REVIEW ARTICLE

Effects of early physiatrist and registered therapist operating rehabilitation (PROr) in patients with stroke

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Abstract

The neurological effects of early post-stroke mobilization have recently been reported in animal and clinical studies. In this review, we summarize previous findings on the effects of early post-stroke mobilization. Focusing upon stroke patients, the *A Very Early Rehabilitation Trial* (AVERT) Phase II and Phase III trials examined the effects of early mobilization within 24 h of a stroke. Early mobilization, results suggest, could be both potentially harmful to and potentially beneficial to the post-stroke recovery process. However, while the effect of early rehabilitation on ADL in most previous studies has been examined by nurses and therapists, and only a small number of studies have reported similar assessments conducted by therapists specializing in post-stroke rehabilitation. Conversely, at our hospital, first assessment is by a physician, who then refers patients to a physiatrist, who in turn evaluates the specific needs for rehabilitation, and then refers them to a registered physical therapist and occupational therapist with the aim of providing early mobilization (physiatrist and registered therapist operating rehabilitation: PROr). Based on this background, we conducted two studies to examine the effects of PROr in patients that have had a stroke. Rehabilitation within 24 h of stroke onset did not increase the risk of mortality or recurrence, but several benefits were suggested.

Key words: *early rehabilitation, cerebrovascular disease, activities of daily living.*

INTRODUCTION

Under the current medical care system in Japan, stroke patients showing good recovery are typically discharged directly from acute care facilities to their homes, whereas those with poor recovery are typically discharged to long-term care facilities (Ikegami, 2011). Improvement of physical function is critical to maintaining the ability to perform activities of daily living (ADLs) in patients after a stroke. Increasing physical fitness could therefore shorten the time to home-discharge after a stroke, consequently reducing medical costs. Immediate hospitalization, tissue plasminogen activator, and early mobilization have been proposed to be effective in improving the prognosis of patients after a stroke (Winstein, 2016). Early mobilization includes procedures that facilitate the ability of patients to walk or move, which is characterized by a shorter period of hospitalization or bed rest than is normally practiced, such as early sitting, transfer, standing, and walking. (Bernhardt, 2008; Chippala, 2016; Cumming, 2011; Herisson, 2016; Liu, 2014; Sundseth, 2014). The neurological effects of early post-stroke mobilization have recently been reported in animal and clinical studies. In this review, we summarize reported findings on the effects of early post-stroke mobilization. We explore the idea that patients that have had a stroke seem to benefit from rehabilitation applied within 24 h after a stroke.

Experiments with animals

Animal studies have shown that early mobilization protects against further ischemic brain injury and improves exercise performance by promoting angiogenesis, inhibiting acute inflammatory responses and neuronal apoptosis, and protecting the blood-brain barrier (Zhang, 2015). Mobilization from the first day after a stroke improved brain plasticity more than mobilization beginning on the seventh day, suggesting that the first 24 h may be a crucial time to implement mobilization (Ng, 2015; Zeiler, 2016). Another study (Yang, 2003) involved the ligation of the middle cerebral artery of rats for 60 min. One-week mild treadmill training starting

within 24 h after ligation caused a higher reduction in infarction volume and resulted in a better recovery of locomotive function at two weeks after ligation, compared with that observed in the no-training group. Conversely, functional improvement was similar to that of the control group when training was initiated seven days after ligation (Yang, 2003). In another study, ischemia was experimentally induced in the hindlimb area of the left motor cortex. An immediate increase in the neuronal firing rate in that area was noted when the treadmill training of the rats was initiated within 24 h, but not when training was initiated seven days after ligation (Nielsen, 2013). The effects of early mobility on neurotransmitter levels were examined in another study, (Chang, 2009). Strokes were induced in rats by occluding their middle cerebral artery for 1 h, and then they were subjected to exercise on a treadmill for 2 weeks starting 24 h after the occlusion. This early mobilization increased their levels of striatal extracellular glutamate, brain-derived neurotropic factor, and p-Synapsin I compared with those in the control rats that did not exercise. Early mobilization after cerebral ischemia seems to decrease histological damage and enhance functional recovery.

Experiments with humans

For patients after a stroke, early mobilization within 24 h did not increase the mortality rate at three months post onset, and the outcome of ADL at 12 months was improved compared with when starting mobilization from 24 h to 48 h, as reported by the *A Very Early Rehabilitation Trial* (AVERT) phase II studies (Bernhardt, 2008; Cumming, 2008, 2011; Sorbello, 2009; Tay-Teo, 2008; Tyedin, 2010). Furthermore, early mobilization did not affect the incidence of adverse events in the AVERT phase III trial, but resulted in a smaller chance of a favorable outcome on the modified Rankin Scale (mRS) score compared with usual care (AVERT Trial Collaboration group, 2015). Early mobilization has been reported to be both potentially harmful and potentially beneficial to the post-stroke recovery process (Li, 2018). However, the effect of early rehabilitation on ADLs has been examined in most previous studies by nurses and therapists, and only a few studies have reported similar assessments conducted by therapists specializing in post-stroke rehabilitation. Furthermore, the rate of home-discharge during post-stroke rehabilitation has not been the focus of previous studies.

Physiatrist and registered therapist operating rehabilitation: PROr

At our hospital, first assessment of all patients is by a physician, who then refers them to a physiatrist, who evaluates the specific needs for rehabilitation. Patients are then referred to a registered physical therapist (PT) and occupational therapist (OT) who provide early mobilization (physiatrist and registered therapist operating rehabilitation: PROr). We believe that a well-trained PT and OT can provide intensive and long-term rehabilitation and early mobilization. Such differences in rehabilitation programs could possibly result in differences in the risks associated with such programs. The patients were mobilized out of bed during the first rehabilitation. Mobilization, which refers to all out-of-bed activities, was performed by the PT and OT. Mobilization on the first day was conducted under continuous monitoring of the patients' vital signs and consciousness levels. Rehabilitation typically involved resistance exercises, exercises of daily living, standing position, and gait training with a long-leg orthosis. PROr aims for high-intensity and high-frequency mobilization as much as possible for each patient. The rehabilitation program was applied five days per week. Based on the above-described background, we conducted two studies to examine the effects of PROr in patients after a stroke. First, we investigated whether early PROr increases ADL recovery during acute hospital stay (Study 1) (Kinoshita, 2017). Secondly, we examined the effect of early PROr implementation for 6 months (Study 2) (Kinoshita, 2021).

Subjects and study design

This prospective cohort study was conducted at the Department of Rehabilitation Medicine, Wakayama Medical University Hospital. At our hospital, physiatrists select early mobilization tailored to the severity, type, and time since the stroke. A total of 233 eligible patients were admitted to the emergency room of our hospital between June 2014 and April 2015 and were referred to our department for consultation regarding their suitability for rehabilitation therapy. Eligibility criteria were as follows: acute stroke (ischemic or hemorrhagic) diagnosed by neurosurgeons and/or neurologists, age >18 years, and no concurrent chronic or progressive disorder, such as amyotrophic lateral sclerosis, severe heart failure, or lower-limb fracture preventing mobilization, at the time of first examination in the emergency room before the start of rehabilitation therapy. Of the 233 patients, six were excluded: five non-ambulatory

patients (mRS >4) and one patient with cancer who required palliative care. The remaining 227 patients were divided into the following three groups according to the time from the onset of stroke: patients with very early mobilization (VEM, *n* = 47) started the rehabilitation program within 24 h of stroke onset, patients with early mobilization (EM, *n* = 77) started the same program between 24 and 48 h of stroke onset, and patients with late mobilization (LM, *n* = 103) started after 48 of stroke onset. The start time of the rehabilitation program depended on the treatment plans set by neurosurgery doctors. All patients started PROr under the management of physiatrists as soon as possible. A study flow diagram is shown in Figure 1, which outlines the reasons for exclusion of patients. The duration of hospitalization was significantly longer in the LM group than that in the VEM group (Table 1).

Outcome measures

All patients included in this study were assessed during their first rehabilitation and discharge, six months after their stroke. The outcome measures were the mortality, recurrence rate, functional independence measure (FIM), mRS, National Institute of Health score scale (NIHSS) score and Glasgow coma scale (GCS), the home-discharge rate (to home, to inpatient rehabilitation facilities, or to other medical facilities). Each measured parameter was evaluated by a skilled PT with no association with the present study. The mortality and recurrence rates were calculated during the entire period of the six-month fol-

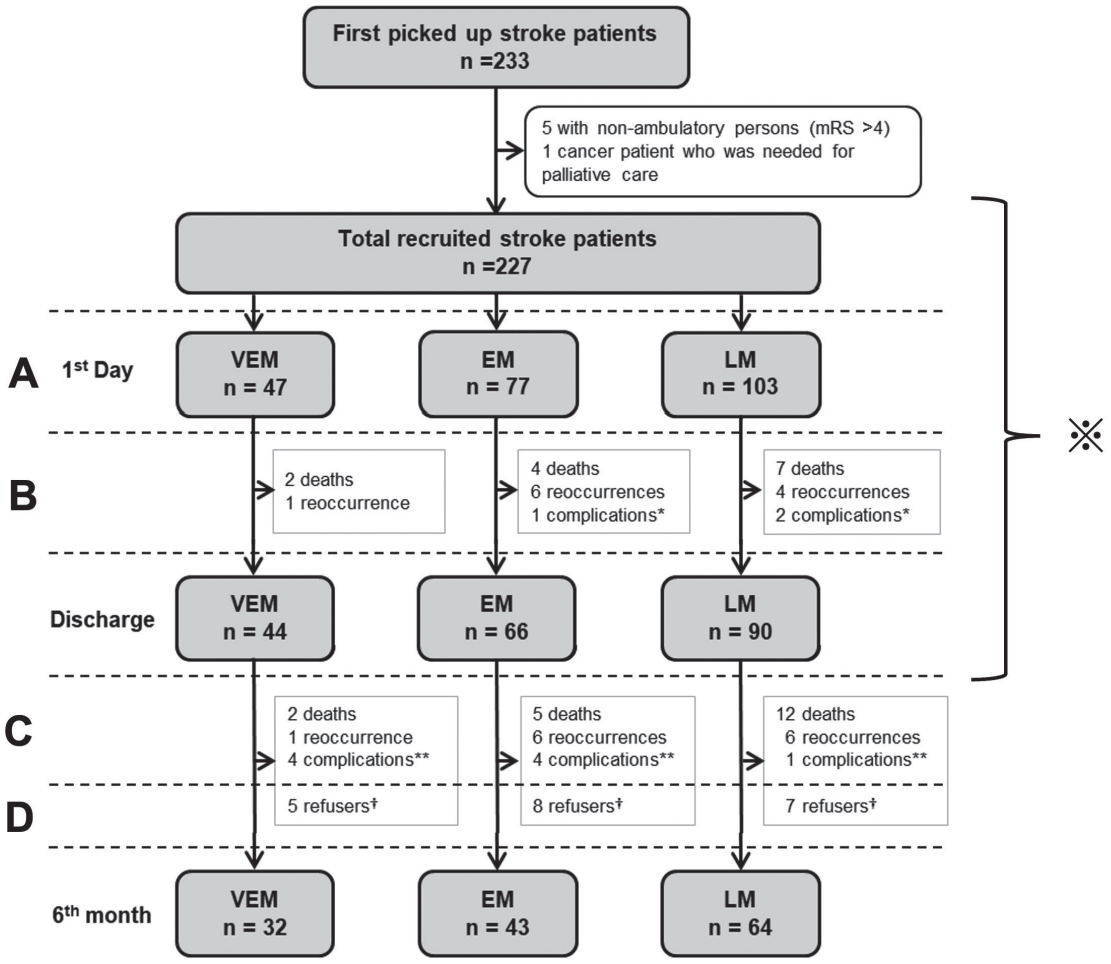

Figure 1. Flow chart of patients' enrolment and number of patients at each stage. VEM: very early mobilization (rehabilitation therapy started within 24 h of onset of stroke), EM: early mobilization (started 24–48 h), LM: late mobilization (started 48 h after), mRS: modified Rankin Scale score, 1st day: the first day of rehabilitation therapy, Discharge: at discharge from the acute hospital, 6 months: 6 months after stroke onset. Number of patients at first day are represented as 'A'. Number of deaths: reoccurrences of stroke and additionally got complications between first day and discharge (B), between discharge and sixth month (C), and number of refusers between discharge and sixth month (D) are shown. (※) *Number of patients who were excluded due to severe heart failure and acute myocardial infarction; **Number of patients who were excluded due to presence of heart failure, pancreatic cancer, brain cancer, epilepsy, or liver cirrhosis; † Family and patients who did not accept our estimation of functional independence measure or who failed to reply to our questions about outcomes after discharge from our hospital

Table 1. Baseline characteristics of patients

	VEM group	EM group	LM group
n	47	77	103
Age (years)	72.4±2.2	77.3±1.4	77.3±1.2
Gender (females/males)	23 / 24	39 / 38	44 / 59
Height (cm)	159±1.5	158±1.0	158±0.9
Weight (kg)	60±2.1	57±1.3	56±1.2
Type of stroke (Hemorrhage / infarction)	18 / 29	12 / 65	34 / 69
Duration of hospital stay (days)	14.2±1.1 (n=44)	16.3±1.2 (n=66)	19.5±1.1† (n=90)
Time spent in rehabilitation per person (min/day)	73.9±3.3 (n=44)	69.4±3.0 (n=66)	69.3±2.4 (n=90)

The duration of hospitalization and rehabilitation are expressed as mean ± SEM, and one-way ANOVA was used to compare differences among groups. $^{\dagger}p<0.05$, compared with the VEM group. VEM: very early mobilization (started within 24 h), EM: early mobilization (started within 24–48 h), LM: later mobilization (started 48 h after).

low-up after the exclusion of refusers (populations A–D, Figure 1). The FIM (total 18 items) consists of the motor subscale (13 items) and cognition subscale (5 items), with each item scored on a seven-point ordinal scale. The mRS defines six levels of disability (de Haan, 1995; van Swieten, 1988), while the FIM is a basic indicator of severity of disability (Chumney, 2010; Heinemann, 1993; Linacre, 1994). Several studies have concluded that the FIM is more sensitive for the evaluation of ADL than the mRS and Barthel Index (BI) (Dromerick, 2003; Granger, 1990; Keith, 1987; Mahoney, 1965; Roberts,1998). NIHSS is a 15-item neurological examination scale used to evaluate the effects of acute cerebral infarction on the level of consciousness, language, neglect, visual field loss, extraocular movement, motor strength, ataxia, dysarthria, and sensory loss (Brott, 1989; Goldstein, 1989). GCS is a tool used by medical professionals to objectively evaluate the degree of consciousness or coma, and the results are scaled between 3 and 15, with high scores indicating higher levels of consciousness (Teasdale, 1979, 2014). The home-discharge rate was compared using the following two models: the percentage of patients who returned home in each population that included all patients (excluding refusers) after discharge (= A – D) and additionally excluding patients who died, had recurrent stroke or additional complications (= A – [B + C + D]), indicated as Models 1 and 2, respectively (Figure 1).

STUDY 1: Effects of early PROr during acute hospitalization (Kinoshita, 2017)

Mortality and recurrent stroke

The total number of deaths was 13 out of 227 (5.7%), and 11 patients (4.8%) developed another stroke during the study period. There were two deaths in the VEM group (4.3%), four in the EM group (5.2%), and seven in the LM groups (6.8%). There was one incidence of repeat strokes in the VEM group (2.1%), six repeat strokes in the EM group (7.8%), and four in the LM group (3.9%). There was no significant difference in the number of deaths and recurrent strokes among the three groups.

Functional independence measure

The total FIM scores improved significantly in the VEM (86.0±5.1), EM (74.3±4.7), and LM (71.2±3.9) groups at discharge compared with the respective values before the first rehabilitation (53.4±3.9, 54.3±4.2, and 51.3±3.5) (Table 2). In addition, the motor and cognition subscales of FIM scores were significantly improved compared with the value before the first rehabilitation (Table 2). The gains in the total FIM (32.6±3.0) and motor subscale (28.5±2.7) scores in the VEM group were significantly greater than those in the EM (20.2±2.3 and 17.7±2.1, respectively) and LM (19.9±2.2 and 15.9±1.8, respectively) groups. However, the gain in the cognition subscale of FIM (VEM, 4.1±0.8; EM, 2.7±0.5; and LM, 4.0±0.7) scores was not significantly different among the three groups (Figure 2).

Modified Rankin scale

The mRS improved significantly in the VEM (3.0±0.2), EM (3.5±0.2), and LM (3.6±0.1) groups at discharge compared with the respective values before the first rehabilitation (4.0±0.2, 4.1±0.2, and 4.3±0.1) (Table 2). However, there was no significant difference in the gain of the mRS score (VEM, -1.0±0.1; EM, -0.5±0.1; and LM, -0.7±0.1) among the three groups.

National Institute of Health stroke scale

The NIHSS score improved significantly in the VEM (4.4±1.0), EM (8.1±1.1), and LM (8.3±1.0) groups at discharge compared with the respective values before the first rehabilitation (7.3±1.1, 10.6±1.3, and 12.2±1.2). Further analysis showed that the NIHSS score of the VEM group at discharge was significantly lower than that of the LM group (Table 2), but there was no significant difference in the gain of the NIHSS score (VEM, -2.9±0.5; EM, -2.5±0.4; and LM, -3.9±0.5) among the three groups.

Glasgow coma scale

The GCS score improved significantly in the VEM (14.7±0.1), EM (13.7±0.3), and LM (13.8±0.3) groups at discharge (range: 3–62 days) compared with the respective values before the first rehabilitation (13.8±0.3, 13.0±0.4, and 12.6±0.4). Further analysis

Table 2. Changes in Functional Independence Measure (FIM), modified Rankin Scale (mRS), National Institute of Health Stroke Scale (NIHSS) and Glasgow Coma Scale (GCS).

	First rehabilitation			Discharge		
	VEM	EM	LM	VEM	EM	LM
	n = 44	n = 66	n = 90	n = 44	n = 66	n = 90
Total FIM	53.4±3.9	54.3±4.2	51.3±3.5	86.0±5.1†	74.3±4.7†	71.2±3.9†
Motor subscale	30.3±2.8	33.3±2.9	31.7±2.4	58.8±4.0†	50.9±3.5†	47.6±3.0†
Cognition subscale	23.1±1.6	21.0±1.5	19.6±1.3	27.3±1.3†	23.4±1.4†	23.6±1.2†
mRS	4.0±0.2	4.1±0.2	4.3±0.1	3.0±0.2†	3.5±0.2†	3.6±0.1†
NIHSS	7.3±1.1	10.6±1.3	12.2±1.2	4.4±1.0†	8.1±1.1†	8.3±1.0†,*
GCS	13.8±0.3	13.0±0.4	12.6±0.4	14.7±0.1†	13.7±0.3†,*	13.8±0.3†,*

Data are mean±SEM.
Differences between the parameters before and after rehabilitation were examined using the Wilcoxon signed rank test. $^{\dagger}p<0.05$, compared with the first rehabilitation and discharge.
The FIM, mRS, NIHSS and GCS data were tested using the Kruskal-Wallis test. Dunn's test was used for subsequent post hoc tests to determine the significance of the differences among the three groups.
* $p<0.05$, compared with the VEM group. VEM, very early mobilization (started within 24 h); EM, early mobilization (started within 24–48 h); LM, later mobilization (started 48 h after).

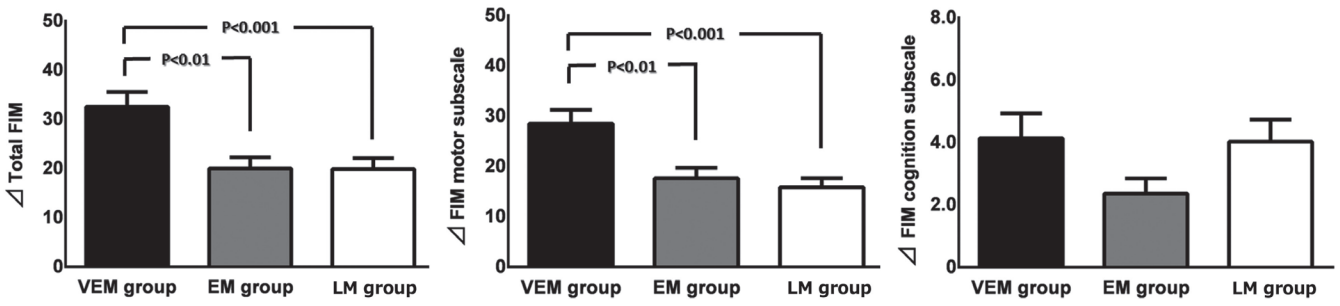

Figure 2. Gain in Functional Independence Measure (FIM). Data are mean±SEM.
VEM: very early mobilization (started within 24 h), EM: early mobilization (started 24–48 h), LM: late mobilization (started 48 h after).

showed that the GCS of the VEM group at discharge was significantly higher than that of the EM and LM groups (Table 2), but there was no significant difference in the GCS gain (VEM, 0.9±0.2; EM, 0.7±0.2; and LM, 1.2±0.2) among the three groups.

STUDY 2: Effect of early PROr implementation for six months (Kinoshita, 2021)

Follow-up survey

Exclusion criteria was met by 12, 23, and 26 patients in the VEM, EM, and LM groups, respectively (Figure 1), because of death, recurrence of stroke, complications, such as severe heart failure, acute myocardial infarction, pancreatic and brain cancers, epilepsy, liver cirrhosis, or due to refusal (C + D). Thus, 32, 43, and 64 patients completed the six-month follow-up in the VEM, EM, and LM groups, respectively (Figure 1).

Mortality and recurrent stroke

The stroke recurrence rates were between 4.8% to 17.4% during the entire study period, and there were no significant differences among the groups (all, p >0.12) (Table 5). The mortality rate was between 9.5% and 19.8% during the entire study period, also with no significant differences among the groups (all p > 0.25).

Home-discharge rate

The home-discharge rates during the entire period based on the two models applied in this study are shown in Table 3. In Model 1, the home-discharge rate was significantly higher in the VEM group than in the EM and LM groups (p = 0.009 and p = 0.038, respectively). In Model 2, the home-discharge rate was significantly higher in the VEM group than in the EM group (p = 0.034) and tended to be higher than that in the LM group (p = 0.084).

Functional independence measure

The total FIM score was significantly higher at discharge and further increased at the sixth months after stroke onset in all groups (data not shown), but the increase in score throughout the entire period was greater in the VEM group than in the LM group (Table 4). The improvement in the motor subscale of the FIM contributed to a larger improvement in the total FIM score (Table 4).

Modified Rankin scale, and National Institutes of Health stroke scale

The mRS and NIHSS scores significantly decreased (i.e., improved) at discharge and six months after the

Table 3. Mortality and recurrence rates during the entire observation period.

	VEM	EM	LM	p value
Number of deaths (Mortality %)	4/42 (9.5%)	9/69 (13.0%)	19/96 (19.8%)	0.244
Number of recurrent stroke (recurrent rate %)	2/42 (4.8%)	12/69 (17.4%)	10/96 (10.4%)	0.116

Values are the number and rate (%) of death and recurrent stroke. p values represent the results of the χ^2 test. VEM: very early mobilization (started within 24 h), EM: early mobilization (started between 24 and 48 h), LM: later mobilization (started 48 h after).

Table 4. Home-discharge rate during the entire observation period

	VEM	EM	LM	p value
Model 1	26/42 (62%)	25/69 (36%)	41/96 (43%)	0.028
Model 2	26/32 (81%)	25/43 (58%)	41/64 (64%)	0.099

Models 1 and 2 show the home-discharge rates calculated from the populations of A – D and A – (B + C + D), respectively, as shown in Figure 1. p values represent the results of the χ^2 test. VEM: very early mobilization (started within 24 h), EM: early mobilization (started between 24 and 48 h), LM: later mobilization (started 48 h after).

onset of stroke in all groups (data not shown), and there was no significant difference in the decreases among the groups (Table 4).

Glasgow coma scale

The GCS score was significantly improved in all groups, compared with that on the first day of rehabilitation (data not shown), while the improvements were not different among the groups at any time period (Table 4).

DISCUSSION

There were four major findings of Study 1. The number of deaths and recurrent strokes were not significantly different among the three groups. Secondly, the gains in total FIM and motor subscale scores during hospitalization showed significantly higher improvement in the VEM than in the EM and LM groups. Thirdly, the GCS score at discharge showed a significantly better improvement in the VEM group than in the EM and LM groups. Finally, the improvements

Table 5. Changes (Δ) in FIM, mRS, NIHSS and GCS.

		Before discharge	After discharge	Entire period
ΔTotal FIM	VEM	34.5 (21.0–52.8) *,†	18.0 (0.5–32.8)	49.0 (33.8–74.0) †
	EM	15.0 (7.0–35.0)	12.0 (2.0–29.0)	32.0 (15.0–65.0)
	LM	17.5 (7.0–28.8)	12.5 (0–29.8)	34.5 (8.3–61.0)
ΔMotor subscale	VEM	32.0 (17.3–45.5) *,†	10.5 (0.3–27.5)	45.0 (30.0–66.0) †
	EM	15.0 (5.0–27.0)	10.0 (1.0–27.0)	28.0 (8.0–54.0)
	LM	14.0 (6.0–24.0)	10.5 (0–23.0)	28.0 (7.3–50.8)
ΔCognition subscale	VEM	4.5 (0–6.8)	2.0 (0–5.8)	5.0 (1.5–11.5)
	EM	0 (0–6.0)	1.0 (0–6.0)	3.0 (0–14.0)
	LM	0 (0–.0)	0 (0–5.0)	3.5 (0–11.0)
ΔmRS	VEM	-1.0 (-2.0–0)	-1.0 (-1.8–0)	-2.0 (-3.0 to -1.0)
	EM	0 (-1.0–0)	-1.0 (-1.0–0)	-1.0 (-3.0–0)
	LM	-1.0 (-1.0–0)	-1.0 (-2.0–0)	-2.0 (-3.0–0.3)
ΔNIHSS	VEM	-2.0 (-4.0 to -1.0)	-0.5 (-3.0–0)	-3.5 (-5.8 to -2.0)
	EM	-2.0 (-4.0–0)	-1.0 (-5.0–1.0)	-4.0 (-7.0–0)
	LM	-2.0 (-4.8–0)	-1.0 (-3.0–0)	-2.0 (-7.0–1.0)
ΔGCS	VEM	0 (0–1.0)	0 (0–0)	0.5 (0–1.8)
	EM	0 (0–1.0)	0 (0–0)	0 (0–1.0)
	LM	0 (0–1.0)	0 (0–0)	0 (0–2.0)

Values are shown as medians (interquartile range: IQR). Before discharge, between 1st day of rehabilitation and discharge from the acute hospital; after discharge, from discharge to 6 months after the onset of stroke; entire period, from 1st day to 6 months after stroke. The other abbreviations are the same as those in the previous tables. The Kruskal-Wallis test was used to examine differences in the changes in FIM, mRS, NIHSS and GCS scores during each time duration among the three groups, followed by the Dunn test as a post-hoc test.
* $p<0.05$, compared with EM; † $p<0.05$, compared with LM.
VEM, very early mobilization (started within 24 h); EM, early mobilization (started between 24 and 48 h); LM, later mobilization (started 48 h after); FIM, Functional Independence Measure; mRS, modified Rankin Scale; NIHSS, National Institute of Health Stroke Scale; GCS, Glasgow Coma Scale

in the mRS and GCS scores were not significantly different among the three groups. PROr is therefore suggested to pose no risk and it can improve the FIM score during the acute phase of a stroke.

We consider that an important factor responsible for the successful improvement in the FIM score observed in the present study was the application of a 70-min PROr by well-trained PTs and OTs under the guidance of physiatrists in the acute phase. The patients with very early mobilization underwent rehabilitation therapy for only 31 min/day (IQR 16.5–50.5) by nursing staff as well as physiotherapists in AVERT phase III. This issue is important because it was reported that the duration of rehabilitation sessions is an important determinant of improvements in stroke patients (Lohse, 2014), suggesting that the "dose" of rehabilitation therapy was insufficient to result in perceivable benefits in the AVERT study. Physiatrists, PTs, and OTs are familiar with kinesiology and exercise physiology, and recognize the clinical benefits of standing and exercise. In addition to the clinical consequences of a stroke, these specialists can rule out the risks of rehabilitation activities for the cardiovascular and respiratory systems as well as for the spine, bones, and joints. Consequently, PTs and OTs can safely apply very early mobilization, even in comatose patients and those under mechanical ventilation.

The AVERT phase II trial reported no significant difference in the number of deaths between intensive mobilization that started within 24 h, and mobilization that started 24–48 h after stroke onset (Bernhardt, 2008). In the present study, the timing of the start of rehabilitation relative to the onset of stroke did not significantly alter the number of deaths or recurrent strokes. Our results support the findings of the AVERT phase II trial (Bernhardt, 2008). In the AVERT phase II trial, the mortality rate was 8.5% (6/71) when rehabilitation was started within 2 weeks of stroke onset and 13.2% (5/38) when rehabilitation was started within 24 h of stroke onset (Bernhardt, 2008). In our study, the mortality rate was 5.7% when rehabilitation was started at approximately two weeks of stroke onset and 4.3% in the VEM group. PROr is suggested by this and previous studies to be clinically beneficial and is not associated with a worsened mortality in the acute hospitalization period.

In Study 2, the home-discharge rate during the entire study period was significantly higher in the VEM group than in the EM and LM groups, while the rates of stroke recurrence and mortality in the VEM group did not worsen at six months after discharge compared with the other two groups. The higher home-discharge rate at six-month follow-up might be related to the higher total FIM. Very early mobilization (PROr) within 24 h is therefore possibly beneficial for patients after acute stroke.

In the present study, the home-discharge rate was 20% higher in patients who started PROr within 24 h of stroke onset. The discharge destination of patients with acute stroke is influenced by a variety of factors, including demographic background, socioeconomic status, and clinical severity (Freburger, 2011; Pinedo, 2014; Stineman, 2014). Previous studies demonstrated that the stroke type, FIM score on admission, and comorbidities were independent and significant predictors of home return in Japan, and that the home-discharge rate was higher in patients with cerebral infarction than in those with cerebral hemorrhage (Itaya, 2017). However, the ratio of hemorrhage/infarction in patients who could be followed up to six months after stroke tended to be higher in the VEM group than in the other groups. However, there were no differences in the types and severity of stroke among the groups at the time of admission. For every one-point increase in the FIM score, patients were reported to be approximately 1.08 times more likely to be discharged to their homes than to institutionalized care (Thorpe, 2018). In this study, improvements in eight and nine items of the FIM motor subscale between the first day of rehabilitation and discharge, respectively, were significantly larger in the VEM group than in the EM and LM groups. The main reason for the higher home-discharge rate in the VEM group was therefore likely to be the greater improvement of the FIM score during admission compared with that observed in the EM and LM groups due to prescribed PROr. The home-discharge rate cannot be compared directly with the rate reported in previous studies involving other countries due to differences in healthcare systems, timing of measurements, and severity of disease between different countries. Nonetheless, our findings suggest a beneficial effect of very early rehabilitation on the home-discharge rate.

In our study, the mortality rate was less than 10% in the VEM group. In the AVERT phase II trial, there was no significant difference in mortality at 6 months after stroke between mobilization within 24 h and after 24 h of stroke (23.6% and 15.2%, respectively) (Bernhardt, 2008). Similarly, the AVERT phase III trial showed no significant difference in mortality between the early mobilization (8%) and other groups (7%) (AVERT Trial Collaboration group, 2015). Furthermore, the Shiga Stroke Registry in Japan had 13.2% deaths within 28 days after stroke among 2,955 patients, ir-

respective of rehabilitation therapy (Takashima, 2017). The mortality rate in the present study was comparable to those reported in these studies. Our results therefore support the concept that very early post-onset PROr does not increase the risk of mortality or the recurrence rate at six months.

The present study has certain limitations. First, it was a prospective cohort study and not a randomized controlled trial. Second, although the results revealed a better functional outcome in patients who started mobilization within 24 h, we cannot make a definitive claim about the impact of the time of rehabilitation in patients with acute stroke. However, the study extends the message that patients with stroke seem to benefit from rehabilitation applied within 24 h of a stroke.

CONCLUSION

PROr within 24 h of stroke onset resulted in an enhanced rate of home discharge up to six months of follow-up, with no additional risk of mortality or stroke recurrence. The higher rate of home discharge might be the result of a larger improvement in ADL in cases where PROr was started within 24 h of a stroke. This study therefore extends the message that patients possibly benefit from rehabilitation within 24 h of stroke onset.

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