Original Article

Effect of early mobilization on discharge disposition of mechanically ventilated patients

Hideki Ota[1, 2]*, Hideki Kawai[1], Makoto Sato[2, 3], Kazuaki Ito[2, 3], Satoshi Fujishima[1], Hiroko Suzuki[4]

[1] *Department of Thoracic Surgery, Akita Red Cross Hospital: 222-1 Kamikitate, Akita-city, Akita 010-1495, Japan*
[2] *Respiratory Support Team, Akita Red Cross Hospital, Japan*
[3] *Department of Rehabilitation, Akita Red Cross Hospital, Japan*
[4] *Department of Emergency and Critical Care, Akita Red Cross Hospital, Japan*

Abstract. [Purpose] The purpose of this study was to clarify the benefits of early mobilization for mechanically ventilated patients for their survival to discharge to home from the hospital. [Subjects and Methods] Medical records were retrospectively analyzed of patients who satisfied the following criteria: age $\geq$ 18 years; performance status 0–2 and independent living at their home before admission; mechanical ventilation for more than 48 h; and survival after mechanical ventilation. Mechanically ventilated patients in the early mobilization (EM) group (n = 48) received mobilization therapy, limb exercise and chest physiotherapy, whereas those in the control group (n = 60) received bed rest alone. Univariate and multivariate logistic regression analyses were performed to identify clinical variables associated with discharge disposition. [Results] Early mobilization was a positive independent factor and the presence of neurological deficits was a negative factor contributing to discharge to home. Among patients surviving mechanical ventilation without neurological deficits, the rate of discharge to home was significantly higher among patients in the EM group that in the control group (76% vs. 40%). [Conclusion] Early mobilization can improve the rate of discharge to home of patients requiring mechanical ventilation because of non-neurological deficits.
Key words: Mechanical ventilation, Early mobilization, Physiotherapy

INTRODUCTION

Recent developments in the management of mechanically ventilated patients have improved the survival rate of critically ill patients[1–5]. Survivors of prolonged mechanical ventilation frequently suffer from long-term physical dysfunction[6, 7]. Early mobilization is a physiotherapy technique that is usually initiated within one or two days following endotracheal intubation and mechanical ventilation[8], and has been shown to be effective at preventing skeletal muscle wasting and weakness in surviving patients[9–12]. The reported clinical benefits of early mobilization of mechanically ventilated patients are a decreased duration of mechanical ventilation[13, 14], reductions in the incidences of ventilator-associated pneumonia (VAP)[15, 16] and intensive care unit (ICU) delirium[13], shorter ICU and hospital stays[14, 17], and improved functional status upon hospital discharge[13]. Despite these reported clinical benefits, it remains controversial as to whether early mobilization can provide recovery of the fundamental skills necessary for independent living at home after hospital discharge in surviving patients successfully weaned from mechanical ventilation.

The purpose of this retrospective study was to clarify the benefits of early mobilization for mechanically ventilated patients for their survival and discharge to home from the hospital.

SUBJECTS AND METHODS

The review board of the Akita Red Cross Hospital approved the study protocol. The medical records of all patients who had received endotracheal intubation and mechanical ventilation in the ICU and high care unit (HCU) of our hospital from August 2009 to July 2013 were reviewed to identify those who met the following criteria: age $\geq$ 18 years; performance status score of 0–2 and independent living at their home prior to hospitalization; duration of mechanical ventilation for more than 48 h; and survival after mechanical ventilation. Each patient's performance status before admission was evaluated in accordance with the European Cooperative Oncology Group scoring system. Data collection was restricted to the first episode of mechanical ventilation. Patients with cervical spine injury, neuromuscular diseases, or major burns were excluded.

*Corresponding author. Hideki Ota (E-mail: hidekiohta29@ hotmail.com)

The following data were collected from the medical records: age, sex, smoking status, age-adjusted Charlson comorbidity index (ACCI), acute physiology and chronic health evaluation (APACHE) II score, cause of mechanical ventilation, presence of VAP, delirium after weaning from mechanical ventilation, tracheostomy, duration of mechanical ventilation, length of hospital stay after initiating mechanical ventilation, and discharge disposition. The term "discharge to home" was used for patients who were independently living at home after hospital discharge. An elderly patient was defined as a patient over the age of 65. APACHE II scores were calculated from data obtained at the time of initiating mechanical ventilation. Patients were further divided according to the cause of mechanical ventilation into the following overlapping categories: postoperative care after emergency surgery, multiple trauma, neurological deficits, pneumonia, and others. Neurological deficits in the present study included acute onset of cerebrovascular disease, traumatic brain injury, meningitis, encephalitis, hypoxic ischemic encephalopathy following cardiopulmonary arrest, exacerbation of Parkinson's disease, and major epilepsy. Other causes of mechanical ventilation included acute pancreatitis, acute liver failure, septic shock, heart failure, laryngeal edema, and recurrent laryngeal nerve paralysis. A diagnosis of VAP was made on the basis of the criteria recommended by the Japan Nosocomial Infections Surveillance[18].

Patients were divided into two groups based on whether or not they received early mobilization: the early mobilization group (EM group) received our early mobilization program, whereas the control group received bed rest alone. Because the ICU/HCU of our hospital had an open model of organization, the attending physicians made all decisions regarding implementation of early mobilization. The common consensus of intervention criteria was that early mobilization would be implemented for patients who were expected to survive their disease and require prolonged mechanical ventilation (usually greater than 7–10 days). The procedures of our early mobilization program consist of passive and active limb exercise, relaxation of the muscles, deep breathing exercises, chest physiotherapy, elevation of the head up to 30–90 degrees, and changing a patient's position from supine to up to a 135-degree lateral position. The safety of our early mobilization program was monitored by bedside nurses and no adverse side effects were observed. Muscle exercise/relaxation and chest physiotherapy were conducted twice daily at day-time by one or two licensed physical therapists and nurses. Changing a patient's position was performed every 2 hours by bedside nurses. The timing and intensity of early mobilization were adjusted according to the neurological and cardiopulmonary condition of the patients. The median time from initiating mechanical ventilation to the first early mobilization session in the EM group was 2 days (interquartile range, 0–5 days). The main reason for delay in initiation of early mobilization was due to holiday schedules. After weaning from mechanical ventilation, all patients received standard physiotherapy performed by licensed physical therapists, which was adjusted to the individual needs of the patients every day until hospital discharge.

Sedation and analgesia in the mechanically ventilated patients were managed according to the guidelines proposed by the Japan Society of Respiratory Care Medicine[19]. The Richmond Agitation-Sedation Scale (RASS) was used to measure sedation level, and sedation was titrated to a goal RASS score of −1 to −3 at night-time by the ICU/HCU nurses. All patients were ventilated with a Servo-s, Servo ventilator-900c, Newport e360, or Newport e500 ventilator. The decision on weaning and extubation was made by the attending physicians, according to the patient's clinical condition, weaning parameters, and the results of spontaneous breathing trials with a T-piece for 30 minutes to 2 hours. The indications for tracheostomy in our hospital were prolonged mechanical ventilation, upper airway obstruction, re-intubation, difficult airway management, and massive hemoptysis following chest trauma.

Clinical data are expressed as the number (%) or median (interquartile range: 25–75%). To test if the variables were normally distributed, the Kolmogorov-Smirnov test was performed. The nonparametric test of Mann-Whitney U test was used to analyze age, ACCI, APACHE II score, duration of mechanical ventilation, and the length of hospital stay after initiating mechanical ventilation, because the variables were not normally distributed as determined by two-tailed hypothesis testing. The χ^2 test was used to compare the number of males, smokers, VAP, causes of mechanical ventilation, delirium, tracheostomy, and discharge disposition between groups. Fisher's exact test was used for the subgroup analyses of patients with neurological deficits. Variables that were found to be significantly associated with discharge disposition in univariate analyses ($p < 0.10$) were included in a multivariate model, and backwards step-wise logistic regression analysis was performed to evaluate the independent contribution of each variable. All statistical analyses were conducted using EZR software (Saitama Medical Center, Jichi Medical University), which is a graphical user interface for R (The R Foundation for Statistical Computing)[20]. A p value of <0.05 was considered statistically significant.

RESULTS

The medical records of 517 patients requiring mechanical ventilation at our hospital from August 2009 to July 2013 were reviewed retrospectively. Of the 111 patients who met the inclusion criteria, 48 were assigned to the EM group and 60 were assigned to the control group. Three patients were excluded due to incomplete medical records. Because the eligible patients in this study were representative of survivors, 15 patients who received mechanical ventilation for more than 48 hours and died due to the severity of thier disease in hospital were also excluded. Among them were 12 patients who received early mobilization: 3 died while receiving mechanical ventilation, and 9 died after weaning from mechanical ventilation.

The patients' characteristics at the time of initiating mechanical ventilation are described in Table 1. Patients in the EM group were significantly younger than those in the control group (p = 0.009). On admission, 33 patients (69%) in the EM group and 43 patients (72%) in the control group underwent medical treatment for comorbidities. There were no significant differences between the two groups with respect

Table 1. Summary of the patients' characteristics

Variable	EM group (n = 48)	Control group (n = 60)
Male, n (%)	34 (69)	44 (73)
Age, median (IQR), years	64 (46–73)	72 (59–82)*
elderly age, n (%)	22 (46)	42 (68)*
Smoker, n (%)	24 (50)	33 (55)
ACCI, median (IQR)	4 (2–5)	4 (3–5)
Comorbidities, n (%)		
Cardiovascular diseases	20 (42)	36 (60)
Respiratory diseases	6 (13)	1 (2)
Cerebrovascular diseases	11 (23)	16 (27)
Psychological diseases	2 (4)	3 (5)
Diabetes melitus	10 (21)	7 (12)
Endocrine diseases	2 (4)	3 (5)
Malignancies	7 (15)	8 (13)
Hemodialysis for chronic renal failure	0 (0)	4 (7)
None	15 (31)	17 (28)
APACHE II score, median (IQR)	14 (11–20)	16 (12–21)
Causes of mechanical ventilation, n (%)		
Postoperative care after emergency surgery	20 (42)	18 (30)
Multiple trauma	13 (27)	12 (20)
Neurological deficits	14 (29)	23 (38)
Cerebrovascular disease	3	7
Traumatic brain injury	6	6
Hypoxic-ischemic encephalopathy following CPA	2	5
Others	3	5
Pneumonia	9 (19)	16 (27)
Other causes	4 (8)	7 (12)

EM: early mobilization; IQR: interquartile range; SD: standard deviation; ACCI: age-adjusted Charlson comorbidity index; APACHE: the acute physiology and chronic; *: p<0.05

Table 2. The clinical outcomes of each group

Variable	EM group (n = 48)	Control group (n = 60)
Ventilator-associated pneumonia, n (%)	13 (27)	11 (18)
Derilium after weaning from mechanical ventilation, n (%)	13 (27)	17 (28)
Tracheostomy, n (%)	29 (60)*	23 (38)
Duration of mechanical ventilation, median (IQR), days	13 (7–22)*	8 (6–12)
Length of hospital stay, median (IQR), days	56 (38–85)	58 (36–78)
Discharge, n		
Home	28*	18
Another hospital or nursing care home	20	42

EM: early mobilization; IQR: interquartile range; *: p<0.05

to the number of males and smokers, ACCI, or APACHE II score. Of the 38 patients receiving mechanical ventilation due to postoperative care after emergency surgery, two in the EM group had thoracic surgery and the others underwent abdominal surgery. No significant differences were found between groups with respect to the categorical variables.

Table 2 shows the clinical outcomes of each group. Four patients in the EM group and two patients in the control group required reintubation owing to failed extubation of mechanical ventilation. The number of patients undergoing

Table 3. Summary of the results of univariate and multivariate analyses

Covariates	OR (95%CI)
Univariate analysis	
Early mobilization	3.27 (1.47–7.24)*
Male	1.16 (0.49–2.73)
Age ≥65 years	0.75 (0.35–1.63)
Smoker	0.96 (0.45–2.06)
ACCI ≥4 point	1.05 (0.48–2.29)
APACHE II score ≥20 point	0.53 (0.23–1.25)
Postoperative care	5.42 (2.30–12.8)
Multiple trauma	0.70 (0.28–1.76)
Neurological deficits	0.11 (0.04–0.33)*
Pneumonia	0.56 (0.22–1.43)
Multivariate analysis	
Early mobilization	3.47 (1.42–8.44)*
Neurological deficits	0.11 (0.04–0.33)*

OR: odds ratio; CI: confidence intervals; ACCI: age-adjusted Charlson comorbidity index; APACHE: the acute physiology and chronic health evaluation; *: $p<0.05$

Table 4. Subgroup analysis of discharge disposition

Variable	EM group	Control group
	(n = 48)	(n = 60)
Neurological deficits, n		
Home	2	3
Another hospital or nursing home	12	20
Non-neurological deficits, n		
Home	26*	15
Another hospital or nursing home	8	22

EM: early mobilization; *: $p<0.05$

Table 5. Summary of the results of univariate and multivariate analyses of patients without neurological deficits

Covariates	OR (95%CI)
Univariate analysis	
Early mobilization	4.77 (1.70–13.3)*
Male	1.17 (0.41–3.32)
Age ≥65 years	0.43 (0.15–1.23)
Smoker	1.61 (0.62–4.17)
ACCI ≥4 point	0.70 (0.25–1.97)
APACHE II score ≥20 point	0.56 (0.20–1.56)
Postoperative care	2.60 (0.99–6.85)
Multiple trauma	0.68 (0.21–2.19)
Pneumonia	0.34 (0.11–1.08)
Multivariate analysis	
Early mobilization	4.77 (1.70–13.3)*

OR: odds ratio; CI: confidence intervals; ACCI: age-adjusted Charlson comorbidity index; APACHE: the acute physiology and chronic health evaluation; *: $p<0.05$

tracheostomy in the EM group was significantly higher than in the control group (p = 0.03). The duration of mechanical ventilation was significantly longer in the EM group than in the control group (p < 0.001), but the length of hospital stay after initiating mechanical ventilation was similar in both groups. Of the 108 patients, 46 were discharged to home from the hospital, and 62 were transferred to another hospital or to nursing care homes for further rehabilitation. The EM group had a significantly higher rate of discharge to home than the control group (58% vs. 30%, p = 0.003).

The results of univariate and multivariate logistic analyses for the contribution of each covariate on discharge disposition are described in Table 3. The following statistically significant variables derived from the univariate analysis were included in the multivariate model: early mobilization, postoperative care after emergency surgery, and neurological deficits. The results of the multivariate logistic analysis indicate that early mobilization was a positive independent factor and the presence of neurological deficits was a negative factor contributing to discharge home.

Subsequently, subgroup analyses were conducted according to presence or absence of neurological deficits (Table 4). Among survivors without neurological deficits, the rate of discharge to home in the EM group was significantly higher than in the control group (76% vs. 40%, p = 0.004). The results of univariate and multivariate logistic analyses for the contribution of each covariate to the discharge disposition of patients without neurological deficits is shown in Table 5. The patients without neurological deficits, early mobilization and pneumonia factors, that were found to be significantly associated with discharge home in univariate analyses (p<0.10), were included in the multivariate model, and backwards step-wise logistic regression analysis demonstrated that early mobilization was the only significant variable facilitating the discharge to home of mechanically ventilated patients without neurological deficits.

DISCUSSION

The present study revealed that early mobilization improved the rate of discharge to home of mechanical ventilation patients without neurological deficits. Elderly patients were less likely to receive early mobilization, but age had no significant impact on the rate of discharge to home. In this retrospective study, early mobilization treatment had been selected and performed for mechanically ventilated patients based on the clinical expectations of the attending physicians. These findings indicate that when mechanically ventilated patients without neurological deficits are not able to receive early mobilization due to their age, they have a reduced opportunity to recover the fundamental skills necessary for independent living at home upon hospital discharge.

The aim of our early mobilization program is to prevent disuse atrophy and muscle weakness, and to increase the clearance of lung secretions and maintain lung expansion. This program was also designed to be feasible and safe for physical therapists and nurses in daily clinical practice. Since the first reports of early mobilization for mechanically ventilated patients were published in the mid-2000s, the literature on the effectiveness, feasibility, and safety of

early mobilization has grown substantially[21–23]. In addition, fundamental studies on physiological changes in respiratory function associated with physiotherapy have provided insight on new ways to improve the care and management of mechanically ventilated patients[24–27]. Respiratory physiotherapy techniques used for mechanically ventilated patients are divided into three activities: mobilization, chest physiotherapy, and muscle retraining[23, 28]. The procedures of mobilization include posture improvement, passive and active limb exercises, and continuous rotational therapy[28]. Recent studies have demonstrated the efficacy and safety of advanced mobilization programs, which include additional elements such as prone positioning[29–31] or 45 degree rotation in the prone position[32], early exercise using a bedside bicycle ergometer[9], and walking exercises[33]. These additional approaches increase the range of intervention criteria and programs of early mobilization, resulting in some confusion about the implementation of early mobilization in clinical practice. The establishment of consensus guidelines regarding indications for early mobilization of mechanically ventilated patients would be helpful for achieving standardized clinical practice.

Our early mobilization program resulted in an improved rate of discharge to home among survivors after mechanical ventilation. Previous studies have suggested that early mobilization for mechanically ventilated patients can be efficient at improving the functional status of these survivors[13]. However, it remains controversial as to whether the improved functional status resulting from early mobilization also facilitates discharge to home[12]. One randomized control trial demonstrated a trend toward better discharge rates to home[13], whereas three other studies showed no significant impact of early mobilization on the number of survivors discharged to their homes[9, 17, 34]. The results of our study indicate that these discrepancies among studies may depend on the presence or absence of neurological deficits, and the specific components of the early mobilization program adopted.

The results of the present study suggest that elderly age has no significant impact on the rate of discharge to home of surviving patients successfully weaned from mechanical ventilation. Elderly patients frequently suffer from one or more severe chronic illnesses before hospitalization, and are therefore less able to meet the physiological demands of critical illness[35]. Morbidity and mortality are higher among elderly patients than among younger patients admitted to the ICU[36]. In addition, the pivotal prospective studies on early mobilization of mechanically ventilated patients only included patients with a mean age of 50–60 years[13, 17]. Therefore, the conclusion of these previous, that early mobilization provides had few benefits for mechanically ventilated elderly patients, despite the lack of direct evidence of a correlation between age and outcomes of early mobilization[22]. Based on our results, we recommend that the indication for early mobilization should not be based on a patient's age alone.

This study had several limitations. First, we cannot rule out the possibility of selection and survivor bias in this retrospective study. Patients in both groups were recruited at different time points, and the decision to perform early mobilization treatment was not randomly assigned. In addition, the higher mortality rates of patients who received early mobilization during mechanical ventilation may lead to a misunderstanding that a lot of poor prognosis patients received early mobilization, even though it is hard to accurately predict which patients are going to survive their disease. These possible biases in the present study are mainly due to the absence of attending physicians and physical therapists who have specialized in intensive care. According to the ambiguous eligibility criteria of early mobilization used in our hospital, physiotherapy can often be delayed or ignored for elderly patients and patients with severe disease. Therefore, our respiratory support team was established to provide advice, information and support on the management of mechanically ventilated patients for the attending physicians. However, it is often difficult to achieve an appropriate intervention of team activity in a timely manner. Therefore, our team is going to develop clinical practice guidelines for use in our hospital for the early mobilization of mechanically ventilated patients. Second, the control group seems to have more patients with neurological deficits who are more likely to develop aspiration pneumonia and receive permanent tracheostomy, which could be the reason why they were not discharged to home directly from the hospital. Patients who have neurological deficits and/or tracheostomy usually need more nursing care and rehabilitation. To address this possible issue, subgroup analyses revealed the benefits of early mobilization for survivors without neurological deficits. Third, our early mobilization program may be insufficient for the improvement of the functional status of patients with neurological deficits requiring mechanical ventilation. A highly specialized rehabilitation program is necessary for such patients to prevent respiratory complications[37]. Despite these limitations, we believe that this study provides several useful findings that could guide treatment strategies for mechanically ventilated patients. Further studies are required to confirm between the relationship the improvement in physical activity achieved by early mobilization and the facilitation of discharge to home.

In conclusion, early mobilization of critically ill patients requiring mechanical ventilation because of non-neurological deficits can improve the functional status at hospital discharge, resulting in an increased rate of discharge to home. These benefits were also apparent among the elderly population. Thus, we recommend that early mobilization should not be implemented according to a patient's age alone. Consensus guidelines regarding indications of early mobilization for mechanically ventilated patients are necessary to establish a standardized clinical practice to help patients recover the fundamental skills required for independent living at their home following hospital discharge.

REFERENCES

1) Kress JP, Pohlman AS, O'Connor MF, et al.: Daily interruption of sedative infusions in critically ill patients undergoing mechanical ventilation. N Engl J Med, 2000, 342: 1471–1477. [Medline] [CrossRef]
2) Girard TD, Kress JP, Fuchs BD, et al.: Efficacy and safety of a paired sedation and ventilator weaning protocol for mechanically ventilated patients in intensive care (Awakening and Breathing Controlled trial): a randomised controlled trial. Lancet, 2008, 371: 126–134. [Medline] [CrossRef]

3) The Acute Respiratory Distress Syndrome Network: Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. N Engl J Med, 2000, 342: 1301–1308. [Medline] [CrossRef]

4) Santa Cruz R, Rojas JI, Nervi R, et al.: High versus low positive end-expiratory pressure (PEEP) levels for mechanically ventilated adult patients with acute lung injury and acute respiratory distress syndrome. Cochrane Database Syst Rev, 2013, 6: CD009098. [Medline]

5) Papazian L, Forel JM, Gacouin A, et al. ACURASYS Study Investigators: Neuromuscular blockers in early acute respiratory distress syndrome. N Engl J Med, 2010, 363: 1107–1116. [Medline] [CrossRef]

6) Herridge MS, Cheung AM, Tansey CM, et al. Canadian Critical Care Trials Group: One-year outcomes in survivors of the acute respiratory distress syndrome. N Engl J Med, 2003, 348: 683–693. [Medline] [CrossRef]

7) De Jonghe B, Sharshar T, Lefaucheur JP, et al. Groupe de Réflexion et d'Etude des Neuromyopathies en Réanimation: Paresis acquired in the intensive care unit: a prospective multicenter study. JAMA, 2002, 288: 2859–2867. [Medline] [CrossRef]

8) Pohlman MC, Schweickert WD, Pohlman AS, et al.: Feasibility of physical and occupational therapy beginning from initiation of mechanical ventilation. Crit Care Med, 2010, 38: 2089–2094. [Medline] [CrossRef]

9) Burtin C, Clerckx B, Robbeets C, et al.: Early exercise in critically ill patients enhances short-term functional recovery. Crit Care Med, 2009, 37: 2499–2505. [Medline] [CrossRef]

10) Chiang LL, Wang LY, Wu CP, et al.: Effects of physical training on functional status in patients with prolonged mechanical ventilation. Phys Ther, 2006, 86: 1271–1281. [Medline] [CrossRef]

11) Chen YH, Lin HL, Hsiao HF, et al.: Effects of exercise training on pulmonary mechanics and functional status in patients with prolonged mechanical ventilation. Respir Care, 2012, 57: 727–734. [Medline] [CrossRef]

12) Li Z, Peng X, Zhu B, et al.: Active mobilization for mechanically ventilated patients: a systematic review. Arch Phys Med Rehabil, 2013, 94: 551–561. [Medline] [CrossRef]

13) Schweickert WD, Pohlman MC, Pohlman AS, et al.: Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial. Lancet, 2009, 373: 1874–1882. [Medline] [CrossRef]

14) Malkoç M, Karadibak D, Yildirim Y: The effect of physiotherapy on ventilatory dependency and the length of stay in an intensive care unit. Int J Rehabil Res, 2009, 32: 85–88. [Medline] [CrossRef]

15) Ntoumenopoulos G, Presneill JJ, McElholum M, et al.: Chest physiotherapy for the prevention of ventilator-associated pneumonia. Intensive Care Med, 2002, 28: 850–856. [Medline] [CrossRef]

16) Pattanshetty RB, Gaude GS: Effect of multimodality chest physiotherapy in prevention of ventilator-associated pneumonia: a randomized clinical trial. Indian J Crit Care Med, 2010, 14: 70–76. [Medline] [CrossRef]

17) Morris PE, Goad A, Thompson C, et al.: Early intensive care unit mobility therapy in the treatment of acute respiratory failure. Crit Care Med, 2008, 36: 2238–2243. [Medline] [CrossRef]

18) Ministry of Health, Labour and Welfare: Japanease Nasocomial Infections Surveillance (JANIS) http://www.nih-janis.jp/section/standard/standard_icu_ver1.3_20110622.pdf.

19) Japan Society of Respiratory Care Medicine: http://square.umin.ac.jp/jrcm/contents/guide/page03.html.

20) Kanda Y: Investigation of the freely available easy-to-use software 'EZR' for medical statistics. Bone Marrow Transplant, 2013, 48: 452–458. [Medline] [CrossRef]

21) Bailey P, Thomsen GE, Spuhler VJ, et al.: Early activity is feasible and safe in respiratory failure patients. Crit Care Med, 2007, 35: 139–145. [Medline] [CrossRef]

22) Schweickert WD, Kress JP: Implementing early mobilization interventions in mechanically ventilated patients in the ICU. Chest, 2011, 140: 1612–1617. [Medline] [CrossRef]

23) Needham DM: Mobilizing patients in the intensive care unit: improving neuromuscular weakness and physical function. JAMA, 2008, 300: 1685–1690. [Medline] [CrossRef]

24) Ogiwara S, Miyachi T: Effect of posture on ventilatory muscle strength. J Phys Ther Sci, 2002, 14: 1–5. [CrossRef]

25) Sekikawa K, Tabusadani M, Tabira K, et al.: Changes in skeletal muscle oxygenation during dynamic exercise in patients with respiratory failure. J Phys Ther Sci, 2003, 15: 19–23. [CrossRef]

26) Tomita K, Sakai Y, Monm M, et al.: Analysis of diaphragmatic motion with prone positioning using dynamic MRI. J Phys Ther Sci, 2004, 16: 85–89. [CrossRef]

27) Sugiura H, Ohta K, Minatani S, et al.: Relationship between respiratory muscle strength and exercise tolerance. J Phys Ther Sci, 2009, 21: 393–397. [CrossRef]

28) Clini E, Ambrosino N: Early physiotherapy in the respiratory intensive care unit. Respir Med, 2005, 99: 1096–1104. [Medline] [CrossRef]

29) Guérin C, Reignier J, Richard JC, et al. PROSEVA Study Group: Prone positioning in severe acute respiratory distress syndrome. N Engl J Med, 2013, 368: 2159–2168. [Medline] [CrossRef]

30) Abroug F, Ouanes-Besbes L, Dachraoui F, et al.: An updated study-level meta-analysis of randomised controlled trials on proning in ARDS and acute lung injury. Crit Care, 2011, 15: R6. [Medline] [CrossRef]

31) Sud S, Friedrich JO, Taccone P, et al.: Prone ventilation reduces mortality in patients with acute respiratory failure and severe hypoxemia: systematic review and meta-analysis. Intensive Care Med, 2010, 36: 585–599. [Medline] [CrossRef]

32) Tsubaki A, Deguchi S, Yoneda Y: Influence of posture on respiratory function and respiratory muscle strength in normal subjects. J Phys Ther Sci, 2009, 21: 71–74. [CrossRef]

33) Perme C, Chandrashekar R: Early mobility and walking program for patients in intensive care units: creating a standard of care. Am J Crit Care, 2009, 18: 212–221. [Medline] [CrossRef]

34) Chen S, Su CL, Wu YT, et al.: Physical training is beneficial to functional status and survival in patients with prolonged mechanical ventilation. J Formos Med Assoc, 2011, 110: 572–579. [Medline] [CrossRef]

35) Vosylius S, Sipylaite J, Ivaskevicius J: Determinants of outcome in elderly patients admitted to the intensive care unit. Age Ageing, 2005, 34: 157–162. [Medline] [CrossRef]

36) Fuchs L, Chronaki CE, Park S, et al.: ICU admission characteristics and mortality rates among elderly and very elderly patients. Intensive Care Med, 2012, 38: 1654–1661. [Medline] [CrossRef]

37) Yoon J, Park J, Lee D, et al.: Comparisons of respiratory function and activities of daily living between spinal cord injury and stroke patients and normal elderly people. J Phys Ther Sci, 2012, 24: 465–469. [CrossRef]