ORIGINAL ARTICLE

Association Between Early Rehabilitation for Mechanically Ventilated Intensive Care Unit Patients and Oral Ingestion

Shinichi Watanabe, PT, PhD [a] Yasunari Morita, MD [b] Shuichi Suzuki, MD [b] and Fujiko Someya, MD, PhD [c]

Objective: The present study examined the association between early rehabilitation for mechanically ventilated intensive care unit (ICU) patients and oral ingestion. **Method:** Among 1055 consecutive patients who were transported to the study facility via ambulance, newly admitted to the ICU, and treated with rehabilitation during hospitalization, 234 were included in the current study. The patients were allocated to early rehabilitation and control groups to retrospectively examine the proportion able to orally ingest three meals per day, the period needed to achieve such independence, and course-related factors. **Results:** A total of 77 matched pairs were selected using propensity score matching. Analysis using the Kaplan–Meier estimator revealed that the early rehabilitation group needed a markedly shorter period to achieve oral ingestion of three meals per day. There were significant differences between the groups in the periods from hospital admission to first physical therapy and to mobilization as well as differences in the frequency of delirium. **Conclusion:** Early rehabilitation for mechanically ventilated ICU patients may facilitate earlier mobilization. It may also shorten the period needed to achieve oral ingestion of three meals per day by preventing complications such as delirium.

Key words: early rehabilitation; ICU-acquired swallowing disorder; mechanically ventilated; oral ingestion

BACKGROUND

With advances in life-saving and perioperative management techniques for critically ill patients in the intensive care unit (ICU), the survival rate of such patients has markedly increased.[1] However, because the majority of ICU patients undergo mechanical ventilation and sedation, they are at increased risk of functional disorders and impaired mobility as a result of disuse syndrome,[2] and some require long-term rehabilitation.[3]

In recent years, many studies have indicated that early rehabilitation for mechanically ventilated patients can shorten the duration of hospitalization and improve their activities of daily living (ADL) score on discharge from the hospital.

In line with this finding, an increasing number of facilities are actively promoting rehabilitation for ICU patients from the early stage of intensive care.[4,5] Several studies have confirmed the safety of early rehabilitation for ICU patients,[6] whereas others have noted the effectiveness of early rehabilitation in reducing the incidence of delirium and shortening the duration of mechanical ventilation.[7] However, Morris et al.[8] compared standardized early rehabilitation for mechanically ventilated patients and standard care, and reported that standardized early rehabilitation was not more effective than standard care. Consequently, evidence for the effectiveness of such rehabilitation is currently insufficient.

Dysphagia after mechanical ventilation is called postextubation dysphagia,[9] or ICU-acquired swallowing disorder.[10]

The reasons for this condition include physical damage, such as that to the vocal folds caused by intubation or tracheostomy tubes; paralysis; muscle weakness caused by neuromuscular disorders; sensory disorders of the pharynx/larynx; disorientation of consciousness as a result of delirium; intake of sedative drugs; respiration associated with gastroesophageal reflux; and synchronic dysfunction of swallowing.[10] Studies on dysphagia after mechanical ventilation have reported that at least 20% of survivors after extubation had swallowing disorder[11] and in another study, dysphagia was confirmed in 84%.[12] Rehabilitation is extremely important because swallowing disorder can cause dehydration, malnutrition, aspiration pneumonia, suffocation, and loss of eating pleasure. However, little research on the effects of early rehabilitation in the ICU on the prognosis of dysphagia has been performed.

The present study examined the association between early rehabilitation for mechanically ventilated ICU patients and oral ingestion, including the period required to achieve consistent oral ingestion, using adjusted confounding factors.

MATERIALS AND METHODS

Design and Study Participants

This retrospective observational study was conducted between April 1, 2013, and May 31, 2016. Among 1055 consecutive patients who were transported to the study facility via ambulance, newly admitted to the ICU, and treated with rehabilitation during hospitalization, 821 were excluded according to the following criteria: duration of mechanical ventilation shorter than 48 h, motor Glasgow coma scale (GCS) score lower than 5, oral intake inability prior to hospitalization, history of dementia/psychiatric disorders, death in the ICU, hip fracture, unstable spine or pathological fracture, and presence of neuromuscular diseases. After these exclusions, data from 234 patients were analyzed (**Fig. 1**).

The included patients were allocated to one of the following two groups based on when rehabilitation was initiated: the early rehabilitation group (rehabilitation initiated during mechanical ventilation in the ICU) and the control group (rehabilitation initiated after discharge from the ICU). The study was conducted in a medium-sized community hospital with 740 beds, in which two anesthesiologists and other doctors are exclusively allocated to a semi-closed-type ICU with 8 beds to provide intensive care with attending doctors. The period of rehabilitation was determined by each attending doctor.

Data Collection
Sample Characteristics

The following baseline data were collected: patient age, sex, height, weight, acute physiology and chronic health evaluation (APACHE II) score,[13] Charlson comorbidity index (CCI),[14] presence of sepsis, albumin level, admission category (abdominal/pelvic surgery, cardiovascular, gastrointestinal/hepatic, neurosurgery/neurologic, respiratory, and others), and pre-hospital Barthel index (BI) score.[15]

Primary Outcomes

The proportion of patients able to orally ingest three meals per day and the period needed to achieve such oral ingestion were examined as the primary outcomes. The study was continued until hospital discharge. Patients with a food intake scale score ≥ 7[16] (easy-to-swallow food is orally ingested in three meals per day) were considered to have achieved oral ingestion, and such independence during hospitalization was assessed by speech therapists.

Oral ingestion was assessed when the following starting criteria were met: (1) *RASS* consciousness level 0 to −1, (2) respiratory condition was good, (3) there was no oral contamination and the mouth was moderately moistened, (4) the patient's overall condition was good with no fever, (5) vital signs were stable with no progression of disease. When the criteria were met, direct training was conducted by a speech therapist to determine whether oral ingestion was possible.

Secondary Outcomes

The periods from hospital admission to the initiation of physical therapy and to mobilization (days); the durations of mechanical ventilation, ICU stay, and hospitalization (days); hospitalization cost; and the incidence of complications during hospitalization (deep vein thrombosis, ICU-acquired delirium (ICU-AD), hospital-acquired pneumonia, bedsores, and falls) were examined as secondary outcomes.

Pneumonia was diagnosed on the basis of infiltrative shadows newly observed within 48 h after hospital admission; fever involving a temperature of 38° or higher without clear sources other than respiratory organs; clinical pulmonary symptoms, such as coughing and phlegm; abnormal C-reactive protein levels; and/or abnormal peripheral blood leukocyte counts.

ICU-AD was assessed using the following two delirium screening scales: confusion assessment method for the intensive care unit (CAM-ICU)[17] and the intensive care delirium screening checklist (ICDSC).[18]
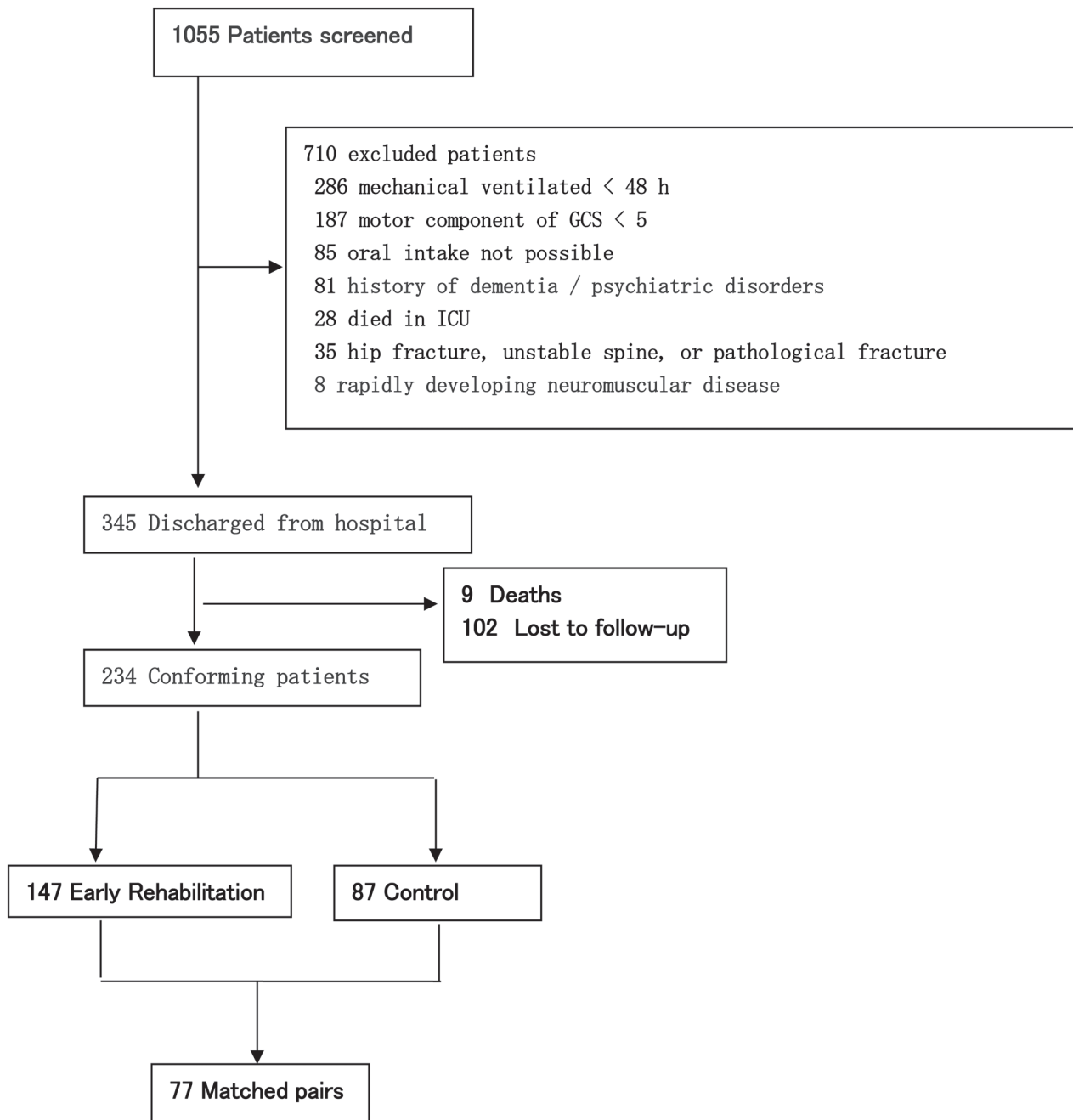
Fig. 1. Flow chart of the patient selection process.

Early Rehabilitation Protocol

Rehabilitation for ICU patients was performed through collaboration with ICU physical therapists, intensive care specialists, and nurses, according to a protocol developed by Morris.[6] Rehabilitation intervention was performed in the following five steps: step 1, perform passive range of motion (ROM) exercise; step 2, maintain the head of the bed at $\geq 60°$ and perform active ROM exercise; step 3, able to sit at the side of the bed, able to sit at the side of bed at bed rest; step 4, stand at the side of the bed and stand and pivot with a chair; step 5 walk with assistance and walk independently. The feasibility of mobilization was confirmed once daily or more frequently. **Table 1** shows the mean number of early rehabilitation sessions during the ICU stay and those at each exercise intensity level (**Table 1**). The activities described in **Table 1** were all carried out with the patient wearing a ventilator.

With regard to swallowing training, both groups under-

Table 1. Intervention frequency and intervention time in the early rehabilitation group

Baseline characteristics	Early rehabilitation (n=147)
Frequency of rehabilitation per person (day)	4.8 ± 0.7
Daily duration of rehabilitation per person (min)	36.6 ± 16.2
Total frequency of rehabilitation	846
Program, n/total (%)	
Step 1	260 (30.7)
Step 2	315 (37.2)
Step 3	142 (16.8)
Step 4	81 (9.6)
Step 5	48 (5.7)
Adverse events	0

The frequency and duration of rehabilitation are given as means ± standard deviations.

went speech therapist intervention after extubation and started swallowing training (direct training or indirect training) from the same day. After discharge from the ICU, training to appropriately execute basic movements, such as walking, was performed only on weekdays, and no specific protocol was followed. The sedation dosage was adjusted in the morning by ICU physicians to target a RASS of −1 or 0 before patients performed rehabilitation.

Statistical Analysis

Background and course-related factors were compared between the early rehabilitation and control groups. Continuous and ordinal variables were compared using the Mann–Whitney U test, whereas nominal variables were compared using the chi-square test. Logistic regression analysis was performed with background factors (APACHE II score, CCI) as independent variables, and the obtained predicted probabilities were used as propensity scores. The value for matching was 0.25 times the standard deviation of the overall propensity score. Lastly, factors influencing oral ingestion were examined by analyzing the period needed to achieve oral ingestion of three meals using the Kaplan–Meier estimator. The log-rank test was also used for comparisons between the groups. All analyses were performed using SPSS Statistics 23.0 (IBM Corp., Armonk, NY, USA), and the significance level was set at <5%.

Ethics and Consent

The study was conducted after receiving approval from the institutional review board (IRB) at Nagoya Medical Center Hospital (IRB approval number 96). We followed a de-identification standard to protect the confidentiality of personal information. The study qualified for exempt status according to the IRB because data were collected from existing patient records. Therefore, the need for patient consent was waived.

RESULTS

Before propensity score matching, significant differences in the APACHE II score (P=0.005) and CCI (P=0.019) were observed between the early rehabilitation and control groups. On propensity score matching with these items entered, 77 pairs were selected, and the background factors adjusted showed markedly similar values (propensity scores: early rehabilitation, 0.378 ± 0.119; control, 0.388 ± 0.120). On comparing background factors after matching, we found no significant differences between the groups for any item (**Table 2**). Analysis of the primary outcomes after matching indicated that there was no significant difference between the groups in the proportion of patients able to orally ingest three meals at hospital discharge. However, the period needed to achieve such oral ingestion was significantly different between the two groups when compared using the log-rank test (P=0.001) (**Fig. 2**).

With respect to the secondary outcomes, both the periods from hospital admission to the initiation of physical therapy and to mobilization were markedly shorter in the early rehabilitation group than in the control group. The incidence of complications during hospitalization was also significantly lower in the early rehabilitation group than in the control group; however, hospitalization costs did not markedly differ between the groups (**Table 3**).

Number at risk
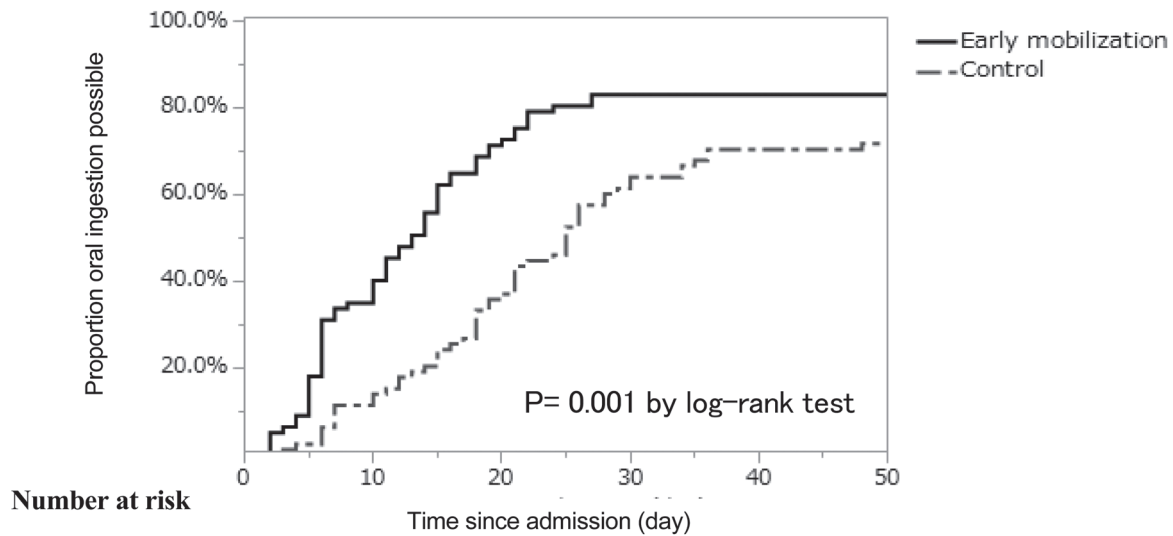
Early Rehabilitation	78	50	35	22	16	13
Control	78	69	50	30	25	22

Fig. 2. Proportion of patients in whom oral ingestion of three meals per day was possible in the early rehabilitation group and the control group. There was a significant difference between the groups (P <0.05, log-rank test).

Table 2. Comparison of patient baseline characteristics between early rehabilitation and control groups for the whole population and for the matched population

	Total population			Matched population		
	Early rehabilitation	Control	P-value	Early rehabilitation	Control	P-value
Baseline characteristics	n=147	n=87		n=77	n=77	
Age, years, median (IQR)	66 (54–73)	64 (50–78)	0.847	66 (55–73)	66 (52–78)	0.991
APACHE II score, median (IQR)	24 (19–32)	28 (24–34)	0.005	27 (24–32)	28 (23–32)	0.514
Male sex, n (%)	84 (57.1)	52 (59.7)	0.747	40 (51.9)	34 (44.2)	0.346
Weight, kg, median (IQR)	54 (46–65)	55 (48–68)	0.384	53 (47–65)	54 (47–67)	0.431
CCI, score, median (IQR)	2 (1–4)	4 (1–5)	0.019	3 (1–4)	3 (1–4)	0.521
Sepsis, n (%)	73 (49.7)	52 (59.7)	0.189	44 (57.1)	45 (58.4)	0.887
Albumin (g/dl)	3.4 (2.5–4.2)	3.5 (2.6–4.2)	0.742	3.3 (2.4–4.1)	3.4 (2.5–4.1)	0.786
Admission category						
Abdominal/pelvic surgery, n (%)	26 (17.7)	15 (17.2)	0.230	13 (16.9)	11 (14.3)	0.869
Cardiovascular, n (%)	24 (16.3)	22 (25.3)		14 (18.2)	20 (26.0)	
Gastrointestinal/hepatic, n (%)	12 (8.2)	6 (6.9)		19 (24.7)	17 (22.1)	
Neurosurgery/neurologic, n (%)	35 (23.8)	12 (13.8)		6 (7.8)	6 (7.8)	
Respiratory, n (%)	40 (27.2)	22 (25.3)		15 (19.5)	16 (20.8)	
Others, n (%)	10 (6.8)	10 (11.5)		10 (13.0)	7 (9.1)	
Prehospital BI, score, median (IQR)	100 (95–100)	99 (90–100)	0.410	100 (95–100)	95 (95–100)	0.639

IQR, interquartile range.

Table 3. Comparison of clinical parameters between early rehabilitation and control groups for the whole population and for the matched population

	Total population			Matched population		
	Early rehabilitation	Control	P-value	Early rehabilitation	Control	P-value
Baseline characteristics	n=147	n=87		n=77	n=77	
Primary outcome						
Oral ingestion of three meals, n (%)	116 (78.9)	67 (77.0)	0.396	64 (83.1)	55 (71.4)	0.241
Secondary outcomes						
Time to first physical therapy assessment, day, median (IQR)	2 (1–3)	8 (7–12)	<0.001	2 (2–3)	8 (7–12)	<0.001
Time to first mobilization, day, median (IQR)	5 (4–7)	9 (7–14)	<0.001	6 (4–8)	9 (7–14)	<0.001
Duration of mechanical ventilation, day, median (IQR)	4 (2–8)	4 (2–10)	0.221	5 (3–10)	4 (3–10)	0.684
ICU length of stay, day, median (IQR)	7 (6–12)	7 (5–12)	0.286	8 (5–12)	7 (4–13)	0.231
Hospital length of stay, day, median (IQR)	37 (26–53)	44 (28–61)	0.044	41 (28–58)	43 (28–61)	0.661
Total billed costs per patient, yen, median (IQR)	3192240 (249321–4585860)	3463690 (254479–5144580)	0.188	3399180 (2727360–4899520)	3447850 (2521040–5050243)	0.684
Complications						
DVT, n (%)	3 (2.0)	4 (4.6)	0.243	2 (1.3)	4 (5.2)	0.462
Delirium, n (%)	46 (31.3)	48 (55.2)	<0.001	23 (29.9)	40 (51.9)	0.008
Pneumonia, n (%)	46 (31.3)	46 (52.9)	0.002	30 (39.0)	40 (51.9)	0.248
Bedsore, n (%)	4 (2.7)	6 (6.9)	0.201	4 (5.2)	6 (7.8)	0.759
Fall, n (%)	10 (6.8)	6 (6.9)	0.912	4 (5.2)	6 (7.8)	0.759

IQR, Interquartile range; DVT, Deep vein thrombosis

DISCUSSION

In this study, the time needed to achieve oral ingestion of three meals per day was significantly shorter among early rehabilitation patients than among control patients. ICU-acquired swallowing disorder can be considered as dysphagia caused by muscle mass reduction and weakness of the muscles associated with the whole body and those associated with swallowing.[19,20] Mechanically ventilated patients may exhibit dysphagia after extubation because of ICU-acquired muscle weakness, impaired tongue strength or perception, pharyngeal disorders, or cognitive complications such as delirium.

To assess the relationship between early rehabilitation and dysphagia in mechanically ventilated critically ill patients, a propensity score-matched analysis was performed, and the ability of patients to orally ingest three meals per day was assessed. Although some patients could ingest three meals per day immediately after extubation, for others, swallowing was impaired after mechanical ventilation, making it difficult to ingest food orally. Early rehabilitation and early ingestion are particularly important for the response to dysphagia after extubation. In elderly patients with aspiration pneumonia, mortality is significantly lower when physical therapy is started within 3 days after admission.[21]

In a study by Moss et al.,[22] intensive rehabilitation, including mobilization, was initiated on day 8 after ICU admission. However, this rehabilitation approach was found not to be more effective than standard care for shortening the duration of hospitalization or improving physical function. Similarly, Walsh et al.[23] performed intensive rehabilitation in patients after discharge from the ICU. They reported that the approach did not improve the functional prognosis of patients, although patient satisfaction levels increased. In both studies, mobilization was initiated late. Moreover, in the study by Walsh et al., the frequency of intervention was limited to twice weekly. These factors may explain the poor outcomes of intensive rehabilitation in these studies. In the present study, intervention in the early rehabilitation group was generally initiated within 2 days after hospital admission, and it was performed every day through collaboration among intensive care specialists, ICU physical therapists, speech therapists, and nurses. This early introduction of rehabilitation possibly contributed to the reduction of the period needed to achieve satisfactory oral ingestion.

Delirium has recently been reported to negatively affect not only short-term prognosis but also long-term prognosis and cognitive function. Additionally, there is a consensus that ICU-AD influences functional prognosis. In the present study, delirium developed markedly less frequently in the early rehabilitation group. Delirium is defined as a reversible cognitive disorder involving disorientation, short-term memory impairment, lack of attention, and/or abnormal patterns of thinking. Schweickert et al.[7] reported that the early initiation of exercise therapy for ICU patients improved their ADL scores and walking distances on discharge from the hospital and reduced the prevalence of ICU-AD. Based on this finding, early rehabilitation employing multi-professional collaboration for ICU patients with tracheal intubation may facilitate changes making earlier mobilization feasible. Furthermore, the prevention of complications associated with delirium may shorten the period needed to achieve oral ingestion.

Early rehabilitation for ICU patients may increase hospitalization cost because of a rise in rehabilitation fees for each disease category. However, on comparing such costs between the early rehabilitation and control groups, we did not identify any significant differences. In previous studies, early rehabilitation increased personnel expenses, but hospitalization cost remained unchanged because of shortened durations of ICU stay and hospitalization.[6] In the present study, although the durations of hospitalization and ICU stay were similar between the two study groups, the overall hospitalization costs were similar. This was possibly because the increased medical fees incurred as a result of early rehabilitation were offset by the prevention of complications, such as delirium, and a reduction in related treatment costs.

The present study has some limitations. The study was conducted in a single facility within a limited period. Because the subjects were not randomly allocated to the two groups, it may be difficult to generalize the results regarding early rehabilitation to all mechanically ventilated ICU patients. Additionally, the study assessed the period needed to achieve oral ingestion without measuring the swallowing function. Thus, it did not fully examine the effects of early rehabilitation. In the future, prospective studies with a higher number of subjects should be conducted.

CONCLUSION

Early rehabilitation for mechanically ventilated ICU patients may facilitate earlier mobilization. Additionally, it may shorten the period required to achieve oral ingestion by preventing complications such as delirium.

CONFLICTS OF INTEREST

The authors declare that there are no conflicts of interest.

REFERENCES

1. Pandharipande PP, Girard TD, Jackson JC, Morandi A, Thompson JL, Pun BT, Brummel NE, Hughes CG, Vasilevskis EE, Shintani AK, Moons KG, Geevarghese SK, Canonico A, Hopkins RO, Bernard GR, Dittus RS, Ely EW, BRAIN-ICU Study Investigators: Long-term cognitive impairment after critical illness. N Engl J Med 2013;369:1306–1316. PMID:24088092, DOI:10.1056/NEJMoa1301372

2. Brahmbhatt N, Murugan R, Milbrandt EB: Early mobilization improves functional outcomes in critically ill patients. Crit Care 2010;14:321–323. PMID:20880413, DOI:10.1186/cc9262

3. Dowdy DW, Eid MP, Dennison CR, Mendez-Tellez PA, Herridge MS, Guallar E, Pronovost PJ, Needham DM: Quality of life after acute respiratory distress syndrome: a meta-analysis. Intensive Care Med 2006;32:1115–1124. PMID:16783553, DOI:10.1007/s00134-006-0217-3

4. Bailey P, Thomsen GE, Spuhler VJ, Blair R, Jewkes J, Bezdjian L, Veale K, Rodriquez L, Hopkins RO: Early activity is feasible and safe in respiratory failure patients. Crit Care Med 2007;35:139–145. PMID:17133183, DOI:10.1097/01.CCM.0000251130.69568.87

5. Burtin C, Clerckx B, Robbeets C, Ferdinande P, Langer D, Troosters T, Hermans G, Decramer M, Gosselink R: Early exercise in critically ill patients enhances short-term functional recovery. Crit Care Med 2009;37:2499–2505. PMID:19623052, DOI:10.1097/CCM.0b013e3181a38937

6. Morris PE, Goad A, Thompson C, Taylor K, Harry B, Passmore L, Ross A, Anderson L, Baker S, Sanchez M, Penley L, Howard A, Dixon L, Leach S, Small R, Hite RD, Haponik E: Early intensive care unit mobility therapy in the treatment of acute respiratory failure. Crit Care Med 2008;36:2238–2243. PMID:18596631, DOI:10.1097/CCM.0b013e318180b90e

7. Schweickert WD, Pohlman MC, Pohlman AS, Nigos C, Pawlik AJ, Esbrook CL, Spears L, Miller M, Franczyk M, Deprizio D, Schmidt GA, Bowman A, Barr R, McCallister KE, Hall JB, Kress JP: Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial. Lancet 2009;373:1874–1882. PMID:19446324, DOI:10.1016/S0140-6736(09)60658-9

8. Morris PE, Berry MJ, Files DC, Thompson JC, Hauser J, Flores L, Dhar S, Chmelo E, Lovato J, Case LD, Bakhru RN, Sarwal A, Parry SM, Campbell P, Mote A, Winkelman C, Hite RD, Nicklas B, Chatterjee A, Young MP: Standardized rehabilitation and hospital length of stay among patients with acute respiratory failure: a randomized clinical trial. JAMA 2016;315:2694–2702. PMID:27367766, DOI:10.1001/jama.2016.7201

9. Rassameehiran S, Klomjit S, Mankongpaisarnrung C, Rakvit A: Postextubation dysphagia. Bayl Univ Med Cent Proc 2015;28:18–20. PMID:25552788, DOI:10.1080/08998280.2015.11929174

10. Macht M, Wimbish T, Bodine C, Moss M: ICU-acquired swallowing disorders. Crit Care Med 2013;41:2396–2405. PMID:23939361, DOI:10.1097/CCM.0b013e31829caf33

11. Macht M, White SD, Moss M: Swallowing dysfunction after critical illness. Chest 2014;146:1681–1689. PMID:25451355, DOI:10.1378/chest.14-1133

12. Macht M, Wimbish T, Clark BJ, Benson AB, Burnham EL, Williams A, Moss M: Postextubation dysphagia is persistent and associated with poor outcomes in survivors of critical illness. Crit Care 2011;15:231–239. PMID:21958475, DOI:10.1186/cc10472

13. Knaus WA, Draper EA, Wagner DP, Zimmerman JE: APACHEII: a severity of disease classification system. Crit Care Med 1985;13:818–829.

14. Charlson ME, Pompei P, Ales KL, MacKenzie CR: A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. J Chronic Dis 1987;40:373–383. PMID:3558716, DOI:10.1016/0021-9681(87)90171-8

15. Katz PP: Measures of adult general functional status: The Barthel Index, Katz Index of Activities of Daily Living, Health Assessment Questionnaire (HAQ), MACTAR Patient Preference Disability Questionnaire, and Modified Health Assessment Questionnaire (MHAQ). Arthritis Care Res 2003;49:l5–l27.

16. Kunieda K, Ohno T, Fujishima I, Hojo K, Morita T: Reliability and validity of a tool to measure the severity of dysphagia: the Food Intake LEVEL Scale. J Pain Symptom Manage 2013;46:201–206. PMID:23159683, DOI:10.1016/j.jpainsymman.2012.07.020

17. Ely EW, Margolin R, Francis J, May L, Truman B, Dittus R, Speroff T, Gautam S, Bernard GR, Inouye SK: Evaluation of delirium in critically ill

patients: validation of the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU). Crit Care Med 2001;29:1370–1379. PMID:11445689, DOI:10.1097/00003246-200107000-00012

18. Bergeron N, Dubois MJ, Dumont M, Dial S, Skrobik Y: Intensive Care Delirium Screening Checklist: evaluation of a new screening tool. Intensive Care Med 2001;27:859–864. PMID:11430542, DOI:10.1007/s001340100909

19. Wakabayashi H: Presbyphagia and sarcopenic dysphagia: association between aging, sarcopenia, and deglutition disorders. J Frailty Aging 2014;3:97–103. PMID:27049901

20. Wakabayashi H, Sakuma K: Rehabilitation nutrition for sarcopenia with disability: a combination of both rehabilitation and nutrition care management. J Cachexia Sarcopenia Muscle 2014;5:269–277. PMID:25223471, DOI:10.1007/s13539-014-0162-x

21. Momosaki R, Yasunaga H, Matsui H, Horiguchi H, Fushimi K, Abo M: Effect of early rehabilitation by physical therapists on in-hospital mortality after aspiration pneumonia in the elderly. Arch Phys Med Rehabil 2015;96:205–209. PMID:25301440, DOI:10.1016/j.apmr.2014.09.014

22. Moss M, Nordon-Craft A, Malone D, Van Pelt D, Frankel SK, Warner ML, Kriekels W, McNulty M, Fairclough DL, Schenkman M: A randomized trial of an intensive physical therapy program for patients with acute respiratory failure. Am J Respir Crit Care Med 2016;193:1101–1110. PMID:26651376, DOI:10.1164/rccm.201505-1039OC

23. Walsh TS, Salisbury LG , Merriweather JL, Boyd JA, Griffith DM, Huby G, Kean S, Mackenzie SJ, Krishan A, Lewis SC, Murray GD, Forbes JF, Smith J, Rattray JE, Hull AM, Ramsay P, RECOVER Investigators: Increased hospital-based physical rehabilitation and information provision after intensive care unit discharge: The RECOVER Randomized Clinical Trial. JAMA Intern Med 2015;175:901–910. PMID:25867659, DOI:10.1001/jamainternmed.2015.0822