Impact of Rehabilitation on Outcomes in Patients With Ischemic Stroke

A Nationwide Retrospective Cohort Study in Japan

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***Background and Purpose*—**We aimed to examine the concurrent effects of timing and intensity of rehabilitation on improving activities of daily living (ADL) among patients with ischemic stroke.

***Methods*—**Using the Japanese Diagnosis Procedure Combination inpatient database, we retrospectively analyzed consecutive patients with ischemic stroke at admission who received rehabilitation (n=100 719) from April 2012 to March 2014. Early rehabilitation was defined as that starting within 3 days after admission. The average rehabilitation intensity per day was calculated as the total units of rehabilitation during hospitalization divided by the length of hospital stay. A multivariable logistic regression analysis with multiple imputation and an instrumental variable analysis were performed to examine the association of early and intensive rehabilitation with the proportion of improved ADL score.

***Results*—**The proportion of improved ADL score was higher in the early and intensive rehabilitation group. The multivariable logistic regression analysis showed that significant improvements in ADL were observed for early rehabilitation (odds ratio: 1.08; 95% confidence interval: 1.04–1.13; *P*<0.01) and intensive rehabilitation of >5.0 U/d (odds ratio: 1.87; 95% confidence interval: 1.69–2.07; *P*<0.01). The instrumental variable analysis showed that an increased proportion of improved ADL was associated with early rehabilitation (risk difference: 2.8%; 95% confidence interval: 2.0–3.4%; *P*<0.001) and intensive rehabilitation (risk difference: 5.6%; 95% confidence interval: 4.6–6.6%; *P*<0.001).

***Conclusions*—**The present results suggested that early and intensive rehabilitation improved ADL during hospitalization in patients with ischemic stroke. **(*Stroke*. 2017;48:740-746. DOI: 10.1161/STROKEAHA.116.015147.)**

Key Words: activities of daily living ■ inpatient ■ rehabilitation ■ retrospective study

Early rehabilitation for stroke patients can potentially prevent negative effects on the musculoskeletal, cardiovascular, respiratory, and immune systems[1] and reduce immobility-related complications.[2] Although many guidelines have recommended early rehabilitation after stroke to improve activities of daily living (ADL), such recommendations are only supported by limited evidence.[3]

The timing of starting rehabilitation and intensity of training remain controversial. About the timing of starting rehabilitation, several studies suggested that post-stroke rehabilitation should be initiated immediately after onset to achieve optimal results. A previous meta-analysis demonstrated a positive correlation between early rehabilitation and improved outcomes.[4] However, a literature review showed inconsistent results for the effects of early rehabilitation versus delayed rehabilitation.[5] Recent randomized controlled studies showed that very early rehabilitation within 24 hours of onset was feasible and likely to be safe[6] and showed promising improvement in walking recovery.[7]

With respect to rehabilitation intensity, several meta-analyses reported weak-to-moderate relationships between rehabilitation intensity and functional improvement of ADL.[8–10] However, these studies did not take into account the timing of starting rehabilitation. Thus, the concurrent effects of timing and intensity of rehabilitation on ADL remain unclear in patients with ischemic stroke.

The purpose of the present retrospective observational study was to examine the effect of rehabilitation, taking into consideration both the timing of starting rehabilitation and training

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intensity, on improving ADL among patients with ischemic stroke, using a national inpatient database in Japan.

Methods

Data Source

The Diagnosis Procedure Combination database is a national acute-care inpatient database in Japan. The database includes administrative claims data and some detailed clinical data for ≈7 million inpatients per year in ≈1000 participating hospitals. The main diagnosis, comorbidities present at admission, and complications occurring during hospitalization are coded using *International Classification of Disease and Related Health Problems 10th Revision* (ICD-10) codes accompanied by text data in Japanese. The database also includes each hospital's unique identifier and the following patient details: age; sex; medical procedures, including types of surgery, coded with original Japanese codes; daily records of drug administration and devices used; modified Rankin scale (mRS) score before admission and at discharge; use of prehospital ambulance service; stroke care unit (SCU) admission; level of consciousness based on the Japan Coma Scale (JCS) score at admission and discharge; and ADL scores that can be converted to the Barthel index (BI) at admission and discharge. The JCS codes 1–3 denote a patient who is awake without any stimuli, 10–30 denote a patient who can be aroused by some stimuli, and 100–300 denote a patient in a coma. Assessments by the JCS and the Glasgow Coma Scale are well correlated.[11]

In Japan, an SCU is defined as a unit that exclusively cares for stroke patients with trained members and a multidisciplinary care approach. An SCU must have ≥1 full-time neurological specialists, nurses, and physical or occupational therapists. As of 2014, the numbers of hospitals with an SCU and with an intensive care unit were 131 and 780, respectively. Patients requiring long-term rehabilitation are transferred to a rehabilitation hospital to receive a long-term rehabilitation program for a maximum of 150 days from onset.

For this study, we extracted data on the following complications occurring during hospitalization: pneumonia (J11–J18, J60), urinary tract infection (N10, N12, N30, M39.0), and heart failure (I50). We also extracted data on each patient's use of activacin and glyceol and receipt of endovascular therapy.

Hospital volume was defined as the average number of ischemic stroke patients admitted to each hospital per year and was categorized into tertiles. Hospital type was categorized into academic and nonacademic hospitals.

Because of the anonymous nature of the data, the requirement for informed consent was waived. This study was approved by the Institutional Review Board of The University of Tokyo.

Patient Selection

We identified patients who were admitted with a diagnosis of ischemic stroke (ICD-10 code: I63) and discharged between April 2012 and March 2014. We included the following patients: those aged >20 years, those with independent daily activities before admission (mRS score ≤2), those admitted within 3 days of onset, those who received rehabilitation during hospitalization, and those admitted to hospitals receiving at least 10 patients with ischemic stroke per year on average.

Timing of Starting Rehabilitation

We defined early rehabilitation as a specialized poststroke rehabilitation program administered by physicians, physical therapists, occupational therapists, and speech therapists within 3 days after admission, in line with the definition in a previous study.[12]

Training Intensity of Rehabilitation

In Japan, rehabilitation provided by physicians and therapists is reimbursed by the universal healthcare insurance system. One rehabilitation unit counts for 20 minutes, and patients can receive ≤9 U/d.

The average training intensity per day was calculated as the total units of rehabilitation during hospitalization divided by the length of hospital stay. The average training intensity was categorized into 6 groups: ≤1.0, 1.1–2.0, 2.1–3.0, 3.1–4.0, 4.1–5.0, and ≥5.1 U/d. We defined intensive rehabilitation as rehabilitation conducted at >3.0 U/d, in line with the definition in a previous study.[13]

Outcome Measures

The primary outcome was the improvement in ADL score between admission and discharge for each patient. The ADL assessment was performed by calculating the BI. In the present study, the differences in the BI between admission and discharge were calculated and categorized into 2 groups: improved group (≥1) and nonimproved group (≤0).

Statistical Analysis

We used the χ^2 test to compare categorical variables and the Mann–Whitney *U* test to compare continuous variables between the early rehabilitation group and the nonearly rehabilitation group and between the groups with different rehabilitation intensity categories.

All statistical analyses were performed using IBM SPSS statistics, version 22.0 (IBM, Armonk, NY) and Stata version 12 (StataCorp, College Station, TX). Values of $P<0.05$ were considered significant.

Multiple Imputation

There were missing values for BI at admission and discharge and the intensity of rehabilitation. To account for missing data values, we planned to use multiple imputation (MI) as a statistical plan. MI is a procedure used to replace missing values with other plausible values by creating multiple filling-in patterns to avert bias caused by missing data. It is also recognized as an alternative approach to analyzing incomplete data.[14] In the present study, we replaced each missing value with a set of substituted plausible values by creating 20 filled-in complete data sets using a MI by chained equation method.[15] In the imputation process, the following covariates were used to create 20 complete data sets: age, sex, mRS before admission, use of prehospital ambulance service, SCU admission, JCS score at admission, use of activacin and glyceol, endovascular intervention, complications, hospital type, hospital volume, and early rehabilitation provision at each hospital.

We also added auxiliary variables to our MI model to meet the missing at random assumption. Auxiliary variables are defined as variables that are either correlates of missingness or correlates of incomplete variables. Inclusion of such auxiliary variables (as well as all the covariates) in the imputation process can make the missing at random assumption more plausible and improve the quality of the imputed values.[16,17] In the present study, we used mRS at discharge and JCS score at discharge as the auxiliary variables because these variables may be related to missingness of the BI (eg, mRS score of 6 indicates in-hospital death, and the BI cannot be measured for dead patients).

All the covariates, as well as the BI at admission and proportion of early rehabilitation at each hospital, were also included as independent variables in the multivariable binary logistic regression analysis for each data set to analyze the association of timing of starting rehabilitation and training intensity with ADL improvement.

SEs are calculated using Rubin's rules.[18] These SEs take into account the variability in results between imputed data sets and reflect the uncertainty associated with the missing data.[19] Estimated associations in each of the imputed data sets were averaged together to give overall estimated associations.

Variance inflation factors were measured to test multicollinearity among the independent variables. Because the data derived from multiple hospitals were structured by 2 strata (hospitals and patients), we accounted for clustering within hospitals using a generalized estimating equation with an exchangeable working correlation matrix and a robust estimator variance–covariance matrix.[20]

We also conducted a multivariable binary logistic regression analysis for the outcome with complete cases.

Table 1. Patient Characteristics and Outcomes

	All Patients (N=100 791)	Early Rehabilitation (n=74 229)	Nonearly Rehabilitation (n=26 562)	*P* Value
Age, y, mean (SD)	73.2 (11.8)	72.8 (11.7)	73.2 (11.9)	<0.001
Female sex, n (%)	38 524 (38.2)	28 110 (37.9)	10 414 (39.2)	<0.001
Modified Rankin scale score before admission, n (%)				<0.001
0	60 070 (59.6)	44 697 (60.2)	15 373 (57.9)	
1	22 059 (21.9)	16 112 (21.7)	5947 (22.4)	
2	18 662 (18.5)	13 420 (18.1)	5242 (19.7)	
Use of prehospital ambulance service, n (%)	47 832 (47.5)	34 271 (46.2)	13 561 (51.1)	<0.001
Stroke care unit admission, n (%)	11 085 (11.0)	9554 (12.9)	1531 (5.8)	<0.001
JCS score at admission, n (%)				<0.001
0	56 512 (56.1)	42 158 (56.8)	14 354 (54.0)	
1 digit	35 012 (34.7)	26 103 (35.2)	8909 (33.5)	
2 digits	6849 (6.8)	4555 (6.1)	2294 (8.6)	
3 digits	2418 (2.4)	1413 (1.9)	1005 (3.8)	
Treatment, n (%)				
Use of activacin	5279 (5.2)	3833 (5.2)	1446 (5.4)	0.080
Use of glyceol	13 198 (13.1)	8751 (11.8)	4447 (16.7)	<0.001
Endovascular intervention	1395 (1.4)	938 (1.3)	457 (1.7)	<0.001
Complication, n (%)				
Pneumonia	5715 (5.7)	3683 (5.0)	2032 (7.7)	<0.001
Urinary tract infection	3259 (3.2)	2216 (3.0)	1043 (3.9)	<0.001
Heart failure	1326 (1.3)	833 (1.1)	493 (1.9)	<0.001
Rehabilitation started from admission, d, median (IQR)	2 (2–4)	2 (2–2)	5 (4–7)	<0.001
Rehabilitation intensity (units/d), n (%)*				<0.001
≤1.0	20 016 (19.9)	13 964 (18.8)	6052 (22.8)	
1.1–2.0	17 324 (17.2)	11 720 (15.8)	5604 (21.1)	
2.1–3.0	16 362 (16.2)	12 030 (16.2)	4332 (16.3)	
3.1–4.0	12 190 (12.1)	9487 (12.8)	2703 (10.2)	
4.1–5.0	8128 (8.1)	6687 (9.0)	1441 (5.4)	
≥5.1	8999 (8.9)	7638 (10.3)	1361 (5.1)	
Missing	17 772 (17.6)	12 703 (17.1)	5069 (19.1)	
Barthel index (scores), mean (SD)				
Admission	44.9 (39.4)	52.9 (38.4)	46.9 (39.8)	<0.001
Discharge	73.9 (35.4)	75.3 (34.4)	67.9 (38.1)	<0.001
Length of hospital stay, d, median (IQR)	20 (13–35)	19 (12–33)	24 (5–41)	<0.001
Hospital type (academic), n (%)	10 282 (10.2)	5464 (7.4)	4818 (18.1)	<0.001
Hospital volume (per year), n (%)				<0.001
≤123	33 528 (33.3)	22 953 (30.9)	10 575 (39.8)	
124–216	32 678 (32.4)	23 245 (31.3)	9433 (35.5)	
≥217	34 585 (34.3)	28 031 (37.8)	6554 (24.7)	
Early rehabilitation provision at each hospital (%), mean (SD)	73.6 (17.3)	78.9 (15.7)	58.9 (21.9)	<0.001
Difference in Barthel index between admission and discharge, n (%)				<0.001
Improved	43 613 (43.3)	33 013 (44.5)	10 600 (39.9)	
Not improved	31 340 (31.1)	22 554 (30.4)	8786 (33.1)	
Missing	25 838 (25.6)	18 662 (25.1)	7176 (27.0)	

IQR indicates interquartile range; and JCS, Japan Coma Scale.
*The mean (SD) values for rehabilitation intensity (units/d) were calculated for those without missing data.

Instrumental Variable Analysis

Conventional approaches, such as multivariable logistic regression analyses, cannot remove hidden biases caused by unmeasured confounders. Therefore, we performed an instrumental variable (IV) analysis as a confirmatory analysis. The key assumptions of an IV analysis are as follows: the IV (1) is highly correlated with the treatment, (2) is not correlated with any measured or unmeasured variables in the patient background characteristics, and (3) does not affect patient outcomes except through treatment.[21]

Provision of intensive poststroke rehabilitation to patients may depend on the attending physicians' preferences toward rehabilitation and human resources for rehabilitation employment at individual hospitals. If each hospital tends to conduct intensive rehabilitation independently of patient characteristics, intensive rehabilitation is determined more strongly by the hospital in which the patient is treated than by their specific risk factors. Under such conditions, the proportion of intensive rehabilitation provision per hospital can act as an IV, thereby allowing a natural experiment for an unbiased estimate of the outcome even in the presence of unmeasured confounders.[21] A consistent result from the IV analysis can serve as a useful confirmation of the conventional analysis. For our IV analysis, we excluded patients whose data on the number of units were missing. We defined the IV as the average number of units of rehabilitation per day in each hospital. The continuous variable of the IV was dichotomized with a cutoff value of 3.0 U/d. We used a 2-stage least-squares method to estimate the risk difference in improving ADL and its 95% confidence interval (CI) between the intensive rehabilitation group and the nonintensive rehabilitation group with adjustment for measured and unmeasured variables. We used the *ivreg2* procedure in Stata version 12 (StataCorp). To confirm that the proportion of intensive rehabilitation provision per hospital was not a weak IV, we used a partial *F* test.[22] An *F* statistic of >10 was considered to suggest that the IV was not weak.[22]

Results

We identified a total of 183 551 patients with ischemic stroke from 874 hospitals. We selected 100 791 eligible patients, including 74 229 patients (73.6%) with early rehabilitation and 29 317 patients (29.1%) with intensive rehabilitation. The overall in-hospital mortality was 3.0% (n=2976), and the mean (SD) length of hospital stay was 30.7 (38.1) days.

The median (25–75 percentile) number of patients in each hospital was 153 (64–297). The median (25–75 percentile) proportion of improved ADL was 55% (41%–66%).

Of all 100 791 patients, 25 838 patients (25.6%) had missing data on the outcome measurement (improvement in ADL between admission and discharge), and 17 772 patients (17.6%) had missing data on rehabilitation intensity. Of the 74 953 patients without missing data on the outcome measurement, 12 299 patients (16.4%) had missing data on rehabilitation intensity. Among the 874 hospitals, there were 2 hospitals for which all of their outcomes were missing, and the number of patients in these hospitals was 362.

Table 1 shows the patient characteristics and outcomes in all patients with and without missing data (n=100 791) and patients in the early (n=74 229) and nonearly (n=26 562) rehabilitation groups. The patients in the early rehabilitation group were significantly more likely to be younger and male and to have lower JCS score and significantly less likely to be using glyceol and undergoing endovascular therapy. Patients in the early rehabilitation group were significantly less likely to have complications. The early rehabilitation group was more likely to show admission to SCU. High-volume hospitals were more likely to conduct early rehabilitation. The BI at admission and discharge in the early rehabilitation group were significantly higher, and the difference in the ADL scores between admission and discharge was also significantly higher in the early rehabilitation group (23.4 versus 20.9; *P*<0.001). Patients with mRS score of 0 were more likely to receive early rehabilitation, and those who used prehospital ambulance service were less likely to receive early rehabilitation. Table I in the online-only Data Supplement compares the characteristics of patients with and without missing outcome data. Twenty of the 21 *P* values showed significant differences; that is, the missing pattern was not missing completely at random. This indicates the need to add the auxiliary variables to our MI model to meet the missing at random assumption.

Table 2 shows the crude proportions of improved ADL in patients without missing data for the BI. The proportions of patients with improved ADL were higher in the more intensive and earlier rehabilitation groups.

Table 3 shows the results of the multivariable binary logistic regression analysis for improvement in ADL with MI. The variance inflation factors were <5 for all of the independent variables. Compared with the nonearly rehabilitation group, the early rehabilitation group had significantly improved ADL (odds ratio: 1.08; 95% CI: 1.04–1.13). With reference to the least intensive rehabilitation group (≤1.0 U/d), the odds ratios (95% CI) for improved ADL were 1.15 (1.07–1.23), 1.36 (1.26–1.47), 1.53 (1.41–1.67), and 1.87 (1.69–1.2.07)

Table 2. Proportion of Patients With Improved Activities of Daily Living in the Early and Nonearly Rehabilitation Groups Divided by Rehabilitation Intensity Category Among Patients Without Missing Data for the Outcome

Rehabilitation Intensity Category (Unit/d)	All Patients (N=74 953)		Early Rehabilitation (n=55 567)		Nonearly Rehabilitation (n=19 386)		*P* Value
	n	Improved (%)	n	Improved (%)	n	Improved (%)	
≥5.1	7116	5065 (71.2)	6092	4386 (72.0)	1024	679 (66.3)	<0.001
4.1–5.0	6276	4054 (64.6)	5178	3391 (65.5)	1098	663 (60.4)	0.001
3.1–4.0	9163	5616 (61.3)	7122	4405 (61.9)	2041	1211 (59.3)	0.042
2.1–3.0	12 217	6943 (56.8)	9013	5127 (56.9)	3204	1816 (56.7)	0.852
1.1–2.0	12 869	6884 (53.5)	8772	4734 (54.0)	4097	2150 (52.5)	0.115
≤1.0	15 013	8129 (54.1)	10 616	5902 (55.6)	4397	2227 (50.6)	<0.001
Missing	12 299	6922 (56.3)	8774	5068 (57.8)	3525	1854 (52.6)	…

Table 3. Multivariable Logistic Regression Analysis With Multiple Imputation for Improvement in Activities of Daily Living in Patients With Ischemic Stroke

	Odds Ratio	95% Confidence Interval	*P* Value
Start timing of rehabilitation			
Nonearly rehabilitation	Reference		
Early rehabilitation	1.08	1.04–1.13	<0.01
Rehabilitation intensity			
≤1.0	Reference		
1.1–2.0	1.02	0.97–1.08	0.410
2.1–3.0	1.15	1.07–1.23	<0.01
3.1–4.0	1.36	1.26–1.47	<0.01
4.1–5.0	1.53	1.41–1.67	<0.01
≥5.1	1.87	1.69–2.07	<0.01
Age, y	0.99	0.99–0.99	<0.01
Sex			
Male	Reference		
Female	0.93	0.90–0.96	<0.01
Modified Rankin Scale score before admission			
0	Reference		
1	0.90	0.86–0.93	<0.01
2	0.89	0.84–0.93	<0.01
Use of prehospital ambulance service			
No	Reference		
Yes	1.01	0.96–1.05	0.76
Stroke care unit admission			
No	Reference		
Yes	1.22	1.06–1.39	0.01
JCS score at admission			
0	Reference		
1 digit	0.81	0.77–0.85	<0.01
2 digits	0.39	0.35–0.43	<0.01
3 digits	0.25	0.22–0.29	<0.01
Barthel index at admission (score)	0.97	0.97–0.98	<0.01
Use of activacin	1.02	0.93–1.11	0.67
Use of glyceol	0.69	0.65–0.74	<0.001
Endovascular intervention	0.85	0.73–0.99	0.03
Complications			
Pneumonia	0.42	0.38–0.47	<0.001
Urinary tract infection	0.56	0.51–0.62	<0.001
Heart failure	0.95	0.80–1.12	0.51
Hospital type			
Nonacademic	Reference		
Academic	0.82	0.71–0.95	0.01
Hospital volume (per year), n (%)			
≤123	Reference		
124–216	1.10	0.99–1.22	0.08
≥217	1.28	1.11–1.46	<0.001
Early rehabilitation provision at each hospital (%)	0.98	0.79–1.21	0.84

JCS indicates Japan Coma Scale.

in the groups with 2.1–3.0, 3.1–4.0, 4.1–5.0, and ≥5.1 U/d, respectively. Higher age, female sex, higher mRS score before admission, non-SCU admission, higher JCS score, lower baseline BI, use of glyceol, and complications of pneumonia and urinary tract infection were significantly associated with less improvement in ADL. The proportion of early rehabilitation at each hospital was not associated with improved ADL.

Table II in the online-only Data Supplement shows the results of the complete-case analysis. The results were similar to those obtained in the MI analysis.

In the IV analysis, we included 62 654 patients without missing data. The *F* statistics showed that the proportion of intensive rehabilitation was a strong IV (F=1381; P<0.001). In the IV analysis, intensive rehabilitation (risk difference: 5.6%; 95% CI: 4.6%–6.6%; P<0.001) and early rehabilitation (risk difference: 2.7%; 95% CI: 1.9%–3.5%; P<0.001) were associated with an increased proportion of improved ADL with adjustment for measured and unmeasured variables.

Discussion

Using a national inpatient database in Japan, the present study examined the effect of early rehabilitation on ADL in patients with ischemic stroke in relation to the intensity of rehabilitation. Our results showed that both early rehabilitation and intensive rehabilitation were independently associated with improved ADL.

In the present study, about a quarter of all patients had missing data on the outcome. Among the patients with outcome data, ≈16% of patients had missing data on rehabilitation intensity. The cumulative effect of missing data can cause substantial losses of precision and power. Such biases can be overcome using MI, which allows patients with incomplete data to be included in analyses.[19] It is appropriate to use MI for outcome variables. MI programs make no distinction between independent and dependent variables, and there is no need to distinguish between response or outcome and predictors or covariates.[23,24] Furthermore, we included auxiliary variables in the imputation model to satisfy the missing at random assumption.[16,17] We think that these statistical methods for imputation successfully mitigated any bias caused by missing data.

In Japan, early and intensive rehabilitation for stroke patients is not standardized. As shown in our results, the intensity of rehabilitation varied substantially, possibly through differences in structures and processes at each hospital. Because of this situation, the proportion of intensive rehabilitation provision per hospital can act as an IV. Our IV analysis showed an association of improved ADL with early and intensive rehabilitation, which supported the results of the multivariable logistic regression analysis.

One of the novelties of the present study is the concurrent analysis of the impact of starting time and training intensity. Previous studies suggested that early rehabilitation[4,6,7] and more intensive rehabilitation[8–10] were associated with better outcomes. However, the concurrent effects of timing and intensity of rehabilitation on ADL improvement remained unclear. Our results suggested that early and intensive rehabilitation for acute-phase ischemic stroke had an important role for improving ADL.

Another novelty of this study is the use of a large national database containing data from 874 hospitals, including those with and without an SCU. In the present study, ≈10% of patients were admitted directly to an SCU, whereas 90% of patients were admitted to general hospitals without an SCU, thus limiting the generalizability of the findings. However, our results showed an association between SCU admission and better outcomes, consistent with a previous study.[25]

A possible mechanism for the effectiveness of early and intensive rehabilitation can be proposed on the basis of the following clinical and physiological reasons. Specifically, early and intensive rehabilitation can enhance early mobilization, possibly resulting in prevention of secondary infectious complications including pneumonia and urinary tract infection,[2] as shown in our study.

In animal studies, early and intensive poststroke rehabilitation can be detrimental to the injured brain.[26,27] However, other studies suggested that shortly poststroke brains were primed and more sensitive in response to rehabilitation.[28,29] About intensity of exercise, some studies showed that more intensive training increased cortical representation and brain plasticity.[30,31] However, clinical evidence has been lacking on the effectiveness of exercise after early stroke in humans. The present study suggests that early and intensive rehabilitation may improve ADL after stroke.

In the present study, the contents of the rehabilitation programs were not unified. In general, rehabilitation programs for acute stroke inpatients are constructed in a multidisciplinary manner by assessment of clinical factors.[32] A previous study showed that the type and duration of therapies were heterogeneous and varied among individuals.[33] The results of the present study suggested the importance of providing a sufficient quantity of early rehabilitation as well as the contents of the program.

The present study had several limitations. First, the Diagnosis Procedure Combination database does not include information about the severity of acute stroke (eg, National Institutes of Health Stroke Scale), mood and cognitive function, pathogenesis of stroke, or occluded vessels. Second, the Diagnosis Procedure Combination database only includes information during hospitalization, so we were unable to analyze prehospital and postdischarge outcomes, including long-term ADL and mortality. Third, we were not able to confirm the timing for onset of complications. Patients with complications in the early stage may have been less likely to receive rehabilitation.

Conclusions

The present retrospective study using a national inpatient database showed that early and intensive rehabilitation were associated with improved ADL status.

Disclosures

None.

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Impact of Rehabilitation on Outcomes in Patients With Ischemic Stroke: A Nationwide Retrospective Cohort Study in Japan

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SUPPLEMENTAL MATERIAL.

Supplemental Table I. Patient Characteristics compared with and without missing outcome data

	All patients (n=100,791)	Group without missing outcome data (n=74,953)	Group with missing outcome data (n=25,838)	p
Age (years), mean (SD)	73.2 (11.8)	72.8 (11.8)	74.3 (11.6)	<0.001
Sex (Female), n (%)	38,524 (38.2)	28,405 (37.9)	10,119 (39.2)	<0.001
Modified Rankin Scale before admission				<0.001
0	60,070 (59.6)	45,166 (60.3)	14,904 (57.7)	
1	22,059 (21.9)	16,309 (21.8)	5,750 (22.3)	
2	18,662 (18.5)	13,478 (18.0)	5,184 (20.1)	
Use of prehospital ambulance service, n (%)	47,832 (47.5)	33,930 (45.3)	13,902 (53.8)	<0.001
Stroke Care Unit admission, n (%)	11,085 (11.0)	8,652 (11.5)	2,433 (9.4)	<0.001
JCS at admission, n (%)				<0.001
0	56,512 (56.1)	43,462 (58.0)	13,050 (50.5)	
1-digit	35,012 (34.7)	25,243 (33.7)	9,769 (37.8)	
2-digit	6,849 (6.8)	4,690 (6.3)	2,159 (8.4)	
3-digit	2,418 (2.4)	1,558 (2.1)	860 (3.3)	
Medical treatment, n (%)				
Use of Activacin	5,279 (5.2)	3,854 (5.1)	1,425 (5.5)	0.020
Use of Glyceol	13,198 (13.1)	9,002 (12.0)	4,196 (16.2)	<0.001
Surgical treatment, n (%)				
Endovascular Intervention	1,395 (1.4)	997 (1.3)	398 (1.5)	0.013
Complication, n (%)				
Pneumonia	5,715 (5.7)	3,549 (4.7)	2,166 (8.4)	<0.001
Urinary Tract Infection	3,259 (3.2)	2,379 (3.2)	880 (3.4)	0.069
Heart Failure	1,326 (1.3)	898 (1.2)	478 (1.8)	<0.001

Rehabilitation started from admission (days), mean (SD)	3.6	(12.7)	3.5	(9.6)	3.8	(17.5)	<0.001
Rehabilitation intensity (units per day), mean (SD)	2.7	(1.7)	2.7	(1.7)	2.6	(1.5)	<0.001
Rehabilitation intensity (units per day), n(%)							<0.001
Intensive rehabilitation	29,317	(29.1)	22,555	(30.1)	6,762	(26.2)	
Non-intensive rehabilitation	53,702	(53.3)	40,099	(53.5)	13,603	(52.6)	
Missing	17,772	(17.6)	12,299	(16.4)	5,473	(21.2)	
Barthel Index (scores), mean (SD)							
Admission	44.9	(39.4)	50.4	(39.1)	28.4	(36.5)	<0.001
Discharge	73.9	(35.4)	73.3	(35.6)	76.6	(33.5)	<0.001
Length of hospital stay (days), mean (SD)	30.7	(38.1)	30.0	(34.8)	32.6	(46.0)	<0.001
Hospital type (Academic), n(%)	10,282	(10.2)	7,446	(9.9)	2,836	(11.0)	<0.001
Hospital volume (per year), n (%)							<0.001
≤123	33,528	(33.3)	24,677	(32.9)	8,851	(34.3)	
124-216	32,678	(32.4)	24,038	(32.1)	8,640	(33.4)	
≥217	34,585	(34.3)	26,238	(35.0)	8,347	(32.3)	
Difference in Barthel Index between admission and discharge, n(%)							<0.001
Improved	43,613	(43.3)	43,613	(58.8)	-	-	
Not improved	31,340	(31.1)	31,340	(42.2)	-	-	

SD, standard deviation; IQR, inter-quartile range

Supplemental Table II. Multivariable logistic regression analysis with complete cases for improvement in activities of daily living in patients with ischemic stroke

	Odds ratio	95% confidence interval	p
Start timing of rehabilitation			
Non-early rehabilitation	Reference		
Early rehabilitation	1.14	1.08 - 1.20	<0.01
Intensity of rehabilitation			
≤1.0	Reference		
1.1-2.0	0.97	0.86 - 1.10	0.68
2.1-3.0	1.03	0.89 - 1.19	0.690
3.1-4.0	1.23	1.05 - 1.43	0.01
4.1-5.0	1.33	1.12 - 1.59	<0.01
≥5.1	1.58	1.30 - 1.91	<0.01
Age (years)	0.98	0.97 - 0.98	<0.01
Sex			
Male	Reference		
Female	0.86	0.83 - 0.90	<0.01
Modified Rankin Scale before admission			
0	Reference		
1	0.85	0.81 - 0.90	<0.01
2	0.78	0.73 - 0.83	<0.01
Use of prehospital ambulance service			
No	Reference		
Yes	0.86	0.81 - 0.92	<0.01
Stroke Care Unit admission			
No	Reference		

Yes	1.31	1.07 - 1.60	0.01
JCS at admission			
0	Reference		
1-digit	0.57	0.53 - 0.62	<0.01
2-digit	0.14	0.12 - 0.16	<0.01
3-digit	0.07	0.06 - 0.09	<0.01
Barthel Index at admission (score)	0.96	0.96 - 0.96	<0.01
Use of Activacin	0.95	0.84 - 1.08	0.44
Use of Glyceol	0.50	0.44 - 0.56	<0.001
Endovascular Intervention	0.79	0.64 - 0.97	0.03
Complication			
Pneumonia	0.19	0.17 - 0.22	<0.001
Urinary Tract Infection	0.35	0.30 - 0.40	<0.001
Heart Failure	0.89	0.71 - 1.11	0.29
Hospital type			
Non-academic	Reference		
Academic	0.69	0.52 - 0.92	0.01
Hospital volume (per year), n(%)			
≤123	Reference		
124-216	1.30	1.08 - 1.55	<0.001
≥217	2.40	1.67 - 3.46	<0.001
Early rehabilitation provision at each hospital (%)	0.78	0.50 - 1.23	0.29