Original Article

Short-Term Impact of Mobilization of Patients who are being Mechanically Ventilated in the Medical Intensive Care Unit

Chaiwong W, MS[1], Phetsuk N, BS[1], Liwsrisakun C, MD[1], Pothirat C, MD, FCCP[1]

[1] Division of Pulmonary, Critical Care and Allergy, Department of Internal Medicine, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand

Objective: To evaluate the short-term effect of mobilization in mechanically ventilated patients in the intensive care unit (ICU).

Materials and Methods: A prospective non-randomized controlled study was carried out in the medical intensive care unit of Maharaj Nakorn Chiang Mai Hospital, Chiang Mai, Thailand. The intervention group received once daily mobilization therapy, whereas the usual care group received usual standard care. The primary outcome was the proportion of patients who could get out of bed (OOB) at day 6 or at ICU discharge date. The secondary outcomes were health related quality of life (EQ-5D-5L), functional status score for the ICU (FSS-ICU), muscle strength, mechanical ventilator (MV) days, ICU length of stay (LOS), and hospital LOS.

Results: There were 19 and 10 patients in the intervention and the usual care groups, respectively. The proportion of patients who could get OOB was significantly higher in the intervention group (78.9% versus 30.0%, p=0.017). Significant improvements were also demonstrated in the EQ-5D-5L and the FSS-ICU scores in favor of the intervention group.

Conclusion: Early mobilization helps the mechanically ventilated patients to retain mobility and improves their functional ability. The present study recognizes the importance of mobilization in critically ill patients.

Keywords: Mechanical ventilation, Mobilization, Intensive care unit, Physical therapy, Functional status

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Immobility, deconditioning, and weakness are common problems in mechanically ventilated patients in intensive care units (ICU) and may contribute to prolonged hospitalization[1,2]. Early mobilization has been defined as the initiation of a mobility program when a mechanically ventilated patient has a stable hemodynamic status and is able to participate in rehabilitation[3]. Previous studies found that mobilization therapy delivered early in the course of acute respiratory failure patients receiving mechanical ventilation (MV) is feasible, safe, does not increase cost, and associates with decreased ICU and hospital length of stay (LOS) in survivors[4-6]. However, most mobilization therapy studies are carried out in high-income countries[2,4,5,7-10] and there are very few studies from low- and middle-income countries[6]. Moreover, in Thailand, there is no research evidence about mobilization in the ICU. Thus, the objective of the present study was to evaluate the effect of mobilization in mechanically ventilated patients in ICU.

Correspondence to:

Pothirat C.

Division of Pulmonary, Critical Care and Allergy, Department of Internal Medicine, Faculty of Medicine, Chiang Mai University, 110, Inthavaroros Road, Sriphum, Muang Chiang Mai, Chiang Mai 50200, Thailand.

Phone: +66-53-936228, **Fax**: +66-53-895117

Email: chaicharn.p@cmu.ac.th

Materials and Methods

Study design

A prospective non-randomized controlled study was done in a single medical intensive care unit (MICU) of the Department of Internal Medicine, Faculty of Medicine, Chiang Mai University between July 1, 2014 and June 30, 2016. The study was approved by the Ethics Committee of the Faculty of Medicine, Chiang Mai University (Study code: MED-2557-02285, Date of approval: June 2014), and filed under Thai Clinical Trials Registry (Study

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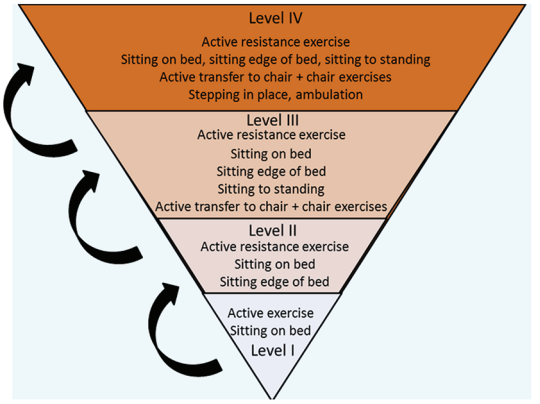

Figure 1. Level of mobilization therapy.

ID: TCTR20160729001). Written informed consents were obtained from all patients.

Study population

Mechanical ventilated patients were screened for eligibility after 48 hours in the MICU. Inclusion criteria were to be at least 18 years of age, required MV for acute respiratory failure for longer than two days, and expected to remain in need of MV for at least another two days. Exclusion criteria were patients with physiological instability, spinal cord injury, stroke, injury preventing the evaluation of six or more muscle groups, inability to follow complex commands, inability to understand Thai, and inability to provide informed consent.

Study procedures

All patients were managed using the same general care protocols and by the same physician and staff (MICU attendants, fellows, and house staff). The patients were allocated into the intervention or usual care groups. The intervention group received mobilization therapy once daily by a physical therapist in accordance with the agreed protocol. Mobilization therapy included active resistance exercise (including elbow flexion and extension, shoulder flexion and abduction, hip flexion, knee flexion and extension, ankle dorsiflexion, and plantar flexion), bed mobility training, transfer training, and ambulation training. Sessions were 30 to 40 minutes long. Progressive resistance was added through the use of manual resistance by a physical therapist. Details of the mobilization therapy protocol are shown in Figure 1. Patients in the intervention group received mobilization therapy until transferred to a general medical ward. The usual care group received usual standard care in mechanically ventilated patients, which, in the authors' center, involved a passive range of motion including 10 repetitions for each upper and lower extremities joint. Standard care did not usually involve active exercise during MV.

Outcome measures

Demographic data, and data pertaining to mortality, baseline assessments, mobilization administration, and hospital outcomes were collected. Baseline assessments included medical history, diagnosis, body mass index (BMI), and Acute Physiology and Chronic Health Evaluation (APACHE II) score. Data were also collected about insulin and steroid use, rates of ventilator-associated pneumonia (VAP), reintubation, pulmonary embolism (PE), and deep vein thrombosis (DVT).

The primary outcome measure was the proportion of patients who could get out of bed (OOB) at day 6 or at ICU discharge date if they were discharged before day 6. The first day OOB was defined as when a patient's feet first touched the floor.

Health-related quality of life (HRQoL) was measured using the Thai version of a five-point Likert scale of EuroQol (EQ-5D-5L) and a EuroQol visual analogue scale (EQ-VAS)[11]. A single score of HRQoL (ranging from –0.205 to 1.0) was calculated, a score of 1 indicating full health, 0 corresponding to death, and negative values corresponding to health states considered to be worse than death[12].

Functional status was assessed using the functional status score for the ICU (FSS-ICU)[13]. The FSS-ICU consists of five categories (rolling, supine-to-sit transfers, unsupported sitting, sit-to-stand, and ambulation). Each functional category is rated using a scale of 1 to 7, with a score of 1 corresponding to total dependence on assistance and score of 7 corresponding to complete independence[14]. A summation of the five categories provided a cumulative FSS-ICU score ranging from 0 to 35[13].

All subjects were assessed using the 12 muscle group strength assessment, bilateral shoulder abduction, elbow flexion, wrist extension, hip flexion, knee extension, and ankle dorsiflexion (the Medical Research Council-Sum Score [MRC-SS])[15]. The patient was positioned in either the sitting or supine position, depending on the patient's condition. Strength in each muscle group was scored according to the six-point MRC system, in which a score of 0 was no contraction, 1 was a flicker of contraction, 2 was active movement with gravity eliminated, 3 was active movement against gravity, 4 was active

movement against gravity and resistance, and 5 was normal power[16]. Summation of the 12 muscle group strength score ranging from 0 to 60.

MV days, ICU LOS, and hospital LOS were collected. A ventilator day was defined as any portion of a calendar day in which the patient required a ventilator. All outcome measurements were collected by a blinded trained nurse at baseline and at day 6 or at ICU discharge date.

Sample size

Sample size calculation was based on the hypothesis from the present pilot study (n = 10); the proportion of patients who could get OOB was 80% for the intervention group and 20% for the usual care group. Allocation was in a 2:1 ratio between the intervention and usual care groups. The study required 24 subjects, 16 in the intervention group and eight in the usual care group to be able to reject the null hypothesis with 80% power. The type I error probability associated with the test of this null hypothesis was 0.05.

Statistical analysis

Descriptive statistics included medians and interquartile range (IQR) for continuous data and absolute frequencies and percentages for categorical data. The groups were compared using the Mann-Whitney U test for continuous data or Fisher's exact test for categorical data. Comparisons between pre and post intervention was done using the Wilcoxon signed-rank test for continuous data or Fisher's exact test for categorical data. Statistical significance was set at a p-value smaller than 0.05. All analyses were carried out using the SPSS statistical package, version 22 for IBM (SPSS Inc., IL, USA).

Results

Out of 46 patients assessed for eligibility, 17 were excluded due to cardiovascular instability (n = 3), neuromuscular disorders (n = 5), dementia (n = 3), and prior discharge from MICU (n = 6). Twenty-nine patients were enrolled, 19 in the intervention group and 10 in the usual care group (Figure 2). The demographic and clinical characteristics between the two groups showed no significant differences (Table 1). The median time of day from MICU admission to the first day of mobilization therapy was 6-day (3 to 11), and median duration per session was 30 (25 to 40) minutes. The proportion of patients who could get OOB was significantly higher in the intervention group) 78.9% versus 30.0%, p=0.017), and the time

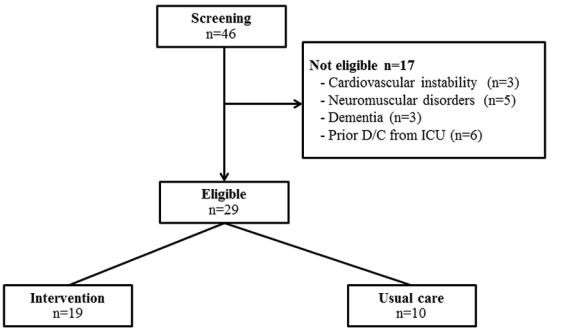

Figure 2. Flow-chart showing participation in the study.

from first mobilization program to get OOB was significantly shorter in the intervention group [3 (2 to 6) days versus 6 (4 to 6) days, p=0.032] (Table 2). Significant improvements were demonstrated for the FSS-ICU scores and the EQ-5D-5L in favor of the intervention group [12 (7 to 15) versus 4 (1.8 to 6.8), p=0.005 and –0.19 (–0.74 to –0.23) versus –0.24 (–0.32 to –0.20), p=0.016, respectively] (Figure 3A, B). However, there was no significant difference in the EQ-VAS and MRC-SS between the groups [50.0 (35.0 to 65.0) versus 35.0 (17.5 to 55.0), p=0.093 and 54.0 (46.0 to 59.0) versus 55 (37.0 to 58.0), p=0.612, respectively] (Figure 3C, D). At day 6 or at ICU discharge date, only patients in the intervention group had statistically significant improvements in FSS-ICU scores, the EQ-5D-5L, EQ-VAS, and MRC-SS (Figure 3A-D). On the last full day of ICU admission, the most activity level was 10.5%, 52.6%, 26.3%, and 10.5% for level I to IV, respectively. The activity level in the intervention group was significantly improved when compared to baseline (Figure 4). Duration of MV days and ICU LOS were shorter in the intervention group, however, the differences were not statistically significant (Table 2). Non-serious adverse events were infrequent, occurring in four out of 80 (5%) activity events, one each in four different patients, these included two orthostatic hypotension, one tachycardia, and one systolic blood pressure above 200 mmHg.

Discussion

Mobilization intervention in the present study, which is similar to the study of Morris et al[4], was based on multiphase treatment tailored to the abilities and progress of the individual patient. Mobilization intervention was carried out without increasing usual ICU staffing. The authors found it was feasible to conduct mobilization that was beneficial not only in increasing the proportion of patients who could

Table 1. Baseline characteristics of subjects in the intervention and usual care groups

Characteristics	Total patients (n = 29), n (%)		p-value
	Intervention (n = 19)	Usual care (n = 10)	
Sex: male	10 (52.6)	4 (40.0)	0.700
Age (years), Median (IQR)	71.0 (62.0 to 79.0)	67.0 (54.0 to 77.5)	0.646
BMI (kg/m^2), Median (IQR)	18.8 (17.8 to 22.4)	20.3 (15.9 to 24.6)	0.748
Primary diagnosis			0.914
Pneumonia	7 (36.8)	3 (30.0)	
Sepsis/severe sepsis/septic shock	6 (31.6)	3 (30.0)	
Acute exacerbation of COPD	4 (21.1)	2 (20.0)	
Other	2 (10.5)	2 (20.0)	
APACHE II score (at admission), Median (IQR)	15.0 (11.0 to 18.0)	14.0 (11.0 to 16.5)	0.675
Patients with previous home O_2 therapy	4 (21.1)	1 (10.0)	0.633
Patients with previous chronic renal failure	2 (10.5)	1 (10.0)	0.733
Co-morbidity			0.737
Cardiovascular disease	4 (21.1)	1 (10.0)	
Respiratory disease	3 (15.8)	1 (10.0)	
Metabolic disease	2 (10.5)	0 (0.0)	
Cardiovascular+respiratory disease	2 (10.5)	3 (30.0)	
Respiratory+metabolic disease	1 (5.3)	1 (10.0)	
Cardiovascular+respiratory+metabolic disease	1 (5.3)	1 (10.0)	
No	6 (31.6)	3 (30.0)	
Patients receiving intravenous insulin in ICU	1 (5.3)	1 (10.0)	0.579
Patients receiving steroids in first 24 hours	6 (31.6)	3 (30.0)	0.636
Highest FiO_2 (%) in ICU, Median (IQR)	40.0 (40.0 to 60.0)	40.0 (37.5 to 50.0)	0.528
Lowest PaO_2 (mmHg) in ICU, Median (IQR)	60.0 (56.5 to 76.5)	71.0 (51.8 to 82.3)	0.880
Lowest PaO_2/FiO_2 in ICU, Median (IQR)	137.5 (112.5 to 186.3)	177.5 (115.0 to 215.0)	0.315

IQR=interquartile range; BMI=body mass index; COPD=chronic obstructive pulmonary disease; APACHE=Acute Physiology and Chronic Health Evaluation; ICU=intensive care unit; FiO_2=fraction of inspired oxygen; PaO_2=partial pressure of arterial oxygen

Table 2. Post enrollment variables of subjects in the intervention and usual care group

Variables	Total patients (n = 29), n (%)		p-value
	Intervention (n = 19)	Usual care (n = 10)	
Patients with VAP	5 (26.3)	4 (40.0)	0.675
Patients with PE	0 (0.0)	1 (10.0)	0.345
Patients with DVT	0 (0.0)	1 (10.0)	0.345
Patients re-intubated	10 (52.6)	5 (50.0)	0.893
Duration of MV (days), Median (IQR)	19.0 (11.0 to 34.0)	24.0 (17.0 to 44.0)	0.422
Total ICU LOS (days), Median (IQR)	22.0 (9.0 to 30.0)	24 (20.0 to 44.0)	0.198
Hospital LOS (days), Median (IQR)	40.0 (21.0 to 47.0)	36.5 (25.3 to 69.3)	0.713
Patients who could get OOB	15 (78.9)	3 (30.0)	0.017*
Time from first MOB to get OOB (days)	3 (2 to 6)	6 (4 to 6)	0.032*
Patients who died at discharge	5 (26.3)	5 (50.0)	0.244

IQR=interquartile range; VAP=ventilator associated pneumonia; PE=pulmonary embolism; DVT=deep vein thrombosis; MV=mechanical ventilation; ICU=intensive care unit; LOS=length of stay; OOB=out of bed

get OOB and their muscle strength, but also led to improvement of HRQoL. Data from a recent systematic review and meta-analysis that included early mobilization, cycle ergometry, and electrical stimulation as physical therapy in ICU have showed benefits on increased peripheral and respiratory muscle strength, shortened duration of MV, ICU and hospital LOS, and improved HRQoL[17]. The present study showed statistically significant improvement in muscle strength in the treatment group despite a short

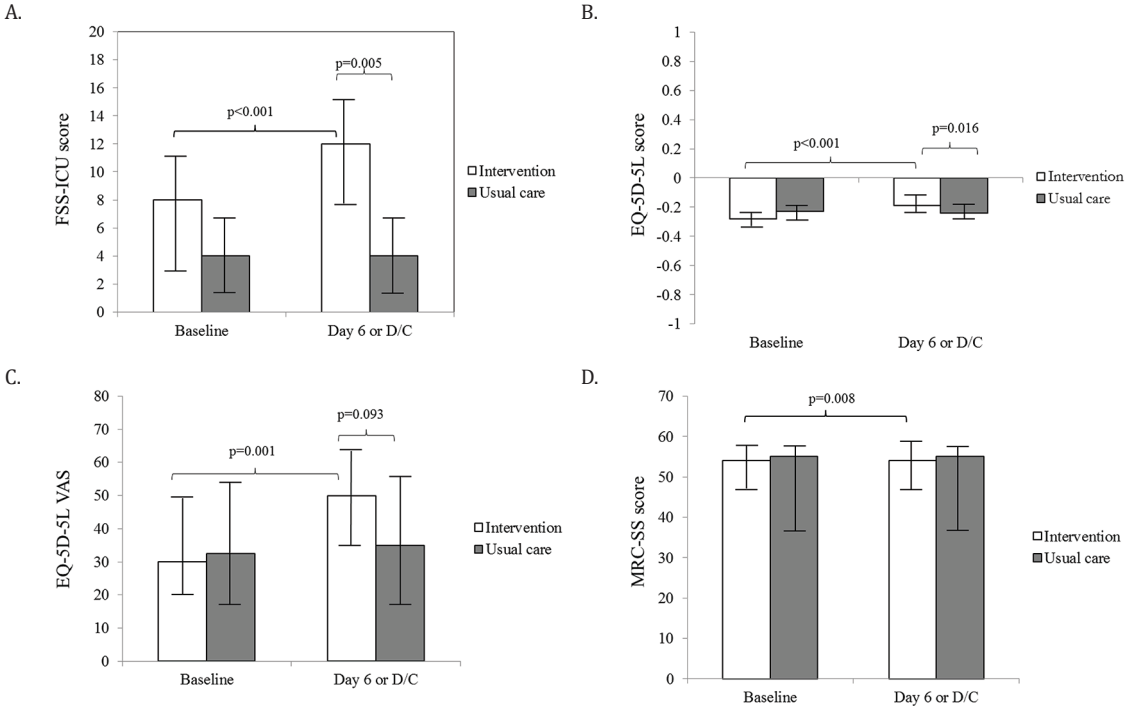

Figure 3. Outcomes in the interventional and usual care groups.
Values and error bars represent the median and interquartile range (IQR)

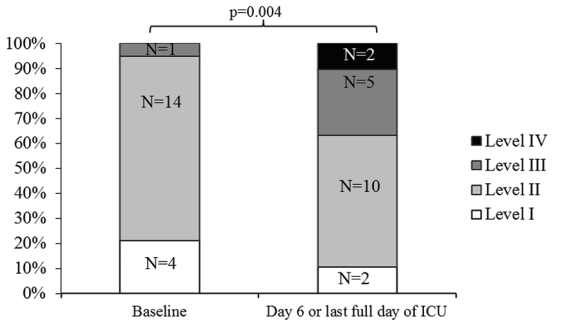

Figure 4. Activity level in the intervention group between baseline and day 6 or the last full day of ICU.

average time (six days) of intervention. However, there was no significant difference in the MRC-SS between the groups. A previous study also showed statistically significant improvement in muscle strength after 72 hours of early mobilization therapy[18].

In the present non-randomized, assessor-blinded study into mobilization therapy versus usual care in mechanical ventilated patients in the MICU, there was no difference in duration of MV days, ICU, and hospital LOS between groups at hospital discharge. Recent studies have also showed non-statistically significant differences in duration of MV days, ICU, and hospital LOS between intervention and control groups[2,19]. However, a previous study showed that early mobilization in ICU patients was associated with statistically significant shortened days in bed, and reduced ICU and hospital LOS for hospital survivors[4]. The present study findings showed non-statistically significant longer hospital LOS in the intervention group compared to the usual group. A previous study has also showed longer duration of hospital LOS in the intervention group[20]. The authors suggest that the longer hospital LOS in the intervention group may have been the result of the mobilization group patients' longer survival; only 26.3% of the mobilization group patients died at discharge, whereas 50.0% patients in the usual care group died in the hospital.

Only four non-serious adverse events occurred on four separate occasions with four separate patients. These included two occurrences of orthostatic hypotension, one tachycardia, and one systolic blood pressure above 200 mmHg. Similar to previous studies[21,22], mobilization was safely performed with a low incidence of non-serious adverse events and only a small number of sessions ceased early as a result of physiological changes.

There were several strengths to the present study. One major strength was that the mobilization

exercises with respiratory failure patients admitted to our MICU were dealt with consistently because every patient in the intervention group received the therapy by the same physical therapist. There were several limitations of the present study. Firstly, the study was not designed as a randomized control trial with sham mobilization therapy in the control group. However, the authors' results are as convincing as maybe a controlled randomized trial. Therefore, the authors' suggest putting this practice into regular clinical use as a good practice procedure. Secondly, the authors' study assessed the muscle strength by manual muscle testing (MMT). An important limitation of MMT using the MRC score system is the 6-point ordinal scale. However, systematic strength assessment and the definition of ICU-acquired weakness according to the MRC-SS have been recommended for both research and clinical practice[23]. Thirdly, the authors' study did not assess long-term outcomes such the readmission rate, exercise performance, or a one-year mortality rate after hospital discharge.

Conclusion

The present study showed that mobilization therapy for patients in MICU who were on MV was feasible and safe. It was associated with an increase in the proportion of patients who could get OOB. In addition, it improved patients' health outcomes and the functional ability when compared with the group that received only usual care. These promising results should encourage healthcare professionals to promote mobilization as a standard in care for mechanically ventilated patients in the ICU.

What is already known on this topic?

Early mobilization therapy delivered early in the course of acute respiratory failure patients receiving mechanical ventilation is feasible, safe, did not increase cost, and associate with decreased ICU and hospital LOS in survivors[4-6]. However, it is not widely utilized in clinical practices in Thailand.

What this study adds?

This study adds the information that mobilization was associated with increase in proportion of the patients who could get OOB. In addition, it also improved patients' health outcomes and the functional ability when compared with the group that received only the usual care.

Acknowledgement

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Conflicts of interest

The authors declare no conflict of interest.

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