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Long-Term Prognosis Following Early Rehabilitation in the ICU: A Retrospective Cohort Study

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OBJECTIVES: Critically ill patients often have residual functional disabilities. Studies have shown that early rehabilitation improves short-term physical function. However, it remains unknown whether early rehabilitation affects long-term prognosis and healthcare resource utilization.

DESIGN: Retrospective cohort study.

SETTING: This study used an administrative claims database in Kumamoto Prefecture, Japan, from April 2012 to February 2017.

PATIENTS: We identified patients who were admitted to the ICU and received rehabilitation. Eligible patients were divided into those who underwent rehabilitation within 3 days (early rehabilitation group) and after 4 or more days of ICU admission (delayed rehabilitation group). Propensity score matching analyses were conducted to compare the number of outpatient consultations within 1 year and 3 years after discharge from the index hospitalization, total duration of hospitalization after discharge, healthcare costs, and survival.

INTERVENTIONS: None.

MEASUREMENTS AND MAIN RESULTS: A total of 6,679 patients were included in the study. Propensity score matching created 2,245 pairs. No difference was observed in the number of outpatient consultations 1 year after discharge, although there were differences between the groups 3 years after discharge. Long-term observation revealed a shorter overall duration of hospitalization (1.9 vs 2.6 mo; $p < 0.001$) and lower total costs ($28,159 vs $38,272; $p < 0.001$), as well as lower average costs per month ($1,690 vs $1,959; $p = 0.001$) in the early compared with the delayed rehabilitation group. No differences in survival were observed (log-rank test; $p = 0.18$).

CONCLUSIONS: Starting rehabilitation within 3 days of ICU admission was associated with shorter durations of future hospitalization and lower healthcare costs. Early rehabilitation for ICU patients might be associated with reduced healthcare resource utilization.

KEY WORDS: administrative claims database; critically ill patients; early rehabilitation; intensive care unit

Over the last decade, patient survival in the ICU has improved, and the proportion of patients discharged home has increased (1). However, studies have shown that critically ill patients in the ICU often suffer post-intensive care syndrome (PICS), a severe physical and mental disorder, even after discharge (2–5).

Early rehabilitation is a potential treatment for PICS. Previous studies reported that early exercise and mobilization improved short-term physical outcomes (6) and functional outcomes at hospital discharge (7), shortened ICU stay, and shortened hospital stay (8–12). However, these studies only examined the prognosis during hospitalization, and few studies have shown a positive

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effect of early mobilization on long-term prognosis (13). Indeed, a previous meta-analysis showed no difference in physical function 6 months after discharge between those receiving early mobilization and those receiving usual care (14).

The impact of early active exercise in critically ill patients on their long-term prognosis and subsequent healthcare resource utilization thus remains unknown. The present study aimed to investigate the association between early rehabilitation and long-term outcomes, in terms of post-discharge outpatient consultations, rehospitalization, healthcare costs, and long-term survival, compared with that for delayed rehabilitation, in patients admitted to the ICU.

MATERIALS AND METHODS

Data Sources

This retrospective cohort study used the administrative claims database for National Health Insurance and Late Elders' Health Insurance of Kumamoto Prefecture, Japan (15, 16). This database covers approximately 780,000 residents of Kumamoto Prefecture (44% of the population) who were beneficiaries of the National Health Insurance system or the Late Elders' Health Insurance system between April 2012 and March 2017. National Health Insurance mainly covers the self-employed, the irregularly employed, and pensioners below 75 years old and their families. The Late Elders' Health Insurance System covers those 75 years old and older (**Table S1**, http://links.lww.com/CCM/H323). Therefore, the majority of beneficiaries in the database are elderly.

The database includes the following patient-level data: age; sex; diagnoses recorded using the *International Statistical Classification of Diseases and Related Health Problems*, 10th Revision (ICD-10) codes; dates of outpatient consultation, hospital admission, discharge, ICU admission, and death; date-stamped procedure and prescription codes; and healthcare costs. As a rule, the physician entered the name of the disease tied to the ICD-10 code. The database is individually numbered, and all data are anonymized.

This study was approved by the institutional review board of Jichi Medical University (approval number: Clinical 19-205). The study was conducted in accordance with the Declaration of Helsinki and Institutional Ethical Guidelines for Medical and Health Research Involving Human Subjects. The need for informed consent was waived because of the anonymous nature of the data.

Patient Selection

We included patients who were admitted to the ICU during any hospitalization between April 2012 and March 2017. Only the first admission was included if patients were admitted to hospitals multiple times. We excluded patients: 1) who did not receive rehabilitation during their hospitalization, because the backgrounds of patients who did not undergo rehabilitation might have been different from those who underwent rehabilitation, 2) who died during hospitalization because we were interested in long-term outcomes after discharge, 3) who did not have records for the 6 months prior to admission, due to our need to obtain sufficient preadmission data, and 4) with no records after discharge.

Exposures

Patients who underwent rehabilitation within 3 days of ICU admission were defined as the early rehabilitation group, and those who underwent rehabilitation after 4 or more days of ICU admission were defined as the delayed rehabilitation group. We chose this grouping according to the definition of early rehabilitation in Japan of rehabilitation "within 48 hours of admission to the ICU." Since most patients admitted due to sepsis reportedly show reduced nerve conduction amplitude within 3 days of admission, starting mobilization within 3 days is considered appropriate (17, 18). The above definition of early rehabilitation is consistent with this evidence.

Under the Japanese insurance system, medical expenses for rehabilitation are covered if the rehabilitation is performed by one of the following specialists: physician, physical therapist, or occupational therapist. Furthermore, rehabilitation is broadly classified into the following five types under the insurance system, depending on the comorbid diseases in the patient: cardiovascular, cerebrovascular, disuse syndrome, musculoskeletal, and respiratory.

Outcomes

If patients were readmitted to a hospital within 1 day of discharge following the index hospitalization, it was considered the same hospitalization, and follow-up was started after the later discharge. The outcomes of this study were: 1) the number of outpatient consultations within 1 year and 3 years after the index hospitalization; 2) total duration of hospitalization after discharge; 3) total healthcare costs and average healthcare costs per month after discharge; and 4) mortality after discharge. Average healthcare costs were calculated as the total healthcare costs divided by the number of months in the observation period after discharge. Costs were calculated at a conversion rate of 1 U.S. dollar = 115 Japanese yen. The number of outpatient consultations was defined as the total number of outpatient visits during the follow-up period. The total duration of hospitalization was defined as the number of days the patient was hospitalized during follow-up. Total healthcare costs were defined as the sum of all inpatient and outpatient reimbursements.

Covariates

Covariates included age at ICU admission, sex, number of days of hospitalization before ICU admission during the index hospitalization, total duration of hospitalization in the 6 months before the index admission, surgical or nonsurgical patient, severe sepsis, number of failing organs, Elixhauser comorbidities (19), and prescribed drugs (categorized according to the Anatomical Therapeutic Chemistry [ATC] classification [20]). Since over-the-counter drugs are not widely used in Japan, almost all drugs administered to patients are included in the database. We also included the following procedures performed within 3 days of ICU admission: intra-aortic balloon pumping, continuous hemodiafiltration, mechanical ventilation, venoarterial extracorporeal membrane oxygenation, therapeutic hypothermia, plasma exchange, and percutaneous coronary intervention, as covariates for analyses. The number of days of hospitalization before ICU admission was defined as the number of days of admission to the hospital before being transferred to the ICU during the index hospitalization. The duration of hospitalization in the 6 months before admission was defined as the total number of days of hospitalization in the 6-month period prior to the index hospitalization. Surgical patients were defined as those who received general anesthesia on the day of ICU admission and were distinguished from nonsurgical patients. Severe sepsis was defined as sepsis with at least one organ system failure. Previous studies used administrative databases to estimate the epidemiology of severe sepsis based on the ICD-9 Clinical Modification and ICD-10 Australian Modification (21, 22). In this study, sepsis was defined as present when patients were diagnosed with any bacterial or fungal infection from admission to the third day of ICU stay using the ICD-10 codes used in previous studies (21, 22) (**Tables S2** and **S3**, http://links.lww.com/CCM/H323). The number of organ failures was also defined based on the presence of ICD-10 codes or drugs indicating failure of cardiovascular, respiratory, neurologic, hematologic, hepatic, or renal organs from admission to the third day of ICU stay (21, 22) (Table S3, http://links.lww.com/CCM/H323). Elixhauser comorbidities were extracted using algorithms developed by Quan et al (23). The presence of these comorbidities within the 6 months prior to the index hospitalization was extracted. The ATC classification system is a drug classification system designed to provide international statistics on the consumption of therapeutic drugs, making it easier to conduct surveys and to compare drugs across different countries using a standard classification system. It is endorsed by the World Health Organization (WHO) and overseen by the WHO Collaborating Centre for Drug Statistics Methodology. Data on the ATC classifications were extracted for the 6 months prior to the index admission and for the period from admission to the third day of ICU stay. Both the ATC classifications before hospitalization and those during hospitalization were used as covariates. Prescription drugs were considered as being used if an insurance claim for the drug was present during each period. Intra-aortic balloon pumping, continuous hemodiafiltration, mechanical ventilation, venoarterial extracorporeal membrane oxygenation, therapeutic hypothermia, plasma exchange, and percutaneous coronary intervention were considered as being used when the corresponding insurance claims for these procedures were present within 3 days of ICU admission. The insurance claim codes for these procedures are shown in **Table S4** (http://links.lww.com/CCM/H323).

Statistical Analysis

Continuous variables are presented as the median and interquartile range, and categorical variables are presented as numbers and proportions. Propensity score matching was used to adjust for measured confounding factors. Please see the **Supplemental Methods** (http://links.lww.com/CCM/H323) for detailed information on propensity score matching. Briefly, we created a logistic regression model to estimate propensity scores, where the dependent variable was the receipt of early rehabilitation and included the following: age, sex, days of hospitalization before the ICU admission, duration of hospitalization in the 6 months prior to admission, surgical or nonsurgical patient, severe sepsis, number of failing organs, intra-aortic balloon pumping, continuous hemodiafiltration, mechanical ventilation, venoarterial extracorporeal membrane oxygenation, therapeutic hypothermia, plasma exchange, percutaneous coronary intervention, medication during the 6 months prior to admission (16 items) and from admission to the third day of ICU admission (16 items) using the ATC classification system, as well as Elixhauser comorbidities (31 items). Patients who received early rehabilitation were matched with those who did not receive early rehabilitation, using nearest neighbor matching without replacement, with the caliper set at 0.2 of the SD of the propensity score. Baseline characteristics were compared using standardized differences, and a standardized difference of less than 10% was considered a negligible imbalance between the groups.

Outcomes were compared between the groups using Fisher exact test or Wilcoxon rank-sum test, as appropriate. We conducted survival analysis comparing time to death between the propensity-matched early and delayed rehabilitation groups using a Kaplan-Meier survival curve and log-rank test. Follow-up began at discharge from the index hospitalization and continued until death, 3 years post-discharge, or the month when the administrative claims were made for the last incurred healthcare costs, whichever came first. A p value of less than 0.05 was considered statistically significant. All statistical analyses were performed with the statistical package R 3.5.3 (The R Foundation, Vienna, Austria).

Sensitivity and Multivariable Regression Analyses

We also performed the following four sensitivity analyses to confirm the robustness of the study results:

1) Patients who did not undergo rehabilitation were included in the delayed rehabilitation group.
2) Patients who did not have records for 3 months prior to admission, instead of 6 months, were evaluated.
3) Patients who underwent rehabilitation within 5 days of ICU admission, rather than within 3 days, were evaluated as the early rehabilitation group.
4) Multivariable regression analyses. Negative binomial regression was used for the number of outpatient consultations within 1 year, the number of outpatient consultations within 3 years, and the duration of hospitalization after discharge, because of the distribution of these outcomes. Linear regression was used for total costs after discharge and average monthly costs after discharge. Among the explanatory variables, the number of days of hospitalization before ICU admission and the duration of hospitalization in the 6 months before admission were not normally distributed. The number of days of hospitalization before ICU admission was classified into 19 categories at 2.5-day intervals. All patients with a hospital stay of 47.5 or more days were grouped into the same category. Similarly, the duration of hospitalization in the 6 months prior to admission was categorized at 5-day intervals, and patients with a duration of hospitalization of 45 or more days were included in the same category. We tested collinearity using a variance inflation factor and ensured all variables had variance inflation factors of less than 10.

RESULTS

A total of 14,160 patients were newly admitted to the ICU from April 1, 2012, to March 31, 2017. After excluding patients who did not receive rehabilitation during their hospitalization (n = 4,764, 33.6%), died during hospitalization (n = 1,632, 11.5%), did not have data for the 6 months prior to hospitalization (n = 2,097, 14.8%), or with no records for the months following discharge (n = 3,149, 22.2%) (numbers include duplicates), 6,679 patients were included in the analyses (**Fig. 1**).

Table 1 shows a comparison of baseline characteristics between the early and delayed rehabilitation groups before and after propensity score matching. The number of patients after propensity score matching was 2,245 in each group. **Tables S5–S7** (http://links.lww.com/CCM/H323) show the use of drugs based on the ATC classification system during the 6 months prior to admission and after admission to the ICU, and Elixhauser comorbidities before and after propensity score matching. All covariates were balanced between the two groups after matching.

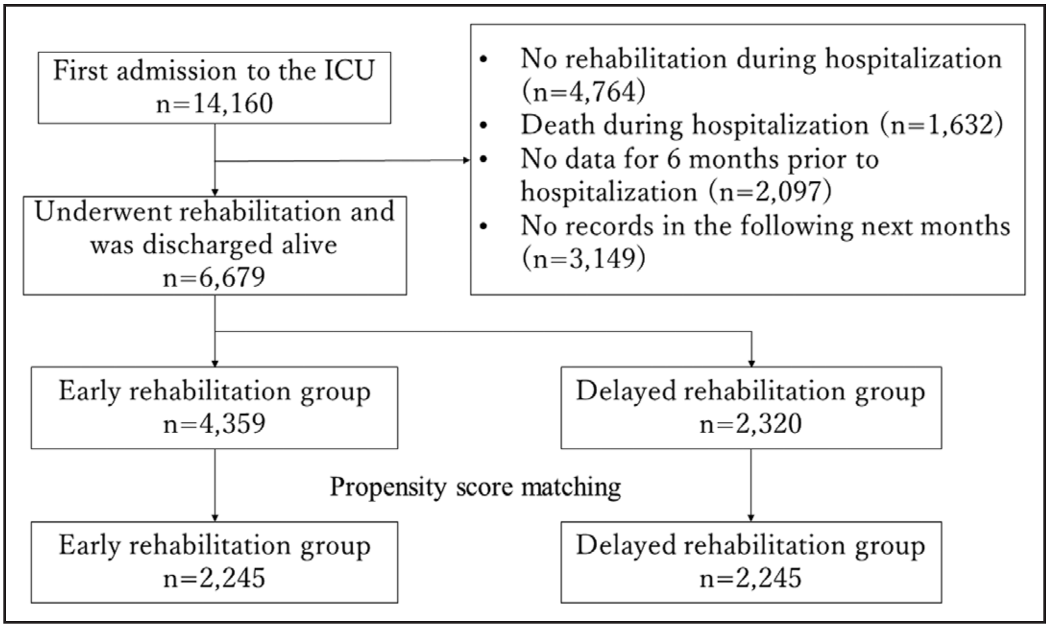

Figure 1. Flow diagram of patient selection.

After propensity score matching, the durations of ICU and hospital stays were shorter in the early rehabilitation group compared with the delayed rehabilitation group (3.4 vs 4.5 d; $p < 0.001$) (50.3 vs 60.7 d; $p < 0.001$) (**Table S8**, http://links.lww.com/CCM/H323). No differences were observed in the total number of outpatient consultations within 1 year after discharge between the two groups. However, the number of hospital visits within 3 years after discharge was lower in the early rehabilitation group compared with the delayed rehabilitation group (61.8 and 68.2 times, respectively; $p = 0.009$). The total duration of hospitalization after the index discharge was shorter in the early rehabilitation group than in the delayed rehabilitation group (1.9 and 2.6 mo, respectively; $p < 0.001$) (**Table 2**).

After propensity score matching, total medical costs and average medical costs per month after discharge were $28,159 and $1,690 in the early rehabilitation group and $38,272 and $1,959 in the delayed rehabilitation group, respectively. Both total and average monthly costs were lower in the early rehabilitation group than in the delayed rehabilitation group (Table 2).

Four hundred ninety-five and 386 patients before propensity score matching, and 297 and 378 patients after propensity score matching died during follow-up in the early and delayed rehabilitation groups, respectively. Survival after hospital discharge was not different in the early rehabilitation group compared with the delayed rehabilitation group ($p = 0.18$) (**Fig. 2**).

Sensitivity analysis for the period of missing prehospital data, performed by changing the exclusion criterion from 6 months to 3 months prehospitalization, showed similar results to those in the primary analysis, except for survival after hospital discharge (**Table S9** and **Fig. S1**, http://links.lww.com/CCM/H323). Sensitivity analysis performed by including patients who did not undergo rehabilitation in the delayed rehabilitation group showed that the number of hospital visits 3 years after discharge, total duration of hospitalization after discharge, and total medical costs were different between the groups (**Table S10** and **Fig. S2**, http://links.lww.com/CCM/H323). Sensitivity analysis of patients who underwent rehabilitation within 5 days of ICU admission as the early rehabilitation group showed differences in the total duration of hospitalization after discharge, total medical costs, and average medical costs per month after discharge (**Table S11** and **Fig. S3**, http://links.lww.com/CCM/H323). Multivariable regression analysis showed similar results to the main results, as shown in **Tables S12–S17** (http://links.lww.com/CCM/H323). There were 2,097 patients without records for the 6 months prior to admission, and the results of a comparison of their baseline characteristics with those of patients who had 6-month preadmission data available are presented in **Table S18** (http://links.lww.com/CCM/H323).

DISCUSSION

This study compared post-discharge outcomes between patients who started rehabilitation within 3 days and those who started rehabilitation 4 or more days after ICU admission. The early rehabilitation group

TABLE 1.
Patients' Characteristics Before and After Propensity Score Matching

Matching Items	Before Matching			After Matching		
	Early Rehabilitation, *n* = 4,359	Delayed Rehabilitation, *n* = 2,320	SMD	Early Rehabilitation, *n* = 2,245	Delayed Rehabilitation, *n* = 2,245	SMD
Age, average (SD)	76.2 (10.2)	75.7 (11.5)	0.049	76.4 (10.7)	75.9 (11.1)	0.047
Sex (male)	2,525 (57.9)	1,343 (57.9)	0.001	1,281 (57.1)	1,293 (57.6)	0.011
Days of hospitalization before ICU admission, average (SD)	5.2 (21.6)	4.2 (12.3)	0.056	4.3 (10.9)	4.3 (12.5)	0.005
Duration of hospitalization in the 6 mo prior to admission, average (SD)	8.1 (19.3)	8.8 (22.3)	0.035	8.3 (20.5)	8.6 (21.6)	0.013
Surgical patient	2,453 (56.3)	922 (39.7)	0.336	873 (38.9)	913 (40.7)	0.036
Severe sepsis	65 (1.5)	49 (2.1)	0.047	43 (1.9)	43 (1.9)	< 0.001
Organ failure (SD)	0.9 (0.9)	0.9 (0.9)	0.008	0.9 (0.8)	0.9 (0.9)	0.052
Intra-aortic balloon pumping	95 (2.2)	58 (2.5)	0.021	52 (2.3)	54 (2.4)	0.006
Continuous hemodiafiltration	36 (0.8)	80 (3.4)	0.182	36 (1.6)	46 (2.0)	0.033
Mechanical ventilation	1,519 (34.8)	818 (35.3)	0.009	732 (32.6)	767 (34.2)	0.033
Therapeutic hypothermia	5 (0.1)	16 (0.7)	0.091	5 (0.2)	7 (0.3)	0.017
Venoarterial extracorporeal membrane oxygenation	4 (0.1)	5 (0.2)	0.032	3 (0.1)	3 (0.1)	< 0.001
Plasma exchange	2 (0.0)	1 (0.0)	0.001	2 (0.1)	1 (0.0)	0.017
Percutaneous coronary intervention	77 (1.8)	54 (2.3)	0.04	53 (2.4)	54 (2.4)	0.003

SMD = standardized mean difference.

Data are presented as numbers (percentages), except for age, days of hospitalization before ICU admission, duration of hospitalization in the 6 mo prior to admission and organ failure.

showed a lower number of hospital visits at 3 years after discharge, shorter duration of hospitalization, and lower healthcare costs after discharge following the initial hospitalization than the delayed rehabilitation group. Early rehabilitation within 3 days of ICU admission was not associated with long-term survival after hospital discharge compared with rehabilitation commencing 4 or more days after ICU admission.

To the best of our knowledge, this is the first study to suggest that the effect of early rehabilitation might be sustained for an extended period of time (up to 3 yr) after discharge. Indeed, although several studies have suggested the short-term effects of early rehabilitation (6–9, 12, 24), few studies have focused on the long-term effects. This study tracked patients for an extended period after leaving the ICU, by utilizing a medical database that includes patient information for the entire prefecture (15, 16). Further, the use of propensity score matching allowed us to compare the early rehabilitation group's long-term prognosis with that of the delayed rehabilitation group, after matching the patients' background characteristics.

Our study showed that early rehabilitation was associated with a shorter duration of hospitalization within 3 years after discharge. A systematic review and meta-analysis, which included 11 studies with 1,322 patients, showed that physical function 6 months after discharge or randomization and health-related quality of life after discharge were not different between the early mobilization and control groups (14). Several possible

TABLE 2.
Comparison of Outcomes Between the Two Groups Before and After Propensity Score Matching

Matching Items	Before Matching: Early Rehabilitation, *n* = 4,359	Before Matching: Delayed Rehabilitation, *n* = 2,320	Before Matching: *p*	After Matching: Early Rehabilitation, *n* = 2,245	After Matching: Delayed Rehabilitation, *n* = 2,245	After Matching: *p*
Number of outpatient consultations within 1 yr	31.6 (35.1)	33.0 (36.9)	0.138	32.44 (37.6)	32.86 (36.8)	0.706
Number of outpatient consultations within 3 yr	61.1 (80.7)	68.6 (87.1)	< 0.001	62.05 (85.9)	67.98 (85.9)	0.021
Duration of hospitalization after discharge (mo)	1.8 (3.3)	2.6 (4.7)	< 0.001	2.04 (3.7)	2.63 (4.7)	< 0.001
Total costs after discharge ($)	25,735.7 (35,544.3)	38,408.8 (52,639.4)	< 0.001	28,820.5 (40,463.9)	38,140.0 (52,374.3)	< 0.001
Average monthly costs after discharge ($)	1,519.5 (2,187.4)	1,987.4 (2,477.5)	< 0.001	1,730.8 (2,425.4)	1,962.5 (2,892.3)	0.004

Data are presented as the average (SD).

explanations were considered for this difference. First, the follow-up duration differed between this meta-analysis and our study. In the meta-analysis (14), the maximum follow-up duration was 6 months, but in our study, we followed up patients for up to 3 years. Our study also found a difference in the number of outpatient consultations after the index discharge. Although the differences were not significant at 1 year, they were significant at 3 years, suggesting that it takes longer for the positive effects of rehabilitation to become apparent. Second, the definition of early rehabilitation differed between the two studies. In the meta-analysis (14), the intervention group was defined as those who started rehabilitation within 1 week, as opposed to within 3 days as in our study. Notably, among previous systematic reviews, only one study showed an increase in patient self-reported physical function and physical role at 6 months. In that study, the exercise group started rehabilitation within 48 hours (24). It is possible that the impact of early rehabilitation is only observed with earlier initiation of rehabilitation. Third, the study population in our study versus the previous study was different. In this study, we restricted the subjects to survivors, whereas the meta-analysis (14) included both survivors and nonsurvivors. Fourth, sample sizes in the studies included in the meta-analysis were small. The 11 previous studies evaluated in the meta-analysis included a total of only 1,322 patients (14). In addition to the small sample size, only 241 patients were available for physical function evaluation 6 months after discharge and 63 for evaluation of health-related quality of life (14). On the other hand, our study included 4,490 patients. Fifth, the outcomes evaluated were different. Our study used duration of hospitalization and number of outpatient consultations after hospital discharge as outcomes, although these might not be related to physical function after hospital discharge. Hence, worsening of these outcomes might not necessarily indicate a decrease in quality of life or physical function.

In the present study, there were no differences within the first year in the total number of outpatient consultations between the groups. However, there was a difference between the groups at 3 years, and the total duration of hospitalization after hospital discharge was shorter in the early rehabilitation group. This might reflect a reduction in serious complications after leaving the ICU, including PICS. Early rehabilitation might

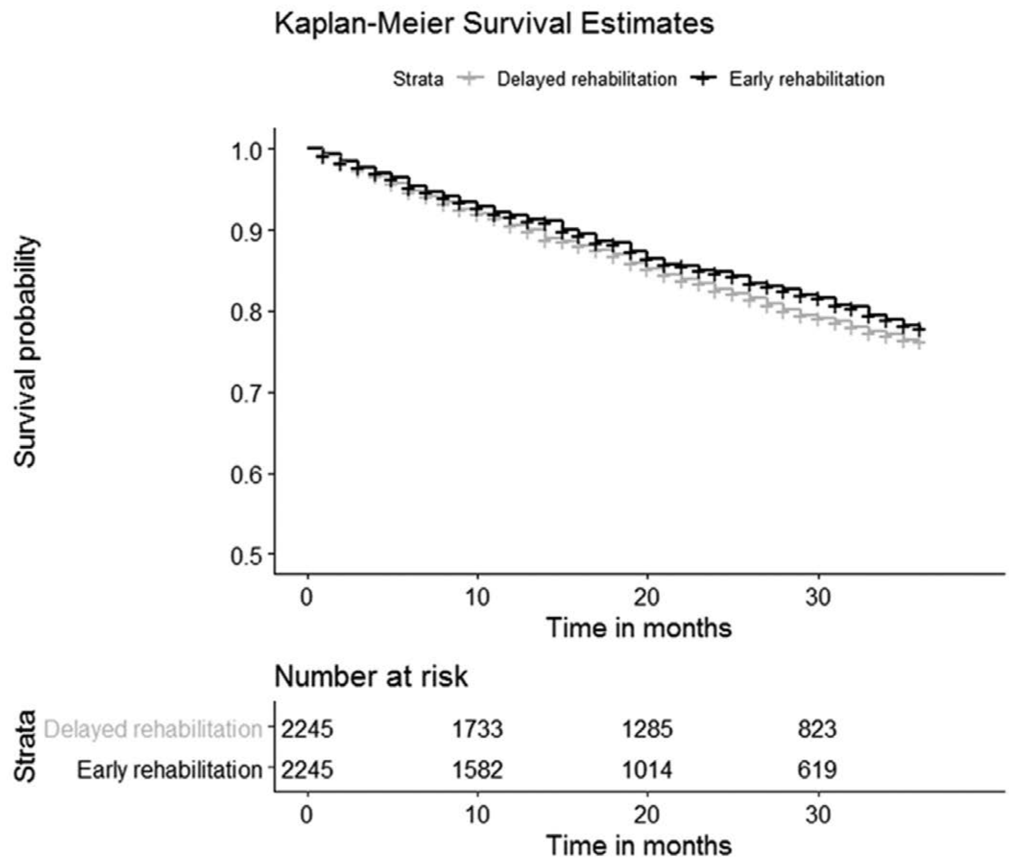

Figure 2. Kaplan-Meier estimates of survival after hospital discharge. Follow-up continued until death, 3 yr post-discharge, or the month when the administrative claims were made for the last incurred healthcare costs, whichever came first. Patients who were lost to follow-up were censored. The number at risk indicates the number of patients who were observed without censoring or death at each time point.

have helped to maintain motor and cognitive function during hospitalization, which might have improved the long-term prognosis of patients in this study. Indeed, early occupational therapy for elderly patients reportedly results in a lower prevalence of delirium, shorter duration of delirium, and maintenance of cognitive function at discharge (25). Early rehabilitation might have prevented delirium and led to favorable results in this study, as delirium has been reported to worsen long-term prognosis (26). In any case, since the mechanism of the positive impact of early rehabilitation on long-term prognosis is unknown, further research is needed in the future.

The strengths of the present study are its inclusion of a large sample size and long-term follow-up. The claim database used in this study includes extensive data that is routinely collected and can be tracked across hospitals. On the other hand, several limitations of this study should be acknowledged. First, the population included in this study was from a limited area of Japan. Due to the differences between the population covered in this study and the general population, it might be difficult to apply these results to other regions. Second, although we excluded patients who did not have records for the 6 months prior to admission in order to obtain sufficient data for propensity score matching, this exclusion criterion might reduce the generalizability of our study. Despite this, it is worth noting that a sensitivity analysis including patients with at least 3 months of history in the database showed similar results to the original analysis. In addition, baseline characteristics after hospitalization were similar between the patients with and without prehospital data for at least 6 months (Table S18, http://links.lww.com/CCM/H323). It must also be considered that we excluded patients without records after discharge following the index hospitalization. Patients without records after discharge from the index hospitalization were older and more severely ill than the included patients (Table S18, http://links.lww.com/CCM/H323). Therefore, excluding these patients might reduce the generalizability of the study results to older and severely ill patients. Third, unmeasured confounders might have biased the results of the present study. The database does not include clinical information such as severity scores. Hence, it is possible that the delayed rehabilitation group might have been too sick (e.g., patients who needed emergency surgery) to begin early rehabilitation. Although propensity score analyses can generally reduce bias due to observed differences between the treatment groups, it is still subject to bias due to unobserved differences. However, we assessed the number of failing organ systems and the use of procedures/therapies to treat them, such as mechanical ventilation or vasopressors, which can be considered partial substitutes for the specific severity scores. For example, in a previous study, the number of failing organ systems was associated with in-hospital mortality (27). Incorporating these substitute factors might have reduced the risk of confounding by indication. Fourth, patient-centered outcomes, such as activities of daily living or quality of life, were not evaluated since they are not included in the database. Fifth, the programs and amount of rehabilitation were not accurately identified. Rehabilitation codes for the highest reimbursement are typically selected. Thus, in practice, the code does not always match the details of the rehabilitation program. Sixth, receiving rehabilitation after discharge might have affected the long-term prognosis. However, the effect of post-discharge rehabilitation might also be the result of the exposure of interest. Finally, sensitivity analysis including patients who did not undergo rehabilitation in the delayed rehabilitation group did not show a difference in the average medical cost per month after discharge from the hospital. It is possible that patients who did not receive rehabilitation during hospitalization were severely ill or had illnesses that were too minor to receive rehabilitation. Thus, although propensity score matching was conducted, unmeasured confounding might have remained.

In conclusion, starting rehabilitation within 3 days of ICU admission was associated with a shorter duration of hospitalization following discharge after the initial hospitalization and lower healthcare costs compared with those who started rehabilitation after 4 days of ICU admission. Early rehabilitation for patients admitted to the ICU might reduce subsequent healthcare resource utilization.

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Drs. Murooka, Sasabuchi, and Takazawa were involved in study conception, study design, data collection, analysis, interpretation of the results, and drafting of the article. Dr. Matsui was involved in study conception, study design, data collection, data cleaning, analysis, and interpretation of the article. Drs. Murooka, Sasabuchi, Matsui, and Yasunaga designed the protocol and collected data. Drs. Matsui, Yasunaga, and Saito revised the draft of the article.

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The data cannot be made publicly available in accordance with an agreement with the data owner. The codes are available to interested researchers upon request to the corresponding author.

This study was approved by the institutional review board of Jichi Medical University (approval number: Clinical 19-205).

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