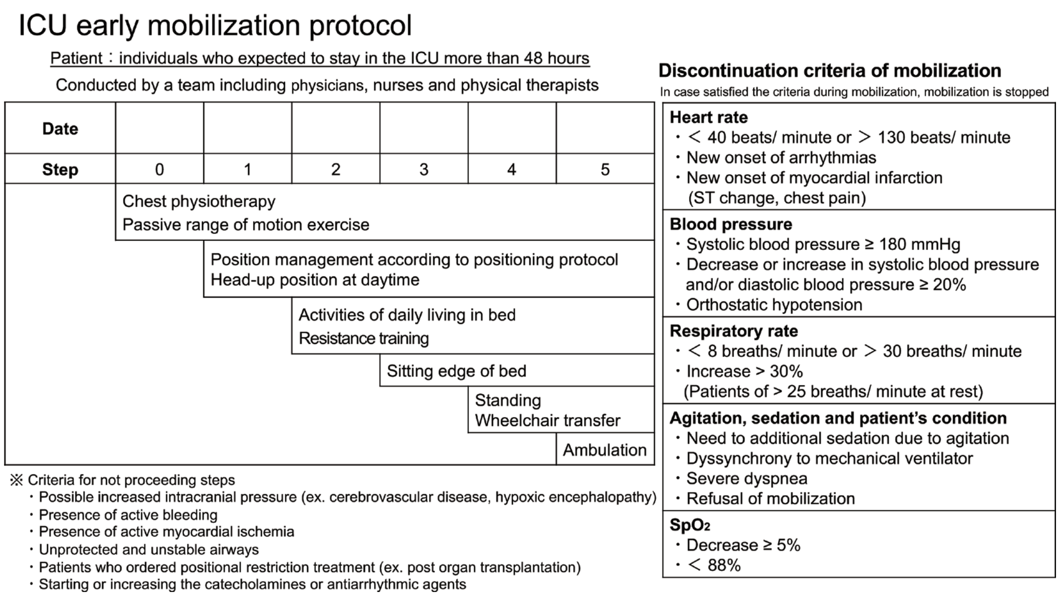

Fig. 2. ICU early mobilization protocol. ICU: intensive care unit; SpO_2: saturation of percutaneous oxygen.

measure (FIM) at hospital discharge. The APACHE II score was the worst value within 24 h of ICU admission.

The definition criteria for ICU-AW proposed by Stevens et al. (4) were used. These defined ICU-AW as an MRC sum score of less than 48 points on 2 occasions separated by 24 h.

Outcome measure

The primary outcome was recovery from ICU-AW at ICU discharge. Secondary outcomes were improvement in the MRC sum score, grip strength, FSS-ICU score, FIM score at discharge, and discharge destination. The improvement efficiency of the MRC sum score, grip strength, and FSS-ICU score was calculated by dividing the difference in these measures at the diagnosis of ICU-AW and at ICU discharge by the same period.

Statistical analyses

Continuous variables are presented as medians and interquartile ranges (IQRs), whereas categorical variables are presented as numbers and percentages. The clinical characteristics, physical function, and discharge destination in both groups were compared using the Wilcoxon sum rank test or Fisher's exact test depending on the type of variable. The effect size was calculated using G*power. All analyses were performed using JMP (version 13.2; SAS Institute Inc., Cary, NC, USA). *P*-values less than 0.05 were considered to indicate statistical significance.

RESULTS

After applying the inclusion and exclusion criteria to 7,489 consecutive patients who were admitted to the ICU during the study period, 23 patients in the ergometer group and 33 patients in the control group were enrolled for analysis (Fig. 3).

The clinical characteristics of the enrolled patients are summarized in Table I. The BMI was significantly higher in the ergometer (23.6 [21.7–25.2] kg/m^2) than in the control group (20.9 [18.4–23.1] kg/m^2) ($p=0.009$). The length of ICU stay (ergometer group: 33 [20.5–37.5] vs. control group: 13 [11–24] days, $p<0.001$) and the duration from ICU admission to the diagnosis of ICU-AW (ergometer group: 13 [8.5–27.5] vs. control group: 6 [3–7] days, $p<0.001$) were significantly longer in the ergometer group.

The in-bed cycling exercise data in the ergometer group are presented in Table II. A total of 284 in-bed cycling exercise sessions were conducted. The number of sessions performed by each patient was 8 [4–16] sessions. The total distance traveled during active cycling was 820 [490–1240] meters per session.

The results of the physical function tests in both groups are shown in Table III. The primary outcome of recovery from ICU-AW at ICU discharge was significantly larger in the ergometer group than in the control group (ergometer group: 87.0% vs. control group: 60.6%, $p=0.039$, effect size$=0.77$). Regarding the secondary outcomes, the ergometer group showed significantly higher improvement efficiency in the MRC sum score (ergometer group: 1.0 [0.7–2.1] vs. control group: 0.1 [0.0–0.2], $p<0.001$, effect size$=1.48$). In addition, the improvement efficiency of the MRC lower limb sum score was significantly higher in the ergometer group (0.6 [0.3–0.9]) than in the control group (0.1 [0.0–0.2], $p<0.001$, effect size$=1.57$), while there was no significant difference in the improvement efficiency of the MRC upper limb sum score ($p=0.382$), FIM at discharge ($p=0.257$), and discharge destination

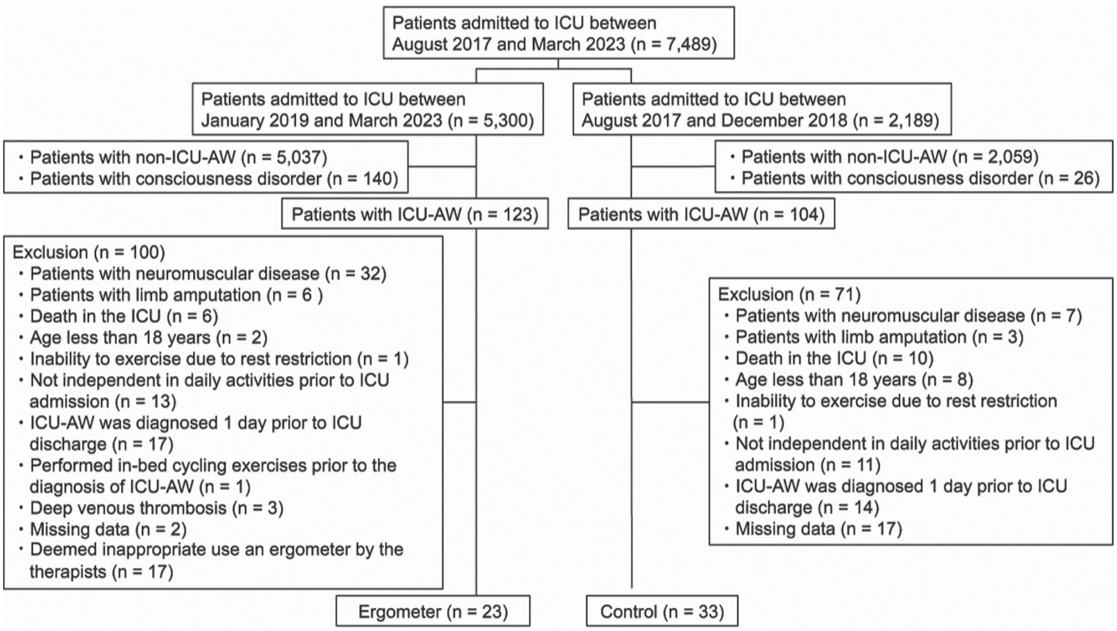

Fig. 3. Participants' flow diagram. ICU: intensive care unit; ICU-AW: intensive care unit acquired weakness; ADL: activities of daily living.

Table I. Participants' characteristics

	Ergometer group ($n=23$)	Control group ($n=33$)	p
Sex, male/female, *n*	11/12	14/19	0.787
Age, years, median [IQR]	70 [49.5–76]	70 [60–76]	0.448
BMI, kg/m², median [IQR]	23.6 [21.7–25.2]	20.9 [18.4–23.1]	0.009
APACHE II score median [IQR]	28 [21–29.5]	22 [19–27]	0.113
SOFA score median [IQR]	10 [9–14]	9 [5–10]	0.037
Location prior to ICU admission, *n* (%)			
Other hospital/emergency department	6 (26.1)	4 (12.1)	0.380
Unplanned from another ward	9 (39.1)	17 (51.5)	
Planned after elective surgery	8 (34.8)	12 (36.4)	
ICU admission diagnosis, *n* (%)			
Medical, *n*			
Respiratory failure	10	9	0.257
Sepsis	1	5	0.384
Circulatory failure	1	2	0.999
Consciousness disorder	1	2	0.999
Other	1	2	0.999
Surgical, *n*			
Cardiovascular	6	8	0.999
Gastrointestinal	3	4	0.496
Other	0	1	0.999
Length of hospital stay, days, median [IQR]	127 [57.5–176]	83 [59–138]	0.147
Length of ICU stay, days, median [IQR]	33 [20.5–37.5]	13 [11–24]	<0.001
Received mechanical ventilation during ICU stay, *n* (%)	21 (91.3)	29 (87.9)	0.999
Length of mechanical ventilation, days, median [IQR]	22 [14–30]	7 [4–17]	<0.001
Duration from ICU admission to first rehabilitation, days, median [IQR]	1 [1–2]	1 [1–1]	0.220
Duration from ICU admission to diagnosis of ICU-AW, days, median [IQR]	13 [8.5–27.5]	6 [3–7]	<0.001
Duration from diagnosis ICU-AW to ICU discharge, days, median [IQR]	12 [5.5–21]	8 [5–13]	0.253
Duration from ICU discharge to hospital discharge, days, median [IQR]	46 [19.5–129.5]	57 [30–95]	0.677

IQR: interquartile range; BMI: body mass index; APACHE II: acute physiology and chronic health disease classification system II; SOFA: sequential organ failure assessment; ICU: intensive care unit; ICU-AW: intensive care unit-acquired weakness.

($p=0.498$) were not significantly different between the 2 groups (Table IV).

DISCUSSION

The main finding of this study was that in-bed leg cycling exercises reduced the number of patients with ICU-AW at ICU discharge and increased lower limb muscle strength in patients with ICU-AW, which supports our hypothesis. To the best of our knowledge, this is the first study to demonstrate the effectiveness of in-bed leg cycling exercises for improving muscle strength in patients with ICU-AW.

The improvement in the MRC score was found only in the lower limbs (not in the upper limbs), indicating that the difference in muscle strength between the 2 groups was attributed to the effect of in-bed cycling exercise which targeted the lower limbs. Previous studies have shown that in-bed cycling exercises improve acute muscle atrophy, quadriceps strength, 6 MWD, and HRQOL (15, 25). A meta-analysis showed that in-bed cycling exercises in critically ill patients can be safely performed but do not show significant effects on physical function, duration of mechanical ventilation, duration of ICU stay, duration of

Table II. Data of in-bed leg cycling exercise

Total number of cycling, sessions per participant	8 [4–16]
Number of active cycling, sessions per participant	7 [4–12.5]
RASS during cycling sessions	0 [-1–0]
Highest intensity level achieved, watt	20 [12–20]
Number of days to achieve the highest intensity level, days	3 [2.5–5.5]
Cycling time, minutes per session	17.1 [11.8–20.0]
Distance by active cycling, meters per session	820 [490–1240]

Values are presented as medians [interquartile ranges]. RASS: Richmond agitation-sedation scale.

Table III. Comparison of physical function between the ergometer and control groups

	Ergometer group ($n=23$)	Control group ($n=33$)	p
Patients who recovered from ICU-AW at ICU discharge, *n* (%)	20 (87.0)	20 (60.6)	0.039
MRC sum score			
ICU-AW diagnosis	35 [28–42.5]	42 [32–45]	0.304
ICU discharge	52 [48–54.5]	48 [44–54]	0.107
Gain	14 [9–20.5]	8 [3–16]	0.026
Improvement efficiency	1.0 [0.7–2.1]	0.1 [0.0–0.2]	<0.001
MRC upper limbs sum score			
ICU-AW diagnosis	19 [14–22.5]	21 [18–22]	0.277
ICU discharge	26 [24.5–27.5]	24 [22–27]	0.205
Gain	7 [4–10.5]	4 [1–8]	0.039
Improvement efficiency	0.5 [0.2–0.9]	0.4 [0.1–1.0]	0.382
MRC lower limbs sum score			
ICU-AW diagnosis	16 [14–20.5]	19 [14–22]	0.493
ICU discharge	26 [23–28]	24 [20–26]	0.104
Gain	9 [4–10]	5 [0–8]	0.041
Improvement efficiency	0.6 [0.3–0.9]	0.1 [0.0–0.2]	<0.001
Grip strength, kgf			
ICU-AW diagnosis	4.8 [1.8–9.5]	5.9 [3.9–9.7]	0.444
ICU discharge	6.5 [5.0–13.0]	9.0 [5.8–12.8]	0.458
Gain	2.5 [0.3–4.3]	2.1 [0.3–5.8]	0.726
Improvement efficiency	0.2 [0.0–0.3]	0.3 [0.0–0.7]	0.532
FSS-ICU sum score			
ICU-AW diagnosis	6 [1.5–8.5]	2 [1–4]	0.208
ICU discharge	13 [10.5–15]	10 [7–14]	0.105
Gain	6 [4–9.5]	5 [2–10]	0.325
Improvement efficiency	0.7 [0.3–1.0]	0.5 [0.1–1.1]	0.577

Values are presented as medians [interquartile ranges] or numbers (%). ICU-AW: intensive care unit-acquired weakness; ICU: intensive care unit; MRC score: Medical Research Council score; FSS-ICU: functional status score for the intensive care unit.

Table IV. Outcomes of activities of daily living and discharge destination of participants after hospital discharge

	Ergometer group (*n* = 23)	Control group (*n* = 33)	*p*
FIM at hospital discharge	91.5 [63.25–121.5]	117 [81.5–125]	0.257
FIM of motor function at hospital discharge	61.5 [33.5–86.5]	82 [57–90]	0.220
FIM of cognitive function at hospital discharge	35 [25.5–35]	35 [30–35]	0.717
FIM of walking at hospital discharge	5.5 [1.25–7]	6 [5–7]	0.430
Discharge destination			
Home, *n* (%)	6 (26.1)	11 (33.3)	0.498
Other hospital, *n* (%)	12 (52.2)	12 (36.4)	
Death, *n* (%)	5 (21.7)	10 (30.3)	

Values are presented as medians [interquartile ranges] or numbers (%).
FIM: functional independence measure.

hospitalization, quality of life, and hospital mortality (26). Although the participants included in the meta-analysis were critically ill, patients with ICU-AW were not specifically included, and there have been no studies of only patients with ICU-AW.

Although the mechanism of ICU-AW has been reported, it is not fully understood. Previous studies identified several potential risk factors of ICU-AW, including multiple organ failure, immobility, hyperglycemia, use of corticosteroids and neuromuscular blockers, and malnutrition (2, 27–29). Although using analgesics and sedatives induces circulatory depression and tissue perfusion defects (30, 31), appropriate analgesic and sedative management is recommended for critically ill patients to relieve pain and other treatment stress (32). In addition, the mechanisms of rapid muscle weakness have been shown to include decreased membrane excitability associated with sodium channel abnormalities (33), damage to the blood-nerve barrier, damage to axonal fibers caused by inflammatory mediators, and damage to muscles due to mitochondrial oxidative stress (34). ICU-AW has been classified into 3 categories: critical illness myopathy (CIM), critical illness polyneuropathy (CIP), and critical illness neuromyopathy (CINM) (4). However, it has been proposed that ICU-AW can also induce transitory reductions in muscle strength due to muscle deconditioning with normal nerve conduction velocity and compound motor action potential (35). Under the current concept of ICU-AW, such a variety of pathologies would be categorized as ICU-AW. The short-term improvement in muscle strength in this study suggests that many of the patients in the present study had pathologies that resulted in transitory reductions in muscle strength due to muscle deconditioning. In-bed cycling exercises are expected to improve proprioceptive sensitivity muscle coordination, and lower limb circulation through continuous repetitive motion. Factors that alter muscle output during muscle strength exercise therapy during the first 2 weeks include changes in the type and total number of motor units mobilized for muscle contraction and the frequency of alpha motor nerve firing, which are central nervous system factors (36). Rhythmic in-bed cycling exercises and the use of an in-bed leg cycling exercise protocol, as in this study, may improve cell perfusion defects, membrane hyperexcitability associated with sodium channelopathies, and damage to the blood-nerve barrier, resulting in an increase in the number of motor units mobilized for muscle contraction and in the frequency of alpha motor nerve firing, thereby improving muscle strength.

This study has some potential limitations. First, it was a single-center retrospective study of patients with critical illnesses, and the results may not necessarily be generalizable to groups with dissimilar demographic characteristics. Second, the BMI was significantly higher in the ergometer group, and the patient backgrounds were not the same. Thus, the effects of the in-bed cycling exercises could have been influenced by the patients' characteristics. Third, although approaches to CIM, CIP, CINM, and muscle deconditioning may differ according to their respective characteristics, electrophysiological testing was not performed in this study, and it was not possible to explore the relationship between the pathophysiological conditions for muscle weakness and the exercise effect. However, this study provides valuable information on the improvement of muscle strength in patients with ICU-AW by combining in-bed leg cycling exercises with early mobilization programs. Further randomized controlled trials of patients with specific ICU-AW types will confirm the effects of in-bed leg cycling exercise for patients with ICU-AW.

In conclusion, in-bed leg cycling exercises, in addition to the early mobilization protocol, significantly improved the efficiency of the MRC sum scores and MRC lower limb sum scores and reduced the number of patients with ICU-AW at ICU discharge. In-bed leg cycling exercises may be a potentially useful exercise therapy for improving muscle strength in critically ill patients with ICU-AW.

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This study was approved by the Medical Research Ethics Review Committee of the Fujita Health University (No. HM23-073, approved on 07 June 2023).

The authors have no conflicts of interest to declare.

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