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Dose-Response Effect of Daily Rehabilitation Time on Functional Gain in Stroke Patients

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Objective To demonstrate the effect of daily treatment time on recovery of functional outcomes and how each type of rehabilitation treatment influences the improvement of subgroups of functional outcomes in stroke patients.

Methods We conducted a retrospective study in 168 patients who were admitted to the Department of Rehabilitation Medicine between 2015 and 2016. Patients who experienced their first-ever stroke and unilateral lesions were included. All patients underwent conventional rehabilitation treatment, and each treatment was administered one to two times a day depending on individual and treatment room schedules. Based on the mean daily treatment time, patients were divided into two groups: a high-amount group (n=54) and low-amount group (n=114). Outcomes were measured through the Korean version of Modified Barthel Index (MBI), Fugl-Meyer Assessment of the upper extremity, Trunk Impairment Scale (TIS), and Berg Balance Scale (BBS) scores on admission and at discharge.

Results The functional change and scores at discharge of MBI, TIS, and BBS were greater in the high-amount group than in the low-amount group. Among various types of rehabilitation treatments, occupational therapy training showed significant correlation with MBI, TIS, and BBS gain from admission to discharge.

Conclusion The amount of daily mean treatment in post-stroke patients plays an important role in recovery. Mean daily rehabilitation treatment time seems to correlate with improved balance and basic activities of daily living after stroke.

Keywords Rehabilitation, Hemiplegia, Cerebrovascular disorders, Gait

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INTRODUCTION

Stroke is a leading cause of disability among adults and can result in survival with permanent sequelae impairing physical function, balance, and daily living [1]. Rehabilitation treatment is crucial for post-stroke patients after they are discharged from the hospital [2]. Previous studies have shown that intensive rehabilitation treatment and early initiation of rehabilitation interventions may be associated with an improvement in functional outcomes after stroke [3-5]. At least 3 hours of rehabilitation treatment per day for at least 5 days/week has been recommended for post-stroke inpatients [4,6]. Recent studies [7,8] have suggested that augmented exercise therapy in the first 6 months post-stroke has small to moderate effects on activities of daily living (ADL), walking ability, and walking speed of patients. Because various components of exercise therapy affect stroke patients' recovery, it is essential to determine the relationship between these components and functional outcomes [9,10]. In the past, studies have been conducted to determine the relationship between the amount of treatment and functional outcomes. However, the effect of treatment time on various subgroups of functional outcomes has not been wellstudied, and standardized therapeutic times have not been established, especially in Asia [11,12]. The purpose of this study was to examine the dose-response effect of daily treatment time on functional outcomes, and to demonstrate how each type of exercise influences improvement in subgroups of functional outcomes in stroke patients. We hypothesized that the higher the amount of rehabilitation treatment, the more likely it is for a poststroke patient to recover.

MATERIALS AND METHODS

Study design and subjects

We conducted a retrospective study in 168 patients, aged 18 years or older, who were admitted to the Department of Rehabilitation Medicine at Chungnam National University Hospital between January 2015 and December 2016. The study protocol was approved by the Institutional Review Board of Chungnam National University Hospital (No. 2019-01-057). Patients with the first-ever stroke, unilateral lesions, those within 1 month from stroke onset to hospitalization time, and those motor grades below fair were included. All stroke patients had undergone computed tomography or magnetic resonance imaging to confirm the diagnosis. Exclusion criteria were (1) patients who failed to perform rehabilitation treatment for more than 1 week during the hospitalization period or more than 1 hour per day due to a comorbidity, (2) patients who were unable to undergo intensive rehabilitation due to a transfer to other departments during hospitalization, (3) a short length of stay in the rehabilitation facility (<7 days), and (4) poor cooperation with 2 points in the National Institutes of Health Stroke Scale (NIHSS) 1c.

The following patient characteristics were obtained by reviewing medical records: age; sex; stroke characteristics (type, side, location); initial functional status determined by the NIHSS, Korean version of Modified Barthel Index (K-MBI), Fugl-Meyer Assessment of the upper extremity (FMA_UE), Trunk Impairment Scale (TIS), and Berg Balance Scale (BBS) scores; time to admission from stroke; total number of treatment sessions; and time of rehabilitation treatment during hospitalization.

Rehabilitation treatment

During inpatient therapy, patients participated in four types of conventional rehabilitation treatment: physiotherapy, occupational therapy (OT), functional gait training, and neuromuscular electrical stimulation (NMES) therapy. Rehabilitation treatments were provided by licensed physical and occupational therapists, and every rehabilitation treatment session was for 30 minutes every day for 5 days a week. Rehabilitation treatment was performed up to twice a day as needed, and the prescription and enforcement of the treatment were modified according to the patient's condition.

Physiotherapy

Physiotherapy is commonly used to enhance the functional recovery of stroke patients in the acute phase, because of its convenience and practicability [3]. It is an integral component to improve patients' mobility, static balance, dynamic balance, and ambulation. The components of physical therapy include trunk and head control, midline orientation, sitting with weight shift, sit-to-stand balance, then stepping in a controlled environment with the help of a physical therapist [13,14]. A single treatment session was 30 minutes.

Functional gait training

Functional gait training can be all therapeutic strategies to improve patients' walking balance and performance with the help of techniques and instruments, such as body weight support gait training, standing table, balance trainer, treadmill, lower extremity strengthening training, and robotic gait assist gait training [15]. A single treatment session was 30 minutes.

Occupational therapy

OT included various practices for upper extremity utilization in which the patient attempts to move their hemiparetic arm in single-joint movements before proceeding gradually to more complex, multi-joint actions. It also contained task-specific practices such as reaching to grasp a cup. Patients also practiced strengthening their hemiparetic arm and fine motor training for their daily living, including constraint-induced movement therapy [15]. Two types of OT were performed: group OT and individual OT. In group OT, 3 patients were matched with 1 therapist for treatment of upper limb function, such as upper limb muscle strength and fine motor training. In individual OT, one patient performed upper limb rehabilitation, manipulation, and ADL training such as eating, dressing, chair/bed transfer, toileting, and ambulation with one therapist. In both treatments, exercise times per session were the same at 30 minutes.

Neuromuscular electrical stimulation

NMES is a technique that utilizes the peripheral nerves and muscles unaffected by damage to the central nervous system. Electrical stimulation was applied to trigger the contraction and relaxation of selected muscle groups by Neurotech 16F (BMR Neurotech Inc., Phoenix, AZ, USA). While walking, excitation of the common peroneal nerve by an externally placed stimulator results in dorsiflexion at the ankle to aid paretic foot clearance [15]. A single treatment session was 30 minutes.

Mean daily treatment time

The total number of treatments was counted as the sum of all rehabilitation sessions during hospitalization. The mean daily treatment time was measured by dividing the total rehabilitation treatment time in minutes (total number of treatments \times 30 minutes) by the length of stay (LOS) in the rehabilitation facility except on Saturdays and Sundays for each type of rehabilitation treatment. Because patients performed rehabilitation treatments for only 5 days in a week, the number of days used for the actual calculation was only 5/7 of the total LOS [4].

Mean daily treatment time= Total number of rehabilitation treatment × 30 minute Length of stay × 5/7

Outcome measures

K-MBI

The K-MBI consists of 10 items including hygiene, bathing, eating, toileting, dressing, and bowel and bladder control. It was used to measure the independence level of the participants. The complete independence score for each item is 10 points, totaling to 100 points [16,17].

FMA_UE

The FMA_UE quantifies the motor function of the lower limbs, with 17 items assessing reflexes, movement, and coordination. Each item is scored on a 3-point ordinal scale ranging from 0 to 2, and the total possible score is 34 [18].

TIS

The TIS consists of three subscales: static sitting balance, dynamic sitting balance, and co-ordination. Each subscale contains 3-10 items. The TIS score ranges from a minimum of 0 to a maximum of 23 [19,20].

BBS

The BBS is a 14-item scale that quantitatively assesses balance and risk for falls in older community-dwelling adults through direct observation of their performance. The scale requires 10 to 20 minutes to complete and measures the patient's ability to maintain balance, either statically or while performing various functional movements, for a specified duration of time. The items are scored from 0 to 4, with a score of 0 representing an inability to complete the task and a score of 4 representing independent item completion. A global score is calculated out of 56 possible points [21].

Each functional outcome was evaluated on admission and at discharge, and functional gain was obtained by the difference between functional outcome between admission and discharge.

Data analysis

All patients were categorized based on a mean daily treatment time of 3hours from the American Stroke Association guideline into two groups: a high-amount group (n=54; mean daily treatment time \geq 3 hr/day) and a lowamount group (n=114; mean daily treatment time <3 hr/day) [6]. Statistical analyses were performed using SPSS version 22 for Windows (IBM, Armonk, NY, USA). The groups were compared using the t-test and chi-squared test according to the characteristics of the variables. Variables were compared to search for associations between the patient's baseline characteristics and functional gain using statistical tests (Spearman correlation for sex, stroke type, and stroke location and Pearson correlation for age, initial functional status, time to admission, LOS). The multiple linear regression was performed to iden-

tify the effect of treatment amount of each rehabilitation strategies.

RESULTS

The descriptive statistics of the study groups are presented in Table 1. A total of 114 patients were included in the low-amount group and 54 patients in the highamount group. There were no significant differences in NIHSS, K-MBI, FMA_UE, TIS, or BBS scores; age, onset time to admission, lesion type, side, or length of stay between the two groups except stroke location. Furthermore, the mean daily rehabilitation treatment time between the two groups was significantly different (2.3 hr/ day in the low-amount group vs. 3.26 hr/day in the highamount group; p<0.001).

| Table 1. General and clinical characteristics of patients at the baseline |
|--|
|--|

| Parameter | Low amount group | High amount group | p-value | |
|---------------------------|-------------------|-------------------|---------|--|
| Sex | | | 0.097 | |
| Male | 56 | 23 | | |
| Female | 58 | 31 | | |
| Age (yr) | 71.22±13.33 | 67.20 ± 12.20 | 0.070 | |
| Туре | | | 0.096 | |
| Ischemic | 90 (78.9) | 39 (72.2) | | |
| Hemorrhagic | 24 (21.1) | 15 (27.8) | | |
| Side | | | 0.131 | |
| Right | 53 (46.5) | 25 (46.3) | | |
| Left | 61 (53.5) | 29 (53.7) | | |
| Lesion | | | 0.001* | |
| Cortical | 44 (38.6) | 9 (16.7) | | |
| Subcortical | 55 (48.2) | 32 (59.3) | | |
| Brainstem | 15 (13.2) | 13 (24.1) | | |
| NIHSS | 7.37±3.96 | 6.42 ± 2.97 | 0.880 | |
| K-MBI | 33.67±21.42 | 39.96 ± 16.97 | 0.060 | |
| FMA_UE | 20.18±18.58 | 19.61±18.02 | 0.849 | |
| TIS | 9.12±7.23 | 11.05 ± 5.85 | 0.091 | |
| BBS | 14.84 ± 17.51 | 13.61 ± 14.24 | 0.651 | |
| Time to admission (day) | 10.28±9.52 | 10.18 ± 7.78 | 0.940 | |
| LOS (day) | 53.89 ± 18.90 | 55.18 ± 16.15 | 0.666 | |
| Daily treatment time (hr) | 2.30±0.55 | 3.26±0.16 | 0.001* | |

Values are presented as mean±standard deviation or number (%).

NIHSS, National Institutes of Health Status of Stroke; K-MBI, Korean version of Modified Barthel Index; FMA_UE, Fugl-Meyer Assessment of the upper extremity; TIS, Trunk Impairment Scale; BBS, Berg Balance Scale; LOS, length of stay.

*p<0.05.

Comparisons of functional gain during hospitalization and functional outcome at discharge between the two groups are described in Table 2. Both groups showed significant improvements in MBI, FMA_UE, BBS, and TIS scores after rehabilitation treatment. Patients in the highamount group showed more functional gain and better functional outcome than patients in the low-amount group. K-MBI, BBS, and TIS scores were significantly different between two groups. However, FMA UE scores were not significantly different. Patients in the highamount group showed a 25.74-point improvement in the MBI score, which was higher than the 18.09-point improvement in the low-amount group (p=0.01). For TIS scores, patients in the high-amount group showed a 7.70-point improvement, which was higher than the 5.75-point improvement in the low-amount group (p=0.039). Patients in the high-amount group showed a 24.42-point improvement in BBS scores, which was higher than the 14.09-point improvement in the low-amount group (p<0.001).

Age, initial functional status (MBI, FMA-UE, TIS, BBS), and LOS showed significant correlation with functional gain. In the Spearman analysis, only stroke location showed significant correlation with functional gain (r=0.241, p=0.002). Table 3 shows the detailed data of correlation between baseline characteristics and functional gain.

Table 4 described results of the relationships between each rehabilitation treatment and patient characteristics and functional gain by multiple linear regression. The correlation between rehabilitation treatment and MBI gain showed significant beta coefficients in the order of individual OT (β =0.325, p=0.011), group OT, and physiotherapy. In TIS gain, significant beta coefficients were ob-

| Outcome | Low amount group | High amount group | p-value | |
|------------------|-------------------|-------------------|---------|--|
| MBI discharge | 51.77±23.47 | 65.70±19.52 | 0.000* | |
| FMA_UE discharge | 31.71±21.73 | 34.09 ± 21.93 | 0.511 | |
| TIS discharge | 14.92 ± 6.94 | 18.90 ± 4.84 | 0.000* | |
| BBS discharge | 29.07±19.42 | 38.03±16.41 | 0.002* | |
| MBI gain | 18.09 ± 15.57 | 25.74±12.39 | 0.010* | |
| FMA_UE gain | 11.53±12.34 | 14.48 ± 11.74 | 0.144 | |
| TIS gain | 5.75±5.46 | 7.70 ± 6.08 | 0.039* | |
| BBS gain | 14.09±13.58 | 24.42±14.47 | 0.000* | |

Table 2. Comparison of functional outcome and functional gain between the two groups

Values are presented as mean±standard deviation.

MBI, Modified Barthel Index; FMA_UE, Fugl-Meyer Assessment of the upper extremity; TIS, Trunk Impairment Scale; BBS, Berg Balance Scale.

*p<0.05.

| Table 3. Pearson correlation analysis for correlation between baseline characteristics and functional gair | n |
|--|---|
|--|---|

| | MBI gain | | FMA_UE gain | | TIS gain | | BBS gain | |
|-------------------|----------|---------|-------------|---------|----------|---------|-----------------|---------|
| | r | p-value | r | p-value | r | p-value | r | p-value |
| Age | -0.233 | 0.017* | -0.127 | 0.100 | 0.046 | 0.557 | -0.235 | 0.010* |
| Time to admission | -0.004 | 0.959 | -0.087 | 0.261 | 0.077 | 0.320 | 0.054 | 0.483 |
| Initial MBI | -0.164 | 0.034* | 0.189 | 0.014* | -0.276 | 0.000* | -0.037 | 0.633 |
| Initial FMA_UE | 0.093 | 0.228 | -0.027 | 0.729 | -0.217 | 0.005* | -0.127 | 0.100 |
| Initial TIS | 0.067 | 0.391 | 0.139 | 0.074 | -0.462 | 0.000* | 0.000 | 0.999 |
| Initial BBS | -0.036 | 0.643 | 0.120 | 0.121 | -0.428 | 0.000* | -0.265 | 0.001* |
| Length of stay | 0.091 | 0.240 | 0.058 | 0.455 | 0.285 | 0.000* | 0.162 | 0.036* |

r, Pearson correlation coefficient; MBI, Modified Barthel Index; FMA_UE, Fugl-Meyer Assessment of the upper extremity; TIS, Trunk Impairment Scale; BBS, Berg Balance Scale. *p<0.05.

| | MBI gain | | FMA_UE gain | | TIS gain | | BBS gain | |
|--------------------------|----------|---------|-------------|---------|----------|---------|----------|---------|
| | β | p-value | β | p-value | β | p-value | β | p-value |
| Physiotherapy | 0.128 | 0.042* | 0.151 | 0.214 | 0.121 | 0.036* | 0.147 | 0.031* |
| Functional gait training | 0.088 | 0.071 | 0.150 | 0.243 | 0.156 | 0.029* | 0.189 | 0.023* |
| Individual OT | 0.325 | 0.011* | 0.192 | 0.122 | 0.255 | 0.002* | 0.266 | 0.010* |
| Group OT | 0.190 | 0.029* | 0.040 | 0.675 | 0.207 | 0.012* | 0.204 | 0.016* |
| Age | -0.363 | 0.014* | 0.012 | 0.896 | -0.152 | 0.083 | -0.406 | 0.001* |
| Stroke location | 0.004 | 0.959 | 0.155 | 0.055 | 0.055 | 0.409 | -0.023 | 0.740 |
| Initial MBI | -0.744 | 0.000* | 0.086 | 0.528 | -0.029 | 0.803 | 0.086 | 0.471 |
| Initial FMA_UE | 0.225 | 0.009* | -0.127 | 0.177 | 0.093 | 0.235 | -0.016 | 0.846 |
| Initial TIS | 0.345 | 0.004* | 0.069 | 0.600 | -0.474 | 0.000* | 0.396 | 0.001* |
| Initial BBS | 0.059 | 0.659 | 0.084 | 0.575 | -0.113 | 0.363 | -0.695 | 0.000* |
| Length of stay | -0.166 | 0.153 | -0.054 | 0.674 | -0.072 | 0.499 | -0.118 | 0.293 |

Table 4. Multiple linear regression analysis for correlation between significant baseline characteristics and rehabilitation treatment on functional gain

β, standardized coefficient for multiple linear regression; MBI, Modified Barthel Index; FMA_UE, Fugl-Meyer Assessment of the upper extremity; TIS, Trunk Impairment Scale; BBS, Berg Balance Scale; OT, occupational therapy. *p<0.05.

served in the order of individual OT (β =0.255, p=0.002), group OT, functional gait training, and physiotherapy. In BBS gain, significant beta coefficients were also observed in the order of individual OT (β =0.266, p=0.010), group OT, functional gait training, and physiotherapy.

Based on the analysis of the relationship between the patients' baseline characteristics and functional gain, age showed a significantly negative correlation with MBI and BBS gain and a negative trend with TIS gain. Initial MBI scores showed a negative correlation (β =-0.744, p<0.001) with MBI gain and initial FMA_UE and TIS showed positive correlations. Each initial functional status showed significant negative correlations with functional gain except FMA_UE. Initial TIS scores showed a negative correlation with TIS gain (β =-0.474, p<0.001), but a positive correlation with BBS gain (β =0.396, p=0.001).

DISCUSSION

The results of this study also confirmed that the mean daily treatment time plays an important role in the recovery and prognosis of patients' functional status after stroke because the functional gain and discharge status based on K-MBI, TIS, and BBS scores were superior in the high-amount group, which supports the positive effect of treatment time on functional gains as shown in previous studies [9,22]. Multiple regression analysis to confirm the relationship between rehabilitation treatment and functional gain showed that individual OT was significantly correlated with improved MBI, TIS, and BBS scores after rehabilitation treatment. It seems that individual OT could play an important role not only in improving ADL, but also in improving balance of patients. It is considered that training such as reaching, grasping, and moving objects in the sitting position positively affected trunk control and balance improvement of patients. In analyzing balance improvement, physiotherapy and functional gait training showed a significant but low coefficient in balance improvement.

Furthermore, it suggests that the amount of rehabilitation treatment plays an important role in patients' recovery. We assumed that the more than 3 hours daily amount of rehabilitation during the hospital stay can increase experience-dependent neural plasticity, and it improved functional gain through sufficient task repetition to induce plasticity during stroke recovery [23].

Age and initial functional status showed strong negative correlations with each functional gain except FMA_ UE. The negative effect of age on ADL in stroke recovery was consistent with previous studies [24], and the negative correlation of initial functional status with functional gain can be interpreted as a ceiling effect where the higher the initial status is, the less the functional gain. TIS and BBS gains, which are indicators of balance, showed opposite correlations with initial TIS scores. Trunk balance is mainly evaluated during the TIS test, whereas in the BBS test, there are comprehensive evaluation items on whole-body balance, such as standing, reaching, turning, and standing on one leg. Therefore, initial trunk stability shows a ceiling effect in terms of TIS improvement, whereas it also can be interpreted as the better the patient's initial trunk stability, the more positive the correlation with functional gain and comprehensive balance improvement. This is also in agreement with a study of Di Monaco et al. [25] of the association between trunk performance and functional ability in stroke recovery.

The present study has a few limitations. First, this was a retrospective study, which may have led to a less detailed correlation between treatment and functional recovery due to the lack of randomization. Thus, there was a significant difference in initial stroke lesions. Second, there was no significant functional recovery in FMA_UE, which was similar to the results of Kwakkel's study [9] demonstrating that a greater intensity of rehabilitation treatment leads to a small improvement in the function of upper extremities. Third, there were some differences between groups in baseline characteristics. There was a significant difference in stroke lesions between groups. In particular, 38% of patients in the low-amount group had cortical lesions, whereas 16% of patients did in the high-amount group. This may have introduced bias affecting the patients' functional gain. In addition, although not significant, age was lower; initial MBI and initial TIS scores were higher in the high-amount group than the lowamount group, which may be an unfavorable tendency in the functional gain in the high-amount group due to negative correlation between initial status and functional gain.

Finally, we could not evaluate patients' participation, interest, or willingness regarding each rehabilitation treatment, which are also important during the rehabilitation process.

In conclusion, this study confirmed that the mean daily treatment time of rehabilitation treatment plays an important role for stroke patients. Among the rehabilitation treatment strategies, OT showed the highest correlation with ADL performance and balance function. Future analyses should focus on improving upper extremity function and consider more robust, prospective studies including those on patient comorbidities.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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AUTHOR CONTRIBUTION

Conceptualization: Jee S, Sohn MK. Methodology: Ko H, Kim H. Formal analysis: Ko H, Kim H. Funding acquisition: Jee S. Project administration: Jee S. Visualization: Ko H, Jee S. Writing – original draft: Ko H, Jee S. Writing – review and editing: Ko H, Jee S, Sohn MK. Approval of final manuscript: all authors.

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