Shorter Interval between Onset and Admission to Convalescent Rehabilitation Wards Is Associated with Improved Outcomes in Ischemic Stroke Patients

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As Japan's population ages, there is a growing interest in regional health care coordination. Our study aimed to evaluate whether the interval between onset and admission to convalescent rehabilitation wards (onset-admission) was associated with outcomes in ischemic stroke patients. We conducted a retrospective cohort study in a single rehabilitation hospital. Ischemic stroke patients consecutively admitted to the wards were eligible to enroll. Outcomes included Functional Independence Measure (FIM)-motor gain, the Food Intake Level Scale (FILS) and a discharge rate to home. FIM assesses functional independence, including motor (FIM-motor) and cognitive domains, and is a measure of activities of daily living (ADLs). The FIM-motor gain indicates the difference between the FIM-motor scores at admission and discharge. FILS is a 10-point observer-rated scale to measure swallowing. After enrollment, 481 patients (mean age 74.4 years; 45.7% women) were included. The median [interquartile range] onset-admission interval was 13 [10-20] days and the median National Institute of Health Stroke Scale score, a measure of stroke severity, was 8 [3-13]. In multivariate analysis, the onset-admission interval was independently associated with FIM-motor gain ($\beta = -0.107$, $p = 0.024$), FILS score at discharge ($\beta = -0.159$, $p = 0.041$), and the rate of discharge to home (odds ratio: 0.946, $p = 0.032$). In conclusion, a shorter interval between stroke onset and admission to convalescent rehabilitation wards contributes to improved outcomes, including ADLs, dysphagia, and a discharge rate to home, in ischemic stroke patients, regardless of stroke severity.

Keywords: activities of daily living; community-based integrated care system; dysphagia; early rehabilitation; home discharge
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Introduction

Early rehabilitation is recommended after stroke. The safety and feasibility of early rehabilitation (within 2 weeks) for stroke have been confirmed (Belagaje 2017; more patients will survive stroke with varying degrees of disability. Research in the past decade has expanded our understanding of the mechanisms underlying stroke recovery and has led to the development of new treatment modalities. This article reviews and summarizes the key concepts related to poststroke recovery. Recent Findings: Good data now exist by which one can predict recovery, especially motor recovery, very soon after stroke onset. Recent trials have not demonstrated a clear benefit associated with very early initiation of rehabilitative therapy after stroke in terms of improvement in poststroke outcomes. However, growing evidence suggests that shorter and more frequent sessions of therapy can be safely started in the first 24 to 48 hours after a stroke. The optimal amount or dose of therapy for stroke remains undetermined, as more intensive treatments have not been associated with better outcomes compared to standard intensities of therapy. Poststroke depres-

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sion adversely affects recovery across a variety of measures and is an important target for therapy. Additionally, the use of selective serotonin reuptake inhibitors (SSRIs) (Coleman et al. 2017), although whether very early rehabilitation (within 24 hours) is favorable for stroke remains under debate (Langhorne et al. 2017, 2018). Moreover, it has been recognized that the traditional clinical practice of "forced bedrest" after stroke onset can be harmful, and that mobilizing patients as early as possible might prevent further complications as well as promote functional recovery (Bernhardt et al. 2017; Coleman et al. 2017). Moreover, clinicians sometimes delay the initiation of rehabilitation of patients with acute ischemic stroke to after intensive therapy. Furthermore, intervention of early and intensive rehabilitation therapy in stroke patients on acute wards can help to desirable functional recovery can be expected (Kinoshita et al. 2017; Nakazora et al. 2018).

There is little evidence regarding the timing of subacute rehabilitation in the medical cooperation system in Japan. An interdisciplinary post-acute (convalescent) rehabilitation unit has been incorporated in the national medical insurance system since 2000 (KRWA, Kaifukuki Rehabilitation Ward Association 2016). Stroke is one of the major target diseases for the medical cooperation system. In a 2011 report, the mean onset-admission interval from acute hospitals to convalescent wards was 31.5 (standard deviation; SD, 18.6) days (Miyai et al. 2011). With the development of the Japanese medical system, the onset-admission interval is expected to shorten. Theoretically, it can be expected that a shorter onset-admission interval will be associated with more favorable outcomes for stroke patients. There are, however, little data on the association between the onset-admission interval and rehabilitation outcomes among such patients.

Therefore, studies elucidating the association between the onset-admission interval from acute hospitals to convalescent wards and clinical outcomes in stroke patients are needed. Hence, a retrospective cohort study was conducted to evaluate whether the onset-admission interval is associated with the rehabilitation outcomes, such as the activities of daily living (ADL), swallowing status, and rate of discharge to home in this setting.

Materials and Methods

Participants and setting

We conducted a retrospective cohort study in a post-acute care hospital in Japan. This hospital is a local rehabilitation hospital with the convalescent rehabilitation wards (a total of 135 beds). At the end of March 2016 in Japan, more than 77,000 convalescent ward-beds (60 beds per 100,000 population) were available nationwide.

The patients admitted to our wards were divided mainly into three categories, namely, patients with stroke, those with hospital-associated deconditioning, and those with musculoskeletal disorders. All patients with stroke admitted in our wards were transferred from the acute-care hospitals with Stroke Care Unit in the local medical cooperation system. Also, more than 90% of patients with hospital-associated deconditioning and musculoskeletal disorders were transferred from other acute care hospitals after they became medically stable. There were several major acute care hospitals in the local medical alliance system with which the study hospital was involved. Each year, more than 200 stroke patients were referred to the hospital. Therefore, the patients from minor referral hospitals were excluded in the current study to reduce bias in the characteristics of an acute hospital, namely, patients from acute hospitals with a small number of referral patients (< 20) were excluded, and patients from four acute care hospitals with a high number of referral patients (≥ 20) were included in the study.

The study period was between January 2016 and December 2018. All ischemic stroke patients consecutively admitted to our wards were eligible for enrollment. Exclusion criteria included cerebral hemorrhage, craniotomy performed, missing data, refusal of consent to participate, and altered consciousness (indicated by a Japan Coma Scale level of 3 digits (Shigematsu et al. 2013)).

Rehabilitation and nutritional management

The convalescent rehabilitation program was tailored to fit the patient's individual function and disabilities (up to 3 hours per day) (Nagano et al. 2020). The implementation of this program was a multi-professional collaboration, which includes physical therapists, occupational therapists, speech and language therapists, rehabilitation physicians, nurses, pharmacists, dietitians, dental hygienists, medical social workers, and caregivers. For example, physical therapy included range of motion exercises, basic movement training, facilitation of paralyzed limb, walking and ADL exercise, and resistance exercise. Nutritional management was also tailored to fit the patients' functional and nutritional status, which was multidisciplinary and included nutrition education, high-energy and high-protein delivery to malnourished patients, and lifestyle guidance for stroke prevention.

Data collection

Basic information, including age, sex, ischemic stroke type, stroke severity based on the National Institute of Health Stroke Scale (NIHSS) score at the time of stroke onset (Brott et al. 1989), body mass index (BMI), length (days) from onset of stroke to admission to the wards (defined as "onset-admission interval"), referral acute hospital, and residence type (as well as living alone or not) before onset, was recorded upon admission. A validated nutrition screening tool (Rubenstein et al. 2001) of Mini Nutritional Assessment-Short Form (MNA-SF) was completed in an interview conducted by trained registered dietitians, with an MNA-SF score of 0-7 was considered to be malnourished. The dysphagia status using the Food Intake Level Scale (FILS), a validated 10-point observer-rated scale to measure swallowing (Kunieda et al. 2013), was evaluated by trained nurses. Premorbid ADLs using the modified Rankin Scale (mRS) (Banks and Marotta 2007) and severity of comorbidities using the Charlson Comorbidity Index (CCI) (Charlson et al. 1987) were evaluated by medical doctors. Within 72 hours of admission, trained rehabilitation therapists assessed the physical and cognitive function using the Functional Independence Measure (FIM) (Ottenbacher et al. 1996). In addition, we calculated the total rehabilitation therapy units received during hospitalization (units per day, 1 unit = 20 minutes' therapy) by reviewing the medical charts.

Outcomes

Primary outcome used a motor domain of FIM (FIM-motor) (Ottenbacher et al. 1996), which has a motor domain with 13 sub-items (FIM-motor) and a cognitive domain with five sub-items (FIM-cognitive). Tasks are rated on a seven-point ordinal scale ranging from complete care to complete independence. Scores range from 18-126 for total FIM, 13-91 for FIM exercise, and 5-35 for FIM awareness. The lower the score, the less independent the patient is. "FIM-motor gain" was calculated by subtracting the FIM-motor score at admission from that at discharge. "FIM-motor efficacy" was defined by dividing the "FIM-motor gain" by the length of hospital stay.

Secondary outcomes included the FILS score at discharge and rate of home discharge, both of which were also considered indicators of success in rehabilitation and were used as indicators of patients' quality of care (Kus et al. 2011; Yoshimura et al. 2019). In the current study, dysphagia was defined as a FILS score of < 7.

To reduce study bias, rehabilitation therapists, nurses, and medical doctors who assessed the MNA-SF, CCI, mRS, FILS, and FIM, as well as medical social worker responsible for suggesting where to discharge patients and social resources, were independent of those involved in the collection and analysis of data and interpretation of the results.

Sample size calculation

Sample size calculation was based on our previous study (Shiraishi et al. 2017). The results showed that the FIM-motor at admission for patients in the same setting was normally distributed with a standard deviation of 23.4. If the true difference in the mean between the two groups of early and late referral patients, with a median onset-admission days of hospital cutoff, is 17 (Beninato et al. 2006), in order to reject the null hypothesis, a sample size of at least 91 patients in each group is required, with a power of 0.9 and an alpha error of 0.05. This would support the validity of our results.

Statistical analysis

The parametric data are reported as means (SD); non-parametric data, medians and 25th to 75th percentiles [interquartile range; IQR]; and categorical data, numbers (%). For bivariate analysis, the patients were divided into two groups of early and late referral patients with the median onset-admission days as the cutoff value. Two group comparisons were made using the t-test, Mann-Whitney U test and chi-square test. Multiple linear regression analyses were used to determine whether onset-admission interval (days) was significantly associated with FIM-motor gain and efficacy and FILS score at discharge. Multivariate logistic regression analysis was used to determine whether onset-admission days was significantly associated with discharge to home. Confounders selected to adjust for bias were age, sex, NIHSS score, CCI, premorbid mRS, MNA-SF, admission scores of FIM-motor and FIM-cognitive, length of hospital stay (except when FIM efficiency was the dependent variable), total rehabilitation therapy (units/day), and home residence type before onset. These variables were reported to be clinically relevant to the outcome of rehabilitation (Wakabayashi and Sakuma 2014; Shiraishi et al. 2018; Yoshimura et al. 2018a, b, 2019). In multivariate analysis with the dependent variable of FILS score at discharge, "FILS score on admission" was used instead of "MNA-SF on admission" to adjust for the baseline effects. The referral acute hospitals were also adjusted for. To assess multicollinearity, the Variance Inflation Factor (VIF) was used as follows: a VIF value of 1-10 was considered as the absence of multicollinearity. Statistical analysis was performed using IBM SPSS version 21 (IBM, Armonk, NY, USA). Statistical significance was set at p value < 0.05.

Ethics

Informed consent was obtained from all participants or their legal guardians. The study was approved by the Institutional Review Board of Kumamoto Rehabilitation Hospital where the study was conducted (approval number 2019-12). The research was conducted in accordance with the tenets of the Declaration of Helsinki and the Ethical Guidelines for Medical and Health Research Involving Human Subjects (Provisional Translation as of March 2015).

Results

During the study period, a total of 637 stroke patients were newly admitted to the wards. Those that met the inclusion criteria were further reviewed for eligibility. Among them, the stroke patients with cerebral hemorrhage with or without craniotomy (n = 128), those with missing data (n = 21), or those with altered consciousness (n = 7) were excluded. Finally, 481 participants were enrolled.

Table 1 summarizes the baseline characteristics of the enrolled patients. The mean (SD) age was 72.4 (9.1) years and 46 percent of the participants were female. The ischemic stroke type included lacunar infarction (n = 210; 42.7%), atherothrombotic infarction (n = 180; 37.4%), and cardioembolic infarction (n = 91; 18.9%). The median [IQR] onset-admission days was 13 [10-20] days. The

Table 1. Baseline characteristics of participants and between-group comparison of early and late referral to rehabilitation wards.

	Total (n = 481)	Early referral[1] (n = 241)	Late referral[1] (n = 240)	p value
Age, y, mean (SD)	72.4 (9.1)	74.1 (10.2)	73.8 (11.3)	0.103
Sex, n (%)				
Female	220 (45.7)	107 (44.4)	113 (47.1)	0.555
Male	261 (54.3)	134 (55.6)	127 (52.9)	
Ischemic stroke type, n (%)				
Lacunar stroke	210 (42.7)	108 (44.8)	102 (42.5)	0.249
Atherothrombotic stroke	180 (37.4)	84 (34.9)	96 (40.0)	
Cardioembolic stroke	91 (18.9)	42 (17.4)	49 (20.4)	
Onset NIHSS score, median [IQR]	8 [3-13]	6 [2-13]	10 [6-14]	0.025
Onset-admission days, median [IQR]	13 [10-20]	10 [9-12]	19 [15-24]	-
Referral acute hospital, n (%)				
A / B / C / D	75 (15.6) / 288 (59.9) / 71 (14.8) 47 (9.8)	43 (17.4) / 151 (62.7) / 31 (12.9) / 16 (6.6)	32 (13.3) / 137 (57.1) / 12 (16.7) / 31 (12.9)	0.234
FIM, score, median [IQR]				
Total	60 [28-96]	73 [31-100]	41 [22-74]	< 0.001
Motor domain	42 [15-68]	49 [18-73]	22 [13-54]	0.001
Cognitive domain	19 [11-28]	22 [12-29]	15 [8-24]	0.007
mRS before stroke onset, score, median [IQR]	0 [0-2]	0 [0-2]	0 [0-2]	0.033
mRS at stroke onset, score median [IQR]	5 [4-5]	5 [5-5]	5 [5-5]	0.049
CCI, median [IQR]	2 [1-3]	2 [1-3]	2 [1-3]	0.472
Swallowing status				
FILS, median [IQR]	8 [4-10]	8 [7-10]	7 [2-8]	< 0.001
Dysphagia, n (%)	138 (28.7)	50 (20.7)	88 (36.7)	< 0.001
Nutritional status				
Body mass index, kg/m^2, mean (SD)	22.5 (3.8)	22.7 (4.0)	22.4 (3.8)	0.237
MNA-SF, score, median [IQR]	6 [4-8]	7 [4-9]	5 [3-8]	0.001
Malnutrition, n (%)	221 (45.9)	105 (43.6)	116 (48.3)	0.012
Energy intake, kcal/kg BW/day, mean (SD)	28.0 (8.0)	28.2 (8.2)	28.0 (8.4)	0.694
Protein, g//kg BW/day, mean (SD)	1.1 (0.3)	1.1 (0.4)	1.0 (0.3)	0.127
Residence before onset, n (%)				
Own home	457 (95.0)	232 (96.2)	225 (93.8)	0.343
Nursing home	13 (2.7)	5 (2.1)	8 (3.3)	
Institution	11 (2.3)	4 (1.7)	7 (2.9)	
Living alone before onset (n = 457), n (%)	43 (9.4)	18 (8.1)	25 (10.6)	0.256
Laboratory data, mean (SD)				
Albumin, g/dL	3.7 (0.5)	3.6 (0.5)	3.5 (0.6)	0.066
Hemoglobin, g/dL	13.1 (1.8)	13.3 (1.9)	12.8 (2.0)	0.015
C-reactive protein, mg/dL	1.2 (2.2)	1.1 (3.3)	1.4 (3.1)	0.260
Rehabilitation therapy[2], units/day, median [IQR]	8.0 [7.2-8.3]	8.0 [7.1-8.4]	8.0 [7.3-8.3]	0.365
Lengths of hospital stay, day, median [IQR]	86 [50-115]	73 [48-110]	101 [52-122]	0.001

CCI, Charlson's comorbidity index; FILS, food intake level scale; FIM, functional independence measure; MNA-SF, mini nutritional assessment-short form; mRS, modified Rankin Scale; NIHSS, National Institute of Health Stroke Scale.
[1]Early and late referrals: two groups with median referral days of 13 days as cutoff.
[2]Rehabilitation therapy performed during hospitalization (1 unit = 20 min).

median [IQR] scores of FIM-motor and FIM-cognitive were 42 [15-68] and 19 [11-28], respectively. The median [IQR] FILS score was 8 [4-10], and dysphagia was observed in 28.7% of patients at baseline. In bivariate analyses at baseline, early referral patients (onset-admission days < 13) had lower FIM-motor and FIM-cognition scores and higher mRS scores (lower physical independence) before and at the onset of stroke and were more likely to

Table 2. Univariate analyses for clinical outcomes between groups of early and late referral to rehabilitation wards.

	Early referral (n = 241)	Late referral (n = 240)	p value
FIM at discharge, score, median [IQR]			
Total	111 [72-123]	101 [52-120]	0.008
Motor domain	82 [49-90]	75 [34-89]	0.008
Cognitive domain	30 [19-29]	27 [17-33]	0.025
FIM gain, score, median [IQR]			
Total	22 [10-41]	22 [7-46]	0.259
Motor domain	18 [8-33]	18 [4-35]	0.388
Cognitive domain	5 [1-9]	4 [1-10]	0.427
FIM efficacy, score/day, median [IQR]			
Total	0.34 [.14-.52]	0.30 [.11-.46]	0.027
Motor domain	0.26 [.11-.39]	0.23 [.06-.37]	0.044
Cognitive domain	0.06 [.02-.12]	0.05 [.01-.10]	0.075
Swallowing status at discharge			
FILS, score, median [IQR]	10 [8-10]	10 [7-10]	0.009
Dysphagia at discharge, n (%)	14 (5.8)	33 (13.8)	0.044
Home discharge, n (%)	189 (78.4)	169 (70.4)	0.003

Early and late referrals: two groups with median referral days of 13 days as cutoff.
FILS, food intake level scale; FIM, functional independence measure.

Table 3. Multiple linear regression analyses for FIM-motor gain and efficacy.

	FIM-motor gain		FIM-motor efficacy	
	β	p value	β	p value
Age	−0.110	0.041	−0.042	0.125
Sex	0.002	0.746	−0.024	0.730
Onset-admission days	−0.102	0.032	−0.149	0.021
FIM-motor on admission	−0.241	< 0.001	−0.134	< 0.001
FIM-cognitive on admission	0.139	0.011	0.264	0.012
Onset NIHSS score	−0.055	0.312	−0.024	0.411
Length of hospital stay	0.138	0.035	-	-
CCI	−0.079	0.092	−0.092	0.068
MNA-SF on admission	0.262	< 0.001	0.281	< 0.001
Rehabilitation therapy	0.137	0.004	0.096	0.086
Premorbid mRS	−0.187	< 0.001	−0.221	< 0.001
Referral acute hospital				
A hospital	0.051	0.557	−0.029	0.618
B hospital	0.102	0.213	0.010	0.761
C hospital	−0.023	0.644	−0.013	0.510
D hospital (reference)	-	-	-	-
Home residence before onset	0.112	0.070	0.181	0.023

CCI, Charlson's comorbidity index; FIM, functional independence measure; MNA-SF, mini nutritional assessment-short form; mRS, modified Rankin Scale; NIHSS, National Institute of Health Stroke Scale.

experience dysphagia, compared with late referral patients (Table 1).

The results of the univariate analyses of the clinical outcomes between the early and late referral patients are shown in Table 2. Early referral patients compared with late referral patients had a higher median [IQR] FIM-motor

Table 4. Multiple linear regression analysis for FILS at discharge.

	β	p value
Age	−0.131	0.010
Sex	0.041	0.175
Onset-admission days	−0.149	0.040
FIM-motor on admission	0.185	0.027
FIM-cognitive on admission	0.217	0.022
Onset NIHSS score	0.127	0.110
Length of hospital stay	0.057	0.162
CCI	−0.010	0.510
FILS on admission	0.421	< 0.001
Rehabilitation therapy	0.223	0.012
Premorbid mRS	−0.062	0.218
Referral acute hospital		
A hospital	−0.029	0.454
B hospital	0.054	0.824
C hospital	−0.061	0.312
D hospital (reference)	-	-
Home residence before onset	0.012	0.132

CCI, Charlson's comorbidity index; FILS, food intake level scale; FIM, functional independence measure; mRS, modified Rankin Scale; NIHSS, National Institute of Health Stroke Scale.

Table 5. Multiple logistic regression analysis for home discharge.

	OR (95% CI)	p value
Age	0.911 (0.885-0.991)	0.036
Sex	0.741 (0.358-1.413)	0.414
Onset-admission days	0.948 (0.910-0.989)	0.038
FIM-motor on admission	1.115 (1.034-1.189)	< 0.001
FIM-cognitive on admission	1.069 (0.996-1.159)	0.085
Onset NIHSS score	0.711 (0.421-1.123)	0.122
Length of hospital stay	1.009 (0.997-1.018)	0.121
CCI	0.766 (0.491-1.101)	0.131
MNA-SF on admission	1.249 (1.005-1.512)	0.020
Rehabilitation therapy	1.029 (0.562-1.581)	0.434
Premorbid mRS	0.751 (0.470-1.071)	0.114
Referral acute hospital		
A hospital	0.175 (0.119-1.81)	0.112
B hospital	0.712 (0.153-3.545)	0.511
C hospital	0.552 (0.029-1.320)	0.123
D hospital (reference)	-	-
Home residence before onset	5.125 (1.035-9.591)	0.011

CCI, Charlson's comorbidity index; FIM, functional independence measure; MNA-SF, mini nutritional assessment-short form; mRS, modified Rankin Scale; NIHSS, National Institute of Health Stroke Scale.

score at discharge (82 [49-90] vs. 75 [34-89], p = 0.008) and a higher median [IQR] efficiency of FIM-motor (0.26 [0.11-0.39] vs. 0.23 [0.06-0.37], p = 0.044), and decreased incidence of dysphagia at discharge (5.8% vs. 13.8%, p = 0.044). In addition, early referral patients were more likely to be discharged from hospital to home than those with late referral (78.4% vs. 70.4%, p = 0.003).

Tables 3 and 4 show the results of multiple linear regression analyses for FIM-motor gain and efficacy and FILS score at discharge, with adjustment of potential confounding factors. To reduce bias, all multivariate analyses were adjusted for the same confounding factors (except for the baseline scores for MNA-SF and FILS), where no multicollinearity between the variables was detected. The results showed that onset-admission interval was significantly and negatively associated with FIM-motor gain ($\beta = -0.102$, p = 0.032) and efficacy ($\beta = -0.149$, p = 0.021) and FILS score at discharge ($\beta = -0.149$, p = 0.040). However, the strength of the association was weak for all outcomes.

Table 5 show the multivariate logistic regression analysis for discharge to home, after adjusting for potential confounders. No multicollinearity between the variables was detected. The result showed that onset-admission interval was significantly and negatively associated with the rate of discharge to home (odds ratio: 0.948, p = 0.038).

Discussion

In the current study, we aimed to assess the benefits of early admission from onset to convalescent rehabilitation wards regarding clinical outcomes in ischemic stroke patients. Our results highlight three important findings in ischemic stroke patients: (1) early admission from onset to convalescent rehabilitation wards is positively associated with ADL improvement, (2) early admission is positively associated with dysphagia improvement, and (3) early admission is associated with a higher rate of home discharge.

Early admission from onset to convalescent rehabilitation wards was positively associated with ADL improvement in ischemic stroke patients. Early commencement of rehabilitation after stroke is recommended in many clinical practice guidelines (Belagaje 2017; Bernhardt et al. 2017; Coleman et al. 2017). Moreover, in the medical cooperation system in Japan, intensive rehabilitation therapy is reported to lead to preferable functional outcomes after stroke in convalescent rehabilitation wards (Kamo et al. 2019), where intensive and comprehensive multidisciplinary inpatient rehabilitation is performed (KRWA 2016). To make progress in this field, we aimed to determine whether the onset-admission interval had any associations with the rehabilitation outcomes in this setting. This study addressed the evidence gap by reporting that a shorter time from the onset of stroke to admission to convalescent rehabilitation wards was associated with greater functional improvement.

Early admission to convalescent rehabilitation wards was positively associated with dysphagia improvement. Here, we speculate that this may be because convalescent rehabilitation wards in Japan have a large number of medical personnel, including speech-language-hearing therapists, specialist nurses, and dental hygienists, who are involved in eating and swallowing rehabilitation, while the proportion of such personnel is low in acute care hospitals (Miyai et al. 2011; Okamoto et al. 2014; Shiraishi et al. 2019b, 2020). Consequently, late admission to convalescent wards may lead to poor recovery of dysphagia. Previous studies reported that early commencement of intensive dysphagia rehabilitation was associated with a greater improvement in the swallowing function (Lee et al. 2014; Du et al. 2016) and lower aspiration rates (Bakhtiyari et al. 2015) in stroke patients, which also support our results.

Early admission was associated with a higher rate of discharge to home. The factors influencing the rate of home discharge after stroke rehabilitation include higher age, lower ADL, limited mobility, cognitive impairment, dysphagia, impaired oral status, malnutrition, sarcopenia, and medical needs (Massucci et al. 2006; Yoshimura et al. 2019; Shiraishi et al. 2019a). Here, we showed that early admission was associated with improved ADL and dysphagia. This indirectly suggests that early admission also increases the likelihood of returning home after discharge.

There are some limitations of the current study. First, the retrospective study design and limited number of hospitals might limit the generalizability of the results. Moreover, we could not rule out the possibility that baseline differences between the groups may have influenced the results. We need future multicenter studies to support our results. Second, there could be unmeasured confounders that might affect the results. Accordingly, we were unable to obtain detailed information regarding whether complications were treated, whether intravenous treatment of recombinant tissue plasminogen activator was administered, and the quality and quantity of treatment and rehabilitation in acute care hospitals, which might affect the functional outcomes. High-quality prospective studies are warranted to adjust for these confounding factors. Third, the Kumamoto earthquake occurred in 2016, which was not treated as an adjustment variable in the current study. However, the earthquake may have had a significant impact on the regional health care coordination system in Kumamoto; thus, the results must be carefully interpreted.

In conclusion, the onset-admission interval from acute hospital to convalescent rehabilitation wards is associated with clinical outcomes, including ADLs, swallowing status, and the rate of discharge to home, in ischemic stroke patients, regardless of stroke severity. Based on these findings, we emphasize the importance of close medical cooperation in the regional medical system and transfer to convalescent rehabilitation wards as early as medically acceptable in such patients.

Conflict of Interest

The authors declare no conflict of interest.

References

Bakhtiyari, J., Sarraf, P., Nakhostin-Ansari, N., Tafakhori, A., Logemann, J., Faghihzadeh, S. & Harirchian, M.H. (2015) Effects of early intervention of swallowing therapy on recovery from dysphagia following stroke. *Iran. J. Neurol.*, **14**, 119-124.

Banks, J.L. & Marotta, C.A. (2007) Outcomes validity and reliability of the modified Rankin scale: implications for stroke clinical trials: a literature review and synthesis. *Stroke*, **38**, 1091-1096.

Belagaje, S.R. (2017) Stroke rehabilitation. *Continuum* (*Minneap. Minn.*), **23**, 238-253.

Beninato, M., Gill-Body, K.M., Salles, S., Stark, P.C., Black-Schaffer, R.M. & Stein, J. (2006) Determination of the minimal clinically important difference in the FIM instrument in patients with stroke. *Arch. Phys. Med. Rehabil.*, **87**, 32-39.

Bernhardt, J., Godecke, E., Johnson, L. & Langhorne, P. (2017) Early rehabilitation after stroke. *Curr. Opin. Neurol.*, **30**, 48-54.

Brott, T., Adams, H.P. Jr., Olinger, C.P., Marler, J.R., Barsan, W.G., Biller, J., Spilker, J., Holleran, R., Eberle, R., Hertzberg, V., Rorick, M., Moomaw, C. J. & Walker, M. (1989) Measurements of acute cerebral infarction: a clinical examination scale. *Stroke*, **20**, 864-870.

Charlson, M.E., Pompei, P., Ales, K.L. & MacKenzie, C.R. (1987) A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J. Chronic Dis.*, **40**, 373-383.

Coleman, E.R., Moudgal, R., Lang, K., Hyacinth, H.I., Awosika, O.O., Kissela, B.M. & Feng, W. (2017) Early rehabilitation after stroke: a narrative review. *Curr. Atheroscler. Rep.*, **19**, 59.

Du, J., Yang, F., Liu, L., Hu, J., Cai, B., Liu, W., Xu, G. & Liu, X. (2016) Repetitive transcranial magnetic stimulation for rehabilitation of poststroke dysphagia: a randomized, double-blind clinical trial. *Clin. Neurophysiol.*, **127**, 1907-1913.

Kaifukuki Rehabilitation Ward Association (KRWA) (2016) Kaifukuki Rehabilitation Ward Association. http://www.rehabili.jp/eng/eng_page.html [*Accessed*: June 14, 2020].

Kamo, T., Momosaki, R., Suzuki, K., Asahi, R., Azami, M., Ogihara, H. & Nishida, Y. (2019) Effectiveness of intensive rehabilitation therapy on functional outcomes after stroke: a propensity score analysis based on Japan rehabilitation database. *J. Stroke Cerebrovasc. Dis.*, **28**, 2537-2542.

Kinoshita, S., Momosaki, R., Kakuda, W., Okamoto, T. & Abo, M. (2017) Association between 7 days per week rehabilitation and functional recovery of patients with acute stroke: a retrospective cohort study based on the Japan rehabilitation database. *Arch. Phys. Med. Rehabil.*, **98**, 701-706.

Kunieda, K., Ohno, T., Fujishima, I., Hojo, K. & Morita, T. (2013) Reliability and validity of a tool to measure the severity of dysphagia: the Food Intake LEVEL Scale. *J. Pain Symptom Manage.*, **46**, 201-206.

Kus, S., Muller, M., Strobl, R. & Grill, E. (2011) Patient goals in post-acute geriatric rehabilitation: goal attainment is an indicator for improved functioning. *J. Rehabil. Med.*, **43**, 156-161.

Langhorne, P., Collier, J.M., Bate, P.J., Thuy, M.N. & Bernhardt, J.

(2018) Very early versus delayed mobilisation after stroke. *Cochrane Database Syst. Rev.*, **10**, CD006187.

Langhorne, P., Wu, O., Rodgers, H., Ashburn, A. & Bernhardt, J. (2017) A very early rehabilitation trial after stroke (AVERT): a Phase III, multicentre, randomised controlled trial. *Health Technol. Assess.*, **21**, 1-120.

Lee, K.W., Kim, S.B., Lee, J.H., Lee, S.J., Ri, J.W. & Park, J.G. (2014) The effect of early neuromuscular electrical stimulation therapy in acute/subacute ischemic stroke patients with Dysphagia. *Ann. Rehabil. Med.*, **38**, 153-159.

Massucci, M., Perdon, L., Agosti, M., Celani, M.G., Righetti, E., Recupero, E., Todeschini, E. & Franceschini, M.; Italian Cooperative Research (ICR2) (2006) Prognostic factors of activity limitation and discharge destination after stroke rehabilitation. *Am. J. Phys. Med. Rehabil.*, **85**, 963-970.

Miyai, I., Sonoda, S., Nagai, S., Takayama, Y., Inoue, Y., Kakehi, A., Kurihara, M. & Ishikawa, M. (2011) Results of new policies for inpatient rehabilitation coverage in Japan. *Neurorehabil. Neural Repair*, **25**, 540-547.

Nagano, F., Yoshimura, Y., Bise, T., Shimazu, S. & Shiraishi, A. (2020) Muscle mass gain is positively associated with functional recovery in patients with sarcopenia after stroke. *J. Stroke Cerebrovasc. Dis*., **29**, 105017.

Nakazora, T., Iwamoto, K., Kiyozuka, T., Arimoto, H., Shirotani, T. & Domen, K. (2018) Effectiveness of 7-day versus weekday-only rehabilitation for stroke patients in an acute-care hospital: a retrospective cohort study. *Disabil. Rehabil.*, **40**, 3050-3053.

Okamoto, T., Ando, S., Sonoda, S., Miyai, I. & Ishikawa, M. (2014) "Kaifukuki Rehabilitation Ward" in Japan. *Jpn. J. Rehabil. Med*., **51**, 629-633.

Ottenbacher, K.J., Hsu, Y., Granger, C.V. & Fiedler, R.C. (1996) The reliability of the functional independence measure: a quantitative review. *Arch. Phys. Med. Rehabil.*, **77**, 1226-1232.

Rubenstein, L.Z., Harker, J.O., Salvà, A., Guigoz, Y. & Vellas, B. (2001) Screening for undernutrition in geriatric practice: developing the short-form mini-nutritional assessment (MNA-SF). *J. Gerontol. A Biol. Sci. Med. Sci.*, **56**, M366-372.

Shigematsu, K., Nakano, H. & Watanabe, Y. (2013) The eye response test alone is sufficient to predict stroke outcome: reintroduction of Japan Coma Scale: a cohort study. *BMJ Open*, **3**, e002736.

Shiraishi, A., Wakabayashi, H. & Yoshimura, Y. (2020) Oral management in rehabilitation medicine: oral frailty, oral sarcopenia, and hospital-associated oral problems. *J. Nutr. Health Aging*, **10**, 1-6.

Shiraishi, A., Yoshimura, Y., Wakabayashi, H. & Tsuji, Y. (2017) Poor oral status is associated with rehabilitation outcome in older people. *Geriatr. Gerontol. Int.*, **17**, 598-604.

Shiraishi, A., Yoshimura, Y., Wakabayashi, H. & Tsuji, Y. (2018) Prevalence of stroke-related sarcopenia and its association with poor oral status in post-acute stroke patients: implications for oral sarcopenia. *Clin. Nutr.*, **37**, 204-207.

Shiraishi, A., Yoshimura, Y., Wakabayashi, H., Tsuji, Y., Shimazu, S. & Jeong, S. (2019a) Impaired oral health status on admission is associated with poor clinical outcomes in post-acute inpatients: a prospective cohort study. *Clin. Nutr.*, **38**, 2677-2683.

Shiraishi, A., Yoshimura, Y., Wakabayashi, H., Tsuji, Y., Yamaga, M. & Koga, H. (2019b) Hospital dental hygienist intervention improves activities of daily living, home discharge and mortality in post-acute rehabilitation. *Geriatr. Gerontol. Int.*, **19**, 189-196.

Wakabayashi, H. & Sakuma, K. (2014) Rehabilitation nutrition for sarcopenia with disability: a combination of both rehabilitation and nutrition care management. *J. Cachexia Sarcopenia Muscle*, **5**, 269-277.

Yoshimura, Y., Bise, T., Nagano, F. & Shimazu, S. (2018a) Systemic inflammation in the recovery stage of stroke : its association with sarcopenia and poor functional rehabilitation outcomes. *Prog. Rehabil. Med.*, **3**, 1-10.

Yoshimura, Y., Wakabayashi, H., Bise, T. & Tanoue, M. (2018b) Prevalence of sarcopenia and its association with activities of daily living and dysphagia in convalescent rehabilitation ward inpatients. *Clin. Nutr.*, **37**, 2022-2028.

Yoshimura, Y., Wakabayashi, H., Bise, T., Nagano, F., Shimazu, S., Shiraishi, A., Yamaga, M. & Koga, H. (2019) Sarcopenia is associated with worse recovery of physical function and dysphagia and a lower rate of home discharge in Japanese hospitalized adults undergoing convalescent rehabilitation. *Nutrition*, **61**, 111-118.