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Research Article

Association between Early Rehabilitation for Mechanically Ventilated ICU Patients and their Walking Independence: A Propensity Score-matched Analysis

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Abstract

Background: To examine the association between early rehabilitation for mechanically ventilated Intensive Care Unit (ICU) patients and their walking independence.

Methods: Among the 1,024 consecutive patientswho had been transported to the study facility using ambulance services, newly admitted to the ICU, and treated with rehabilitation during hospitalization, 236 were included, excluding those meeting the exclusion criteria. The patients were divided into early rehabilitation and control groups to retrospectively examine the rate of walking independence, period needed to achieve such independence, and course-related factors.

Results: On propensity score matching, 78 pairs were selected. Analysis using the Kaplan-Meier estimator revealed thatthe early rehabilitation group needed a markedly shorter period to achieve walking independence. As for course-related factors, there were significant differences between the groups in the periods from hospital admission to the initiation of physical therapy andmobilization, as well as the frequency of delirium.

Conclusion: Early rehabilitation for mechanically ventilated ICU patients may facilitate earlier mobilization. It may alsoshorten the period they need to achieve walking independence by preventing complications, such as delirium.

Abbreviations: ICU: Intensive Care Unit; ICU-AD: ICU-Acquired Delirium; APACHE II: Second version of the Acute Physiology and Chronic Health Evaluation; GCS: Glasgow Coma Scale; CCI: Charlson Comorbidity Index; BI: Barthel Index; CAM-ICU: Confusion Assessment Method for the Intensive Care Unit; ROM: Range of Motion; IRB: Institutional Review Board.

Keywords: Delirium; Early Rehabilitation; Mechanically ventilated; Walking independence.

Background

With the progress of 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, as the majority of ICU patients are generally under management using mechanical ventilation and sedation, they have increased risks of functional disorders and impaired mobility due to disuse syndrome [2], requiring long-term rehabilitation in some cases [3].

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In recent years, a large number of reports have indicated thatearly rehabilitation for mechanically ventilated patients shortensthe duration of hospitalization and improves their ADL on discharge from the hospital. In line with this, an increasing number of facilities are actively performingrehabilitation for ICU patients from the early stage of intensive care [4,5]. Some previous studies confirmed the safety of early rehabilitation for ICU patients [6], while others noted its effectiveness to reduce the incidence of deliriumand shorten the duration of mechanical ventilation [7]. On the other hand, Morris et al. [8] compared standardizedearly rehabilitation for mechanically ventilated patients and standard care, and reported that the former was not shown to be more effective [8]. Thus, evidence for the effectiveness of such rehabilitation is not necessarily sufficient.

When focusing on ICU patients' functional prognosis after discharge from the ICU, walking independence is regarded as the primary determinant of their discharge destination. Therefore, physical therapy programs frequentlyaim at the achievement of such independence. Some systematic reviews [9,10]confirmed that walking training for mechanically ventilated patients isfeasible and safe, but its effectiveness has yet to be confirmed. According to Kayambu et al. [11]the early initiation of exercise therapy, including walking, for mechanically ventilated patients may improve their walking abilities, but its long-term functional outcomes are unclear [11].

Under these circumstances, the present study examined the association between early rehabilitation for mechanically ventilated ICU patients and their walking independence, including the period they need to achieve it, using adjusted confounding factors.

Methods

Study design and subjects

This retrospective observational study was conducted between April 1, 2013 and December 31, 2016. From 1,024 consecutive patients who had been transported to the study facility using ambulance services, newly admitted to the ICU, and treated with rehabilitation during hospitalization, 788 were excluded based on the following criteria:a duration of mechanical ventilation shorter than 48 hours; anda motor-Glasgow coma scale (GCS) lower than 5; unable to walk prior to hospitalization, died in ICU, hip fracture, unstable spine, or pathological fracture, elevated intracranial pressure, unrecoverable disease predicted to have a 6-month mortality rate of over 50%, cardiopulmonary arrest rapidly developing neuromuscular disease. Thus, 236 were analyzed (Figure 1). The included patients were divided into 2 groups based on the period when rehabilitation was initiated: early rehabilitation: during mechanical ventilation in the ICU; and control: after discharge from the ICU. The study was conducted in a medium-scale community hospital with 740 beds, in which 2 anesthesiologists and other doctors are exclusively allocated to a semi-closed-type ICU consisting of 8 beds to provide intensive care with attending doctors, and the period of rehabilitation is determined by each attending doctor, without clear standards.

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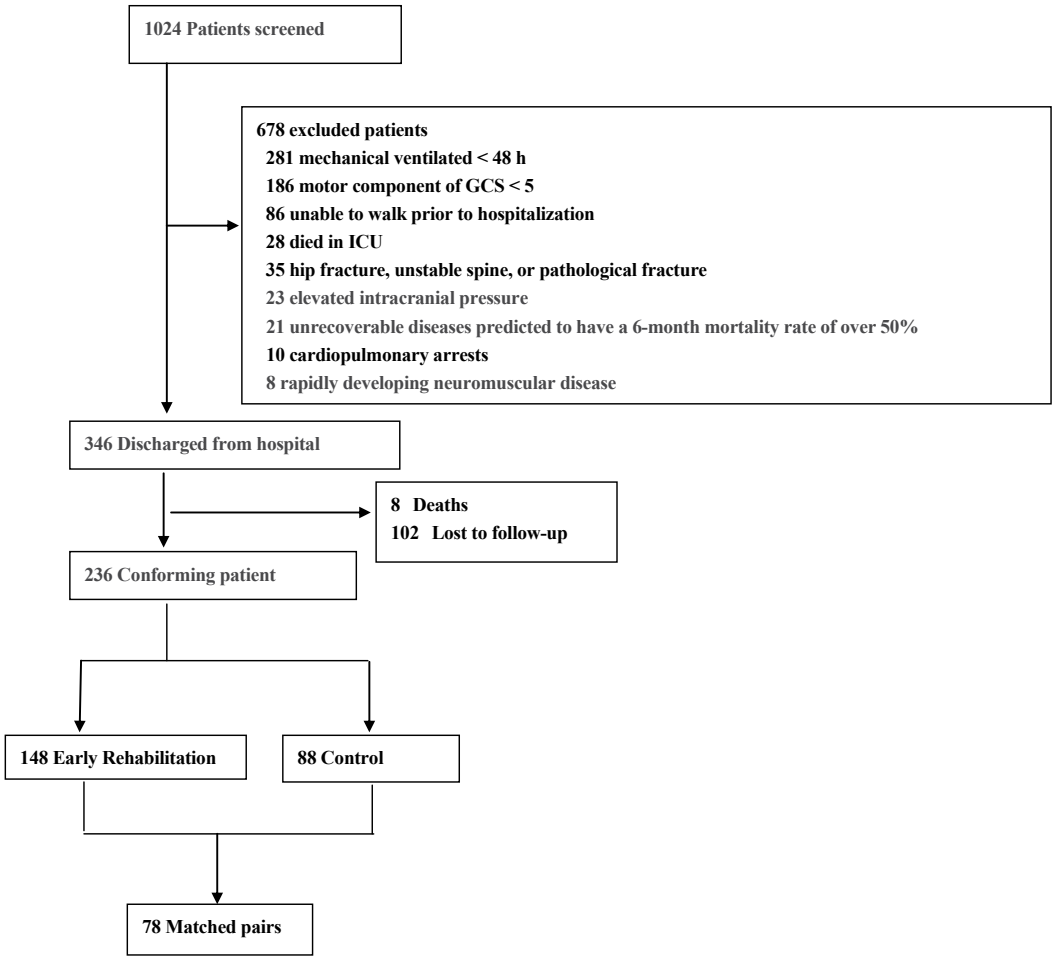


Figure 1: Flow chart of patient selection process.

Study and measurement items

1) Basic information: As baseline data, the age, sex, height, weight, acute physiology and chronic health evaluation (APACHE II) score [12], charlson comorbidity index (CCI)[13], rate of sepsis, admission category (Abdominal/pelvic surgery, cardiovascular, Gastrointestinal/hepatic, Neurosurgery/Neurologic, Respiratory, Others), and pre-hospital barthel index (BI) score[14]were examined.

2) Primary outcomes: The rate of walking independence and the period needed to achieve such independence were examined as the primary outcomes. The study was continued for 90 days. Patients with a walking-related BI score of 15 (being able to walk 45 m or further using or not using an orthosis) were regarded as independent in walking, and such independence during hospitalization was assessed by physical therapists and nurses.After discharge from the hospital, the same rater assessed such independence through telephone interviews with the patients themselves or their families.

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

Pneumonia was diagnosed based on infiltrative shadows newly observed within 48 hours after hospital admission, a fever of 38 degrees or higher without clear sources other than the respiratory organs, clinical pulmonary symptoms such as coughing and phlegm, abnormal C-reactive protein C test values, and/or abnormal peripheral blood leukocyte counts.

ICU-acquired delirium was assessed using 2 delirium screening scales: confusion assessment method for the intensive care unit (CAM-ICU) [15].

Early Rehabilitation Protocol

Rehabilitation for the ICU patients was performed through collaboration with ICU physical therapists, intensive care specialists, and nurses based on a protocol developed by Morris [6]. The rehabilitation intervene was performed for the following 5 steps; Step 1) passive range of motion (ROM), Step 2) head of bed ≥ 60 degrees, active ROM, Step 3) Side of bed, side of bed at bed rest, Step 4) Stand at side of bed, stand and pivot to chair, Step 5) Walk with assistance, walk independently. The feasibility of mobilization was confirmed once daily or more frequently. Table 1 shows the mean numbers of early rehabilitation sessions during the ICU stay and those at each exercise intensity level (Table 1).

As for rehabilitation after discharge from the ICU, training to appropriately execute basic movements, such as walking, was only performed on weekdays, without a specific protocol.

Statistical Processing

Background and course-related factors were compared between the early rehabilitation and control groups. For each item, continuous and ordinal variables were compared using the Mann-Whitney U test, while nominal variables were compared using the chi-square test.

Logistic regression analysis was performed with background factors as independent variables, andthe obtained predicted probabilities were used as propensity scores. The value for matching was 0.25 times higher than the standard deviation of the overall propensity score. Lastly, factors influencing walking independence were examined by analyzing the period needed to achieve walking independence using the Kaplan-Meier estimator. The log-rank test was also used for comparison between the groups. For statistical processing, SPSS Statistics 23.0 was used (IBM Corp., Armonk, NY, USA), with the significance level set at <5%.

Results

Before matching, significant differences in the APACHE II score (p=0.034) and CCI (p=0.020) were observed between the early rehabilitation and control groups. On propensity score matching with these items entered, 78 pairs were selected, and the background factors adjusted showed markedly similar values (Propensity score: Early Rehabilitation 0.396 ± 0.122, Control 0.395 ± 0.122). On comparing background factors after matching, there were no significant differences between the groups in any item (Table 2).On comparing the primary outcomes after matching, there were no significant differences between the groups in the rate of walking independence at 90 days after hospital admission. In contrast, the period needed to achieve such independence significantly varied between the groups when comparing them using the log-rank test (p=0.001) (Figure 2).

On comparing the secondary outcomes, both the periods from hospital admission to the initiation of physical therapy and mobilization were markedly shorter inthe early rehabilitation compared with control group. The incidence of complications during hospitalization was also significantly lower in the former, while hospitalization costs did not markedly vary between them (Table 3).

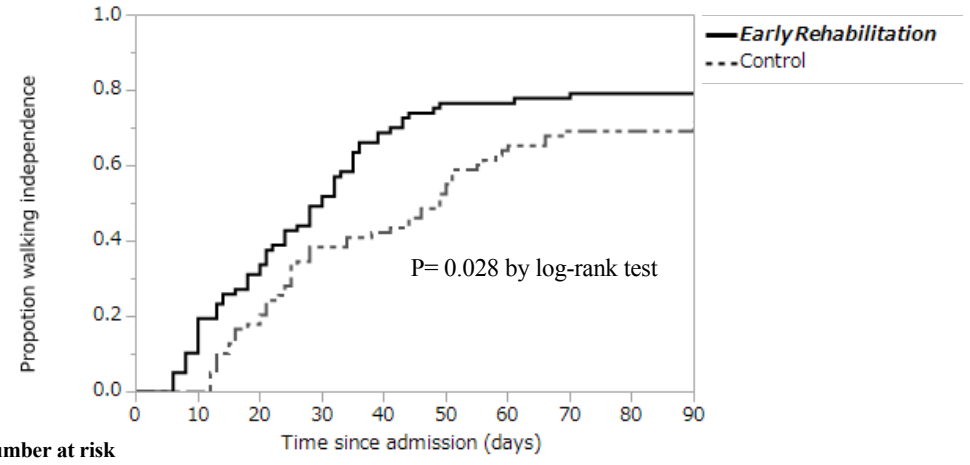
Discussion

In the present study, patients were divided into 2 groupsbased on the period when rehabilitation was initiated: early rehabilitation: during mechanical ventilation in the ICU; and control: after discharge from the ICU.The period needed to achieve walking independencewas significantly shorter in the former. In a study by Moss et al., in which intensive rehabilitation including mobilization was initiated on Day 8 after ICU admission, such an approach was not shown to be more effective than standard care to shorten the duration of hospitalization or improve physical functions[16]. Similarly, Walsh et al. performed intensive rehabilitation after dischargefrom the ICU, and reported that the approach did not improve patients' functional prognosis, although their levels of satisfaction increased [17]. In both cases, mobilization was initiated late. In addition, in the study by Walsh et al. [17], the

Baseline characteristics	Early mobilization (n=148)
Frequency per person of rehabilitation* (day)	4.8 ± 0.8
Daily amount per person of rehabilitation* (min)	36.8 ± 16.5
Total frequency of rehabilitation (time)	848
Program, n/Total (%)	
Step1	262(30.9)
Step2	315(37.1)
Step3	142(16.7)
Step4	81(9.6)
Step5	48(5.7)
Adverse event	0

*Plus–minus values are means ±standard Deviation.

Table 1: Intervention frequency and intervention time in early rehabilitation at ICU admission.



Number at risk

Early Rehabilitation	78	51	28	24
Control	78	39	18	16

Figure 2: 90-day walking independence with early rehabilitation group vs Control group analysis using the log-rank test revealed significant differences between the early rehabilitation and control groups.

	Total Population			Matched Population		
	Early mobilization	Control	P Value	Early mobilization	Control	P Value
Baseline characteristics	N= 148	N = 88		N = 78	N = 78	
Age, yr, median (IQR)	67(54-73)	64(50-78)	0.825	67(58-73)	66(52-78)	0.966
APACHE II score, median (IQR)	25(20-32)	28(24-33)	0.034	27(24-32)	28(22-32)	0.599
Male sex, n (%)	84(56.8)	52(59.1)	0.726	41(52.6)	34(43.6)	0.262
Weight, kg, median (IQR)	53(47-65)	55(48-68)	0.234	52(46-65)	54(47-67)	0.301
CCI, point, median (IQR)	2(1-4)	4(1-5)	0.020	3(1-4)	3(1-4)	0.539
Sepsis, n (%)	73(49.3)	52(59.1)	0.145	44(56.4)	45(57.7)	0.872
Admission category						
Abdominal/pelvic surgery, n (%)	26(15.6)	16(18.2)	0.223	14(18.0)	12(15.4)	0.863
Cardiovascular, n (%)	24(16.2)	22(25.0)		14(18.0)	20(25.6)	
Gastrointestinal/hepatic, n (%)	12(8.1)	6(6.8)		19(24.3)	17(21.8)	
Neurosurgery/Neurologic, n (%)	35(24.3)	12(13.6)		6(7.7)	6(7.7)	
Respiratory, n (%)	40(27.0)	22(25.0)		15(19.2)	16(20.5)	
Other, n (%)	10(6.8)	10(11.4)		10(12.8)	7(9.0)	
Pre-hospital BI, point, median, (IQR)	100(95-100)	98(90-100)	0.206	100(95-100)	98(90-100)	0.366

Median (25th–75th percentile) or the number of patients.
Independent-samples Mann–Whitney U-test or X2 test.
APACHE II = Acute Physiology and Chronic Health Evaluation; IQR = Interquartile range; CCI = Charlson comorbidity index; BI = Barthel index.

Table 2: Comparison of the items related to the baseline data.

	Total Population			Matched Population		
	Early mobilization	Control	P Value	Early mobilization	Control	P Value
Baseline characteristics	148	88		78	78	
Primary outcome						
90-day walking independence, n (%)	128(86.5)	70(79.6)	0.165	61(78.2)	57(73.1)	0.455
Secondary outcome						
The periods from hospital admission to first physical therapy, day median(IQR)	2(1-3)	8(7-12)	<0.001	2(2-3)	8(7-12)	<0.001
The periods from hospital admission 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(2-7)	4(2-10)	0.248	5(3-9)	4(3-10)	0.392
ICU length of stay, day, median(IQR)	7(6-11)	7(5-12)	0.291	8(6-12)	7(4-13)	0.076
Hospital length of stay, day, median(IQR)	36(25-53)	44(28-61)	0.009	41(28-57)	43(28-61)	0.451
Hospitalization costs, yen, median(IQR)	3185580 (248279-4591850)	3463690 (253385-5132490)	0.169	3399180 (2717360-4900910)	3450760 (2515160-5047610)	0.169 0.684
Complications						
DVT, n (%)	4(2.7)	4(4.6)	0.475	1(1.3)	4(5.1)	0.367
ICU-AD, n (%)	46(31.1)	48(54.6)	<0.001	24(30.8)	41(52.6)	0.006
Pneumonia, n (%)	46(31.1)	46(52.3)	0.001	31(39.7)	40(51.3)	0.147
Bedsore, n (%)	4(2.7)	6(6.8)	0.181	4(5.1)	6(7.7)	0.746
Fall, n (%)	10(6.8)	6(6.8)	0.985	4(5.1)	6(7.7)	0.746

Median (25th–75th percentile) or the number of patients.
Independent-samples Mann–Whitney U-test or X2 test.
Definition of abbreviations: IQR = Interquartile range; DVT=Deep vein thrombosis: ICU-AD=ICU acquired delirium.

Table 3: Comparison of clinical parameters.

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 for 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, and nurses, possibly contributing to the reduction of the period needed to achieve walking independence.

Delirium has recently been reported to negatively affect not only the short-term prognosis, but also the long-term prognosis and cognitive functions. There has also been a general consensus that ICU-AD influences the functional prognosis. In the present study, delirium developed markedly less frequently in the early rehabilitation group. Deliriumis defined as a reversible cognitive disorder involving disorientation, short-term memory impairment, a lack of attention, and/orabnormal patterns of thinking. Schweickert, et al. [7],reported that the early initiation of exercise therapy for ICU patients improved their ADL and walking distances on discharge from the hospital, while reducing the prevalence ofICU-AD among them. Based on this,

when performing early rehabilitation for ICU patients with tracheal intubation, multi-professional collaboration may facilitate changes of content and temporal arrangements, consequently making earlier mobilization feasible [7]. Furthermore, the prevention of complications represented by deliriummay also shorten the period such patients need to achieve walking independence.

Early rehabilitation for ICU patients may increase hospitalization costs for them due to a risein rehabilitation fees for each category of disease. However, on comparing such costs between the 2 groups, there were no significant differences. In previous studies, early rehabilitation increased personnel expenses, but hospitalization costs remained unchanged, offsetting shortened durations of ICU length of stay and hospitalization [6]. Similarly, in the present study, the durations of hospitalization and ICU stay were similar between the 2 groups, possibly as a result of offsetting increases in medical fees due to early rehabilitationby preventing complications such as delirium and reducing related treatment costs.

The present study has the following limitations: the study was conducted in a single facility within a limited period; as subjects were not randomized into the 2 groups, it may be difficult to generalize the results regarding the association of early rehabilitation for all mechanically ventilated ICU patients; and the study dealt withthe period needed to achieve walking independence without measuring the muscle strength. Thus, it did not fully examine the effects of early rehabilitation. In the future, prospective studies involving increased numbers of subjects should be conducted.

Conclusion

Mechanically ventilated ICU patients were divided into early rehabilitation and control groups for comparison. In the former, the period fromhospital admission to the initiation of mobilization and that needed to achieve walking independence were significantly shorter, with a reduced frequency of delirium.

Early rehabilitation for mechanically ventilated ICU patients may facilitate earlier mobilization. It may also shorten the period they need to achieve walking independence by preventing complications, such asdelirium.

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