Relationship between first mobilization following the onset of stroke and clinical outcomes in patients with ischemic stroke in the general ward of a hospital: A cohort study

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ABSTRACT. Objective: The purpose of this study was to compare the effects of first mobilization following a stroke with independently performing the activities of daily living at discharge in acute phase ischemic stroke patients in a general ward of a hospital. Methods: A total of 158 patients with ischemic strokes were admitted to a general ward from June 1, 2014 to March 31, 2015. Of the 158 patients, 53 met the study’s eligibility criteria. First mobilization was defined as the transfer of a patient from the bed to a wheelchair by a rehabilitation therapist. A favorable primary outcome at discharge was defined as a modified Rankin Scale score of < 3. The outcome was analyzed using the proportional hazards analysis and receiver operating characteristic curves. Results: The age of the participants was 78.2 ± 11.7 years, stroke severity evaluated by the National Institutes of Health Stroke Scale scores on admission was 14.3 ± 10.6 points, and first mobilization of this population was 6.4 ± 5.2 days. Thirteen (25%) patients had a favorable outcome. Hazards analysis showed a favorable outcome due to first mobilization (adjusted hazards ratio 0.80, 95% confidence interval 0.65-0.98; p < 0.05). The cutoff point for first mobilization to produce a favorable outcome was 6.5 days after the stroke onset (area under the curve 0.729; p < 0.05). Conclusion: As seen in stroke units, early first mobilization is associated with improved clinical outcomes in ischemic stroke patients admitted to a general ward.

Key words: early mobilization, stroke, rehabilitation, general ward, clinical outcome

Stroke is the third most frequent cause of death and one of the main causes of acquired adult disability\(^\text{1,2}\). In Japan, approximately more than half of the stroke patients become dependent after acute hospital discharge\(^\text{3}\). In acute-stage rehabilitation, early mobilization is defined as the first mobilization of the patient out of bed following the stroke onset\(^\text{4}\) and is performed in order to facilitate recovery and prevent complications\(^\text{5}\). For example, mortality due to the complications of immobility become is frequently noted in the first week after stroke onset\(^\text{6}\). Furthermore, in many cases, bed rest may delay recovery and even cause harm to the patient\(^\text{7}\). Immobility-related complications were found to be significantly reduced in the Stroke Unit (SU) where early mobilization is part of the standard care protocol\(^\text{8}\). However, the evidence for early mobilization, particularly the timing and intensity, is controversial\(^\text{9}\). Despite the recommendation of early mobilization after a stroke in the guidelines of many countries, a recent study reported possible detrimental effects due to mobilization within 24 hours of a stroke\(^\text{10}\). Furthermore, a recent meta-analysis of early mobilization in patients within 48 hours from stroke onset found that outcomes including degree of independence of Activities of Daily Living (ADL) and immobility-related complications at 3 months were not significantly different compared to the delayed mobilization group\(^\text{11}\). The National Institute for Health and Care Excellence (NICE) committee therefore recommended that very early and intense mobilization should not be routinely offered\(^\text{12}\). Therefore, it is unclear when to initiate mobilization. However, there are some suggestions guiding the intensity of early mobilization. A recent study showed that subjects’ clinical outcomes improved when early mobilization was performed more frequently and at a lower daily duration of activity (i.e., min-
utes of out-of-bed activity per day). However, these studies were executed in a SU that consisted of a specialized stroke-care team. A hallmark of SU is early rehabilitation due to a multidisciplinary team that consists of medical doctors, nurses, rehabilitation therapists, social workers, and other such professionals. In the SU, the patients’ odds of being dead or dependent were reduced by approximately 80% compared to those for patients who were cared for in the general ward. Among the factors that distinguished the SU from the general ward, early mobilization is the strongest predictor of improved outcomes. Previous studies proposed that early mobilization has a powerful effect on the outcome of patients managed in the SU. It may not be possible to carry out systematic rehabilitation for early mobilization, as a specialized stroke-care team, like that in the SU, may not be stationed in the general wards. Therefore, it is also unclear whether frequent lower intensity mobilization can be achieved. Of the 7380 general hospitals in Japan, only 138 (2%) have a specialized stroke care unit (SCU) authorized by the Ministry of Health, Labour and Welfare (MHLW), while majority of hospitals provide stroke care in a general ward. In Europe, the SU and/or stroke centre was certified by the European Stroke Organisation (ESO). It was estimated that only approximately 30% of the stroke patients receive care in the SU. The probability of death or disability was reduced by about 80% for patients with SU care compared to that for patients with conventional care in the general ward in Italian hospitals.

In the United States, comprehensive stroke centers and/or primary stroke centers (PSCs) are certified by the American Heart Association/American Stroke Association and the Joint Commission. It was estimated that only approximately 37% of the stroke patients received care in the PSCs. The probability of 30-day mortality for patients with PSC care was reduced by about 90% compared to that for patients with non-PSC care in the US. Therefore, it is important to investigate the effect of early mobilization on clinical outcomes of stroke patients in a general ward.

In this study, we investigated the relationship between first mobilization out of bed and into a wheelchair following the onset of a stroke and clinical outcomes measured by the modified Rankin Scale (mRS) in a general ward of a hospital.

Materials & Methods

Design & Subjects

This study was designed as a prospective cohort trial with blinded assessment of outcomes, and a modified intention-to-treat (mITT) analysis. Here, mITT analysis only excluded missing data. This study was conducted from June 1, 2014 to March 31, 2015, in Tokyo General Hospital (TGH) in Tokyo, Japan. TGH does not provide critical care medical services but, has a high-care unit for stroke patients and a secondary emergency medical-service center. In addition, TGH has a rehabilitation center for subacute stroke patients aimed at encouraging early discharge of patients home. Eligible patients were aged 18 years or older, had a confirmed first or recurrent ischemic stroke, were admitted to our hospital within 24 hours of the stroke onset, and underwent rehabilitation. Treatment with recombinant tissue plasminogen activator was allowed. Participants were excluded from the study if they had a premorbid mRS score of > 2, which indicated dependence in performing activities of daily living (ADL); length of stay less than 7 days; deterioration within the first hour of admission to our hospital; concurrent progressive neurological disorder; acute coronary syndrome; severe heart failure; lower-limb fracture that prevented mobilization; required palliative care; and mild symptoms with a National Institutes of Health Stroke Scale (NIHSS) score of < 4 on admission. The protocol of this study was approved by TGH research ethics committee (TGH-057) and is in accordance with the Declaration of Helsinki. Informed consent was obtained from patients and/or a legally acceptable representative.

Procedure

All eligible patients received standard care from ward therapists and nursing staff in our hospital. Typically, irrespective of each patient’s state, standard rehabilitation time was 1 hour per day comprising of 20 minutes of physical, occupational, and speech therapy, respectively. Physical therapy included upper and lower extremity stretching, in-bed mobilization, transfer to a wheelchair, walking, climbing stairs, and task-oriented training. Baseline variables included age, sex, stroke severity based on the NIHSS score, a past medical history rated by the Charlson Comorbidity Index (CCI), and pre-stroke independence level graded by the mRS. First mobilization was defined when patients were transferred to a wheelchair from their beds by rehabilitation therapists. In our hospital, the decision to initiate first mobilization was made through discussion by a medical team, including doctors, nurses, and physical therapists based on the patients’ consciousness level, responsiveness, body temperature, blood pressure, and pulse. Consequently, the initiation of first mobilization varied according to the patients’ status. In addition, the first planned mobilization intervention was performed by the rehabilitation therapists. By investigating the relationship between the first mobilization intervention and clinical outcomes in our hospital, we aimed to determine the effect of initiating early mobilization interventions customized to the patients’ status. First mobilization data were extracted from patients’ electronic medical records. Outcome measures were the Barthel Index (BI) and mRS. In the stroke rehabilitation domain, the BI is a valid and reliable measure of dependence in performing ADL and is used to assess independence in 10 everyday activities. The total possible score is 100, and higher scores...
reflect better performance. The mRS is also a valid and reliable measure of functional independence and is commonly used to assess disability after a stroke. The mRS was defined categorically using 7 different grades. A score of \( < 3 \) indicates functional independence and \( > 2 \) indicates functional dependence. A 1-point shift on this scale is often deemed clinically significant because of the large category differences, using independent-samples \( t \) test for the continuous variables and \( \chi^2 \) test for the categorical variables. To investigate the effect of first mobilization on the favorable outcome at discharge, forward selection (likelihood ratio) proportional hazards analysis was performed, with favorable outcome at discharge (mRS \( \leq 2 \)) as an indicator variable. The time variable of this analysis was length of stay. The potential independent variables were first mobilization and baseline confounding variables that were identified as significant variables in the aforementioned univariate analysis (i.e., age, stroke severity on the NIHSS, BI, mRS, CCI, and provided rehabilitation time). Only if early mobilization was found to be significant, was the receiver operating characteristic (ROC) curve plotted, and search optimal cutoff point for favorable outcome. In addition, to investigate the effect of first mobilization on discharge disposition (home), forward selection (likelihood ratio) proportional hazards analysis with discharge disposition (home) as the dependent variable was also performed. Independent variables of this analysis were the same as those above. Again, only if first mobilization was found to be significant was the ROC curve plotted. Finally, using the former cutoff point of first mobilization, baseline characteristics were compared between groups using unpaired \( t \)-tests. The continuous variables were expressed as mean \( \pm \) standard deviation, while the categorical variables were expressed as median (minimum - maximum) for categorical variables, and the nominal variables were expressed as number (percentage). All statistical analyses were performed using SPSS Statistics 22.0 (IBM Corp, Japan).

**Results**

**General results**

During this study period, 158 potentially eligible patients were admitted to our hospital. The 105 excluded patients included 16 patients with a premorbid mRS score \( > 2 \), 9 with a length of stay \( < 7 \) days, 1 with a concurrent progressive neurological disorder, and 80 had mild symptoms. The remaining 53 patients received on-going rehabilitation until discharge and were included in the analyses. Characteristics of this population was 78.2 \( \pm \) 11.7 years, with 31 female patients (58%) and 22 male patients (42%). Median CCI was 1 (0 - 6). Thirty-four patients presented with their first ever stroke (64%), and 19 patients present with a recurrent stroke (36%). Stroke severity on the NIHSS on admission was 14.3 \( \pm \) 10.6 points. The day from stroke onset to first mobilization out of bed was 6.4 \( \pm \) 5.2 days, and length of stay was 78.8 \( \pm \) 59.2 days. A favorable outcome (mRS \( \leq 2 \) at discharge) was found in 13 (25%) patients. A change in mRS score of \( > 2 \) points from admission to discharge was found in 23 (43%) patients. Twenty-five (47%) patients were discharged home, 16 (30%) patients were discharged to a nursing home, 10 (19%) patients were discharged to a sanatorium long-term care hospital, and 3 (6%) patients died before discharge. Mean duration of rehabilitation provided per day at 1 week from the onset of the stroke was 3.1 (1.4 - 6.0) units (1 unit = 20 minutes). Adverse events due to acute-phase rehabilitation did not occur. Results of the baseline assessment at admission and outcome measures at discharge are shown in Table 1, 2.

**The effect of first mobilization on the primary outcome**

The results of comparing the demographic, neurological, and ALD characteristics at baseline between the groups with favorable outcome and poor outcome revealed that there was a significant difference in the age, NIHSS score, mRS score, CCI, and first mobilization. Therefore, the independent variables for the proportional hazards analysis were age, NIHSS score, mRS score, CCI, and first mobilization. Significant variables were not identified. As there were 11 missing datapoints for the NIHSS score where rehabilitation could not be initiated within 24 hours from stroke onset, we excluded the NIHSS score from among the independent variables for this analysis. The result showed that age and mRS score were the significant variables (Table 3). Our purpose of the current study was to investigate the relationship between first mobilization from onset and favorable outcome at discharge, thus, further excluding the mRS score from among the independent variable in this analysis. The result showed that first mobilization and age were the significant variables (Table 3). Adjusted hazards ratio (HR) were 0.80, 95% confidence interval (CI) 0.65 -
A favorable outcome was found to be significantly larger in patients, and the late group consisted of 22 (42%) patients as the early group. The early group consisted of 31 (58%) patients. Therefore, these variables were independent variables for this proportional hazard analysis. The result showed that first mobilization was the independent variable for this proportional hazard analysis. The result showed that first mobilization was the independent variable for this proportional hazard analysis.

The effects of first mobilization on discharge disposition

The results of comparing the demographic, neurological, and ALD characteristics at baseline between the patients discharged to home and those discharged to others revealed that there was a significant difference in the age, NIHSS score, BI, mRS score, CCI, mean duration of rehabilitation provided per day at 1 week from the onset of the stroke, and first mobilization. Therefore, these variables were independent variables for this proportional hazard analysis. The result showed that first mobilization was the independent variable for this proportional hazard analysis.

### Table 1. Baseline characteristics of the participants

|                     | Overall (n=53) | Early group (n=31) | Late group (n=22) | p value |
|---------------------|---------------|--------------------|-------------------|---------|
| **Age (years)**     | 78.2 ± 11.7   | 77.6 ± 12.1        | 79.1 ± 11.2       |         |
| **Sex (number)**    |               |                    |                   |         |
| Male                | 22 (42)       | 12 (39)            | 10 (45)           |         |
| Female              | 31 (58)       | 19 (61)            | 12 (55)           |         |
| **NIHSS (points)**  | 14.3 ± 10.6   | 9.7 ± 7.1          | 22.5 ± 11.1       | **      |
| **mRS (grades)**    | 5 (3 - 5)     | 5 (3 - 5)          | 5 (5 - 5)         |         |
| **BI (points)**     | 6.2 ± 16.5    | 9.5 ± 20.3         | 1.2 ± 5.5         |         |
| **CCI (number)**    | 1 (0 - 6)     | 1 (0 - 4)          | 1 (0 - 6)         |         |

Continuous variables are expressed as mean ± standard deviation, and the categorical variables are expressed as median (minimum - maximum), while the are nominal variables are expressed as number (percentage).

** = p < 0.01, * = p < 0.05

### Table 2. Outcome measures of the participants at discharge

|                     | Overall (n=53) | Early group (n=31) | Late group (n=22) | p value |
|---------------------|---------------|--------------------|-------------------|---------|
| **NIHSS (points)**  | 8.4 ± 9.3     | 5.6 ± 6.9          | 12.5 ± 10.8       | **      |
| **mRS (grades)**    | 4 (1 - 6)     | 3 (1 - 5)          | 5 (2 - 6)         | *       |
| **BI (points)**     | 50.4 ± 36.5   | 62.6 ± 34.4        | 32.8 ± 32.5       | **      |
| **Duration of rehabilitation (units)** | 3.1 (1.4 - 6.0) | 3.5 (2 - 6) | 2.9 (1.4 - 5.3) | * |
| **Discharge disposition (number)** | Home 25 (47) | Home 20 (65) | Home 5 (23) |       |
|                      | Others 28 (53)| Others 11 (35)     | Others 17 (77)    |         |
| **Favorable outcome (nRS ≤ 2 at discharge)** | 13 (25) | 12 (39) | 1 (5) | **      |

Continuous variables are expressed as mean ± standard deviation, and the categorical variables are expressed as median (minimum - maximum), while the are nominal variables are expressed as number (percentage).

** = p < 0.01, * = p < 0.05

0.98 for first mobilization (p < 0.05) and 0.95, 95% CI 0.91 - 0.99, for age (p < 0.05). First mobilization was significant; therefore, we analyzed the ROC curve with first mobilization as a test variable and favorable outcome as an indicator variable. Results showed that the cutoff point of first mobilization to produce a favorable outcome was 6.5 days. Sensitivity was 92.3%, specificity was 52.5%, and the area under the curve (AUC) was 0.73 (p < 0.05, Table 4). Based on this result, we defined early mobilization after > 6.5 days as the late group, and early mobilization of ≤ 6.5 day as the early group. The early group consisted of 31 (58%) patients, and the late group consisted of 22 (42%) patients. A favorable outcome was found to be significantly larger in the early group than in the late group (n=12 [39%] vs. n=1 [5%]; p < 0.01, Table 2).
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Table 3. Results of Cox proportional hazards regression analysis for favorable outcome and discharge to home

| Indicator variable (mRS ≤ 2 at discharge) | Independent variables | Adjusted HR (95% CI) | p value |
|-----------------------------------------|-----------------------|----------------------|---------|
| Model 1                                 | none                  | 0.826 (0.733, 0.932) | **      |
| Model 2                                 | mRS                   | 0.298 (0.096, 0.922) | *       |
| Model 3                                 | Age                   | 0.951 (0.905, 1.00)  | *       |
| Discharge to home                       | First mobilization    | 0.798 (0.649, 0.982) | *       |
| Model 1                                 | First mobilization    | 0.949 (0.905, 0.994) | *       |

First mobilization: days from stroke onset to bed-to-wheelchair transfer; CI: confidence interval; HR: hazard ratio; mRS: modified Rankin scale.

** = p < 0.01, * = p < 0.05

Table 4. Optimal cutoff points of first mobilization for favorable outcome and discharge to home

| Indicator variable (mRS ≤ 2 at discharge) | Test variable | Cutoff points (Days) | Sensitivity (%) | Specificity (%) | AUC  |
|-----------------------------------------|---------------|---------------------|-----------------|-----------------|------|
| Favorable outcome                        | First mobilization | 6.5                | 92.3            | 52.5            | 0.73 |
| Discharge to home                        | First mobilization | 6.5                | 80              | 60.7            | 0.71 |

First mobilization: days from stroke onset to bed-to-wheelchair transfer; AUC: area under the curve.

significant variable (Table 3). Adjusted HR was 0.83, 95% CI 0.73 - 0.93; p < 0.01 for first mobilization. The result of the ROC curve, using discharge disposition as a status variable, showed that cutoff points for first mobilization were 6.5 days. Sensitivity was 80.0%, specificity was 60.7%, and AUC was 0.71 (Table 4). The early group had a significantly larger number of patients who attained discharge home than the late group (n=20 [65%] vs. n=5 [23%]; p < 0.01, Table 2).

Comparison of baseline data between early and late groups

Finally, the comparison of baseline characteristics of subjects was performed by means of having defined early and late groups. Results showed that there were significant differences between stroke severity on the NIHSS (9.7 ± 7.1 vs. 22.5 ± 11.1 for early vs. late, respectively), mRS score (5 [3 - 5] vs. 5 [5 - 5]), and mean daily duration of provided rehabilitation per patient from stroke onset until day 7 (3.5 [2 - 6] units vs. 2.9 [1.4 - 5.3] units, for early vs. late, Table 1, 2). Other variables were not different (Table 1).

Discussion

The purpose of this study was to evaluate the effects of first mobilization following the onset of a stroke on clinical outcomes in ischemic stroke patients in a general ward of a hospital. Due to the varied initiation time of first mobilization due to patients’ states in this study, the study aimed to determine the effect this would have over using predetermined initiation times for early mobilization. The results of this study suggest that patients who mobilize within 1 week of the onset of the stroke are more likely to have favorable outcomes than those who cannot be mobilized. Patients in the early group, who were mobilized out of bed within 6.5 days of the stroke onset, were more likely to attain independence in performing ADL and be discharged home. Similar results have been reported showing that the clinical states found within 7 days of the stroke predict the long-term recovery of motor function and independence in performing ADL. This is the golden period for initiating exogenous restorative therapies such as early mobilization. Cramer stated that during this epoch, endogenous repair-related events reach peak levels. Therefore, the present results indicate that patients who received early mobilization during this golden period have potential for improved recovery after a stroke. In this study, the decision to initiate first mobilization was made by a medical team. Therefore, no patient received forced routine mobilization. This highlights the ability to provide rehabilitation tailored to the patient’s condition. Our study might suggest a natural history of patients treated by standard care, which consists of upper and lower extremity stretching, in bed mobilization, transfer to a wheelchair, walking, climbing stairs, and task-oriented training. It is important that first mobilization out of bed occurs within 7 days after the stroke onset in order
to produce a favorable outcome at discharge.

Generally, early mobilization is defined as out-of-bed activity beginning within 24 or 48 hours after the stroke onset\(^1\). Early mobilization is a very important factor within a stroke unit, and these units have shown better outcomes compared to those in general wards\(^1,5,10,19,21\). However, definitions of a “SU” are not always the same, and significant differences in standards of care can be found\(^31\). Furthermore, the 2014 UK national stroke audit, which used the gold standard of seven SU criteria, reported that the majority of the UK SU beds did not meet this standard\(^31\). Thus, on the one hand, the clinical outcome of stroke patients under SU care was better than that of this in the general wards, on the other hand, the quality of the SUs was not always uniform. As a specialized team for stroke care may not be stationed in the general wards, the quality of care for stroke patients in general wards might be lower than that in the SU. Several patients have been cared for in the general or mixed wards in many countries\(^8,15,16,19,21\). If so, it is important to determine the effects of early mobilization on the clinical outcomes in the general wards. Hence, the advantage of the current study is that it has partially revealed the effects of first mobilization on the favorable outcomes at discharge in the general wards. However, our observational study did not provide all patients with early mobilization and was carried out in a general ward of a hospital. Therefore, it is difficult to make a direct comparison of the present study and previous studies. Nevertheless, the evidence for early mobilization, particularly the timing and intensity, is still controversial\(^8,15,17\). Recently, it is suggested that the efficacy of early mobilization is not determined by the timing of the first mobilization, but rather by the frequency of mobilization\(^30\) and/or time spent in an upright posture\(^32\). Our study did not investigate the frequency of mobilization or time spent in an upright posture but investigated the provided rehabilitation time, which was approximately 1 hour per day. Although this study did not include out-of-bed activity as a form of mobilization, providing approximately 1 hour of rehabilitation time might be useful for preventing immobilization-related complications (IRC\(\)s). For recovery of independence in performing ADL however, patients with mild symptoms received a large amount of rehabilitation time. The early group had significantly milder severity on the NIHSS and received a larger amount of rehabilitation time (Table 1, 2).

Our observational study has several limitations. First, baseline data of participants were not equally distributed between early and late groups. Second limitation is the small sample size. However, the study excluded those patients with mild symptoms. Those included in the study had a baseline NIHSS of 14.3 ± 10.7 points, resulting in a uniform distribution of patients with mild to severe symptoms. The third limitation was that the decision to time of first mobilization after stroke onset was performed by the rehabilitation therapists only. As the NICE guidelines pointed out, the AVERT phase III trial did not include duration of mobilization analyses performed by nurses\(^32\), and the same applies to this study. Fourth, the patients in our observational study were not followed-up after discharge. In Japan, there are rehabilitation hospitals that provide intensive rehabilitation and encourage discharge to home after acute care of a stroke. Therefore, participants in this study had a relatively long period of hospital stay (78.8 ± 59.2 days). Fifth, the effect on the favorable outcome was greater with respect to the mRS score than with first mobilization. After excluding the mRS score from the hazard analysis, first mobilization was extracted as a significant variable. Finally, the definition of first mobilization is qualitative and generalization of the results is difficult. Although it is difficult to directly compare the present study and previous studies\(^8,15,16,19,21\), to the best of our knowledge, the present study reports the effects of first mobilization on the clinical outcomes in the general ward of a hospital for the first time.

The present study investigated the relationship between the time from stroke onset to mobilization and clinical outcomes for ischemic stroke patients in a secondary emergency general hospital. Although this observational study could not exclude the possibility that those with mild symptoms would achieve mobilization earlier, the results showed that the day from stroke onset to the first mobilization out of bed was related to improve clinical outcomes. Further research is needed to clarify the relationship between stroke severity, rehabilitation intensity, and clinical outcomes in a randomized controlled trial.

Conflict of Interest: The authors report no conflict of interest.

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