Effect of hybrid assistive limb treatment on maximal walking speed and six-minute walking distance during stroke rehabilitation: a pilot study

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Abstract. [Purpose] In stroke rehabilitation, gait assessment measures the maximal walking speed and six-minute walking distance, both of which have not been thoroughly investigated as determinants of walking ability. Here, we assessed the methods for evaluating these gait parameters using clinical data on hybrid assistive limb treatment compared with conventional training. [Participants and Methods] In total, 20 stroke patients (hybrid assistive limb group, n=9; conventional group, n=11) participated in this randomized controlled trial. For 12 sessions (three times per week in 4 weeks), the hybrid assistive limb and conventional groups performed gait treatment with hybrid assistive limb and conventional gait training, respectively. Short physical performance battery and walking ability (maximal walking speed and six-minute walking distance) were evaluated pre- and post-intervention. Subsequently, the patients were divided further into two groups: low- and high-balance score groups. [Results] Maximum walking speed and six-minute walking distance were significantly associated, with a positive relationship observed post-intervention. The high-balance score group showed a significant improvement in the six-minute walking distance compared to the low-balance score group. However, no significant improvement in maximum walking speed was observed between both groups. [Conclusion] Due to its sensitivity in detecting differences in balance, six-minute walking distance may be a useful assessment parameter for stroke rehabilitation, particularly in the recovery of physiological walking ability.

Key words: Gait assessment, Stroke rehabilitation, Hybrid assistive limb

INTRODUCTION

There are many evaluation methods in the stroke rehabilitation field, including motor and gait function, activities of daily living, and quality of life1). Walking ability includes the degree of independent walking, walking speed, and walking endurance; indicators for evaluating these include the functional ambulation category (FAC), walking speed (maximal walking speed, MWS or comfortable walking speed, CWS), and the six-minute walking distance (6MWD)2-4). Independent walking, gait speed, and gait endurance are important to many stroke patients5, 6). Walking endurance, motor function, and balance play an essential role in post-stroke home and community walking activity7).

Independent walking is significantly associated with affected lower limb function, balance ability, and CWS6). Furthermore, 6MWD correlates with balance ability in stroke patients5). More so than exercise tolerance, 6MWD as an assessment tool is related to better walking ability, muscle strength for paretic lower limbs, and balance ability6, 11). In addition to the affected lower limb function, balance is an important parameter that affects 6MWD11).
Recently, studies have compared the characteristics of MWS and 6MWD in assessing walking ability\(^7,\ 12\). Fulk et al.\(^7\) found that although both the 6MWD and CWS are strongly related to community walking activity, only 6MWD is a significant predictor. Another study has suggested that 6MWD has better sensitivity and specificity than CWS for determining balance\(^12,\ 13\). Moreover, although CWS can predict home and community ambulators, the cut-off values commonly used to discriminate between home and community ambulators may overestimate actual walking activity\(^7\). Dalgas et al.\(^14\) suggested that there is a strong correlation between the walking speeds of a short walking test (10 m) and a long walking test (6MWD) in patients with stroke (r=0.94), whereas correlations in healthy participants are weak (r=0.69). Therefore, in stroke patients with a walking ability similar to that of a healthy person, the 10-m walk test alone may be insufficient to evaluate walking ability.

In the last decade, gait treatment using a wearable cyborg hybrid assisted limb (HAL) has been promoted in the stroke rehabilitation field. Such a treatment has significantly improved the independent walking, gait speed, gait endurance, and gait posture of stroke patients\(^15-18\).

However, these parameters have been insufficient to assess gait ability due to unclear evaluation methods during HAL treatment. Therefore, a wearable cyborg HAL was used as a new treatment tool for stroke rehabilitation and a randomized, controlled trial of two groups (HAL therapy group or conventional therapy group) was undertaken to measure both MWS and 6MWD before and after therapy. Using most of these data, our research group previously published an article in the *Archives of Physical Medicine and Rehabilitation* about the effects of gait treatment with HAL compared with that of conventional therapy in stroke patients\(^19\). As our observations surpassed the scope of that previous study, however, the pilot study herein reports further clinical data from that study by comparing the abilities of MWS and 6MWD to assess the characteristics of gait parameters in the stroke rehabilitation field.

### PARTICIPANTS AND METHODS

This randomized controlled trial enrolled 47 subacute-to-recovery stroke patients who met eligibility criteria. The data reported herein are additional findings of a previous study; thus, the inclusion and exclusion criteria were same as those of previous studies\(^19,\ 20\). Thirty-three patients were randomly assigned into two groups (HAL or conventional group) at a 1:1 allocation ratio, not including assignment factors. Eight patients withdrew from the study. Therefore, 25 stroke patients (HAL group, n=12; conventional group, n=13) participated in this study. Both groups received normal traditional physical therapy, occupational therapy, and speech therapy. Additionally, the HAL group underwent gait treatment with HAL. By contrast, the conventional group performed conventional gait training for 20 minutes once per day three times per week, for a total of 12 sessions over 4 weeks. As this study was a pilot study to investigate the efficacy and to confirm the variations in data, the sample size was not statistically calculated. FAC, MWS, step length, cadence, 6MWD, short physical performance battery (SPPB), and Fugl-Meyer assessment for lower extremities (FMA-LE) were measured before and after the therapeutic intervention. The ethics committee of the University of Tsukuba approved this study (approval number: 727 and 727-1), and all patients or their legal representatives provided written informed consent. This study is registered in the University Hospital Medical Information Network clinical trials registry in Japan with the registration number UMIN000022335. Differences in the baseline variables between the HAL and conventional groups were determined using the Fisher’s exact test for categorical data and using the Mann-Whitney U test for continuous data. Correlations were calculated using Spearman’s rank correlation coefficient, and the regression coefficient was calculated using simple regression analysis. The outcome measures in each group were compared before and after gait training using the Wilcoxon signed-rank test; the Mann-Whitney U test was used to compare the amount of change between both groups. All statistical analyses were conducted using IBM SPSS version 24.0 (IBM Corp., Armonk, NY, USA). Statistical significance was set at p<0.05.

### RESULTS

Three patients in the HAL group and two patients in the conventional group were excluded from statistical analysis because these patients did not undergo MWS and 6MWD. Therefore, 9 patients in the HAL group and 11 in the conventional group were statistically analyzed after therapeutic intervention. One patient in the conventional group did not undergo MWS and 6MWD after therapeutic intervention. There were no significant differences in baseline characteristics, e.g., gender, time to stroke onset, and eligibility (cerebral infarction or intracerebral hemorrhage) in the groups. However, age, step length, and FMA-LE balance scores were significantly different within the two groups before intervention (p<0.05); the HAL group was younger and had better balance than the conventional group before intervention (Table 1).

Both groups experienced significant improvement in many parameters (Table 2), including FAC, MWS, cadence, 6MWD, SPPB total scores, SPPB balance score, SPPB gait score, SPPB sit-to-stand score, and timed up-and-go (TUG) (p<0.05). Step length and FMA-LE tended to improve, albeit not significantly. In the HAL group, the FAC, 6MWD, and SPPB total scores significantly improvement after therapeutic intervention (p<0.05), and the MWS, SPPB sit-to stand score, FMA-LE, and cadence had only an insignificant trend of improvement. The FAC, MWS, cadence, 6MWD, SPPB total scores, SPPB balance scores, and TUG significantly improved in the conventional group (p<0.05), but other parameters showed no significant differences.
There was a significant positive relationship between post-6MWD and post-MWS treatments, as analyzed using Spearman's rank correlation coefficient. Similar results were obtained for other parameters; however, no significant correlation was found between 6MWD and FMA-LE.

Figure 1 compares MWS and 6MWD changes between low-balance and high-balance score groups after intervention. Based on these parameters, the participants were sub-divided into a low SPPB balance group (0–1 score) and high SPPB balance group (2–4 score). The high SPPB balance group showed significant improvement in 6MWD compared with the low SPPB balance group (p<0.05). MWS was not significantly improved in either group.

### Table 1. Demographic and baseline characteristics of patients

| Characteristics                      | All Participants (n=20) | HAL group (n=9) | Conventional group (n=11) | p value |
|--------------------------------------|------------------------|----------------|--------------------------|---------|
| Age (years)                          | 69.6 ± 15.6            | 60.0 ± 11.7    | 77.4 ± 14.3              | 0.006a  |
| Gender (male/female)                 | 10/10                  | 6/3            | 4/7                      | 0.37b   |
| Height (cm)                          | 157.9 ± 11.3           | 162.1 ± 9.6    | 154.4 ± 11.8             | 0.15a   |
| Weight (kg)                          | 57.5 ± 15.6            | 61.1 ± 9.9     | 54.5 ± 19.1              | 0.09a   |
| Hemiparesis (right/left)             | 8/12                   | 4/5            | 4/7                      | 1.00b   |
| Type of lesion (ischemic/hemorrhagic) | 11/9                  | 5/4            | 6/5                      | 1.00b   |
| Time since stroke (days)             | 52.9 ± 41.9            | 60.7 ± 50.7    | 46.5 ± 34.4              | 0.88a   |

**Baseline data**

| FAC                                  | 2.4 ± 0.7               | 2.5 ± 0.7       | 2.2 ± 0.7                | 0.45a   |
| MWS (m/min)                          | 30.3 ± 29.2             | 33.9 ± 26.2     | 27.5 ± 32.3              | 0.26a   |
| Step length (m)                      | 0.33 ± 0.17             | 0.37 ± 0.16     | 0.29 ± 0.18              | 0.15a   |
| Cadence (steps/min)                  | 78.0 ± 35.9             | 81.5 ± 36.3     | 75.1 ± 37.1              | 0.50a   |
| 6MWD (m)                             | 119.3 ± 118.7           | 122.6 ± 104.1   | 116.7 ± 134.5            | 0.55a   |
| FMA-LE                               | 21.7 ± 4.2              | 21.1 ± 4.6      | 22.2 ± 4.0               | 0.50a   |
| SPPB total                           | 5.3 ± 3.5               | 6.8 ± 1.9       | 4.0 ± 4.0                | 0.06a   |
| SPPB balance                         | 2.1 ± 1.6               | 3.2 ± 0.8       | 1.2 ± 1.6                | 0.01a   |
| SPPB gait                            | 1.8 ± 1.1               | 1.7 ± 1.2       | 1.8 ± 1.2                | 0.94a   |
| SPPB sit-to stand                    | 1.3 ± 1.3               | 1.8 ± 1.0       | 0.9 ± 1.3                | 0.06a   |
| TUG                                  | 40.9 ± 23.8             | 33.9 ± 22.4     | 46.6 ± 24.4              | 0.26a   |

FAC: Functional Ambulation Category; MWS: Maximal Walking Speed; 6MWD: 6-minute walking distance; FMA-LE: Fugl-Meyer Assessment of the lower extremity; SPPB: Short Physical Performance Battery; TUG: Timed Up-and-Go test. Values are Mean ± SD or number, aMann-Whitney U test, bFisher's exact test.

### Table 2. Comparison of the outcomes each group at pre and post intervention

| All participants (n=20) | HAL group (n=9) | Conventional group (n=11) | p value# |
|-------------------------|----------------|--------------------------|---------|
| **Pre**                 | **Post**       | **Pre**                  | **Post** | **change** | **Pre** | **Post** | **change** | **p value** |
| FAC                     | 2.4 ± 0.7      | 3.3 ± 1.07               | 2.5 ± 0.7 | 3.6 ± 0.87   | 1.1     | 2.2 ± 0.7 | 3.0 ± 1.07   | 0.7          | 0.20       |
| MWS (m/min)             | 27.9 ± 27.8    | 40.0 ± 29.07             | 33.9 ± 26.2 | 45.5 ± 29.3  | 11.6    | 22.5 ± 29.4 | 35.0 ± 29.4  | 12.4         | 1.00       |
| Step length (m)         | 0.33 ± 0.17    | 0.37 ± 0.16              | 0.37 ± 0.16 | 0.41 ± 0.15   | 0.03    | 0.29 ± 0.18 | 0.34 ± 0.18   | 0.05         | 0.50       |
| Cadence (steps/min)     | 78.0 ± 35.9    | 98.4 ± 34.37             | 81.5 ± 36.3 | 98.0 ± 43.9  | 16.5    | 75.1 ± 37.1 | 98.7 ± 26.3   | 23.5         | 0.65       |
| 6MWD (m)                | 107.7 ± 109.7  | 168.5 ± 126.57           | 122.6 ± 104.1 | 192.8 ± 125.37 | 70.2    | 94.3 ± 118.4 | 146.6 ± 130.27 | 52.2         | 0.54       |
| FMA-LE                  | 21.7 ± 4.2     | 23.2 ± 4.0               | 21.1 ± 4.6 | 22.6 ± 4.2    | 1.5     | 22.2 ± 4.0 | 23.7 ± 4.0    | 1.4          | 0.76       |
| SPPB total              | 5.3 ± 3.5      | 7.2 ± 3.7               | 6.8 ± 1.9 | 8.4 ± 2.87   | 1.5     | 4.0 ± 4.0 | 6.1 ± 4.2    | 2.1          | 0.65       |
| SPPB balance            | 2.1 ± 1.6      | 2.8 ± 1.5               | 3.2 ± 0.8 | 3.4 ± 1.0    | 0.2     | 1.2 ± 1.6 | 2.2 ± 1.7    | 1.0          | 0.20       |
| SPPB gait               | 1.8 ± 1.1      | 2.2 ± 1.2               | 1.7 ± 1.2 | 2.3 ± 1.3    | 0.5     | 1.8 ± 1.2 | 2.1 ± 1.2    | 0.3          | 0.88       |
| SPPB sit-to stand       | 1.3 ± 1.3      | 2.0 ± 1.7               | 1.8 ± 1.0 | 2.6 ± 1.5    | 0.7     | 0.9 ± 1.3 | 1.5 ± 1.8    | 0.6          | 0.60       |
| TUG                     | 40.9 ± 23.8    | 30.6 ± 34.4              | 33.9 ± 22.4 | 32.9 ± 49.0  | −0.91   | 46.6 ± 24.4 | 28.6 ± 17.9   | −17.9        | 0.33       |

FAC: Functional Ambulation Category; MWS: Maximal Walking Speed; 6MWD: 6-minute walking distance; FMA-LE: Fugl-Meyer Assessment of the lower extremity; SPPB: Short Physical Performance Battery; TUG: Timed Up-and-Go test. Values are Mean ± SD.

#Differences of between HAL and Conventional group, *p<0.05. One patient in the conventional group did not undergo MWS and 6MWD after therapeutic intervention.
The regression coefficient between the pre-treatment and post-treatment groups for MWS and 6MWD were analyzed using simple regression analysis. All patients, the HAL group, and the conventional group had significant coefficients before and after MWS (p<0.05; Fig. 2) and before and after 6MWD (p<0.05; Fig. 3). Slope analyses revealed that the HAL group had some effect regardless of the pre-treatment walking state (Figs. 2 and 3).

**DISCUSSION**

In clinical practice, MWS and 6MWD are used as walking measurements; however, the characteristics of each parameter have not been clarified. Thus, this study evaluated the characteristics of MWS and 6MWD in the stroke rehabilitation field using clinical data on HAL treatment compared with conventional training. This pilot study suggested that 6MWD is an accurate assessment parameter for stroke rehabilitation, particularly when assessing stroke patients undergoing balanced walking recovery. These data are similar to the results of previous studies.

Several recent studies have reported the characteristics of 6MWD, which had the highest ability to predict post-discharge outdoor activities, with a cut-off value of 358.5 m. Thus, the rehabilitation of stroke patients should target a 6MWD of 350 m or longer to enable comfortable outdoor activities after discharge. 6MWD was strongly associated with the function of the affected lower limb and balance than with subjective fatigue in stroke patients in a convalescent rehabilitation ward. In particular, the motor function of the knee was crucial for improving 6MWD in the affected lower limb. Akezaki et al. found that 6MWD is strongly related to the load factor of the paralyzed lower limbs, suggesting the importance of balance ability. Furthermore, Pradon et al. reported that 6MWD is an index of cadence in stroke patients. Oikawa et al. suggested that the advisability of outdoor activities can be determined using MWS, 6MWD, and the 30-second chair-stand test with cut-off points of 0.43 m/s, 112 m, and 5.5 times, respectively. Additionally, a study recently suggested an association between gait posture and 6MWD. Step length asymmetry improvements were only related to improved 6MWT distance (p=0.025; r=−0.49). It is considered that the symmetry of the stride allows efficient walking, and, as a result, the continuous walking distance is extended. Thus, it can be assumed that the stride length on the non-paralyzed side increases due to the extension of the support time for the single leg on the paralyzed side. In the present study, however, the symmetry of stride length and spatiotemporal gait factors could not be measured. These parameters will be addressed in future studies.

The features of MWS and 6MWD are described below. MWS is often measured using a walking path of 10 m to reflect an instantaneous walking ability. Over a short distance, the task can be generally accomplished even if balance or gait ability is poor. Long-distance walking (6MWD) is likely difficult when compensatory walking is strong. Thus, a patient’s walking ability cannot be fully evaluated by an instantaneous measurement of 10 m (MWS). In this study, the high SPPB balance group (2–4 score after intervention) showed significant improvement in 6MWD compared with the low SPPB balance group (0–1 score). However, no significant improvement was found in MWS between groups. Therefore, 6MWD may be a good assessment parameter for stroke rehabilitation, particularly in assessing stroke patients recovering their balance. As in previous studies, long-distance walking and high walking speeds are required for stroke patients to live in the community.
Several studies on HAL treatment use different evaluation parameters, such as improvement of independent walking for acute stroke, improvement of activities of daily living for subacute stroke, improvement of spatiotemporal gait parameters for chronic stroke, improvement of health-related quality of life for chronic spinal cord injury, and a decrease of spasticity for chronic spinal cord injury[17,18,26-28]).

These studies have reported that gait treatment using HAL affects the improvement of walking ability in stroke patients. However, few comparisons with the control group and many unclear points about the effectiveness of HAL have remained unresolved[29]. Indeed, many of them use clinical evaluation indexes, such as independence walking, MWS or CWS, and activities of daily living; however, in recent years, clinical trials have evaluated HAL treatment from various aspects, such as muscle activity, motion analysis, and brain activity[17,30-33]).

According to the other papers reporting on recovery and compensation after stroke, the discrimination between recovery and compensation is increasingly highlighted in stroke rehabilitation, leading to discussions that compensatory strategies early post-stroke might prevent the possibility of true recovery[34-37]). From the early stages of a stroke, it is essential to acquire symmetrical movements and correct posture.

Gait treatment with HAL in stroke patients assists the function of paralyzed lower limbs and allows repeated gait movements. It is thought that such repeated gait movements improve the motor and walking functions of paralyzed lower limbs. Previous studies have also reported improved coordination of paralyzed lower limbs and improved muscle activity patterns after HAL treatment[30-32]). Thus, HAL treatment is a method that restores the function of paralyzed lower limbs and aims for more physiologically efficient walking, which is different from compensatory walking (compensation for the non-paralyzed lower limbs). The data of the present study suggest that HAL treatment has a gait-improving effect in patients with a condi-
tion compared with in the control group (Figs. 2 and 3). It is presumed that these are the results of appropriate walking support by cybernetic control and securing of repeated walking amount\(^{18, 38-40}\). Although many clinical studies have been conducted in the last decade, more clinical studies, particularly high-quality design studies, are needed to elucidate the mechanism of HAL treatment. Additionally, it is crucial to select an appropriate evaluation index according to the walking condition of stroke patients.

The present study has some limitations. The statistical power was low because of the small number of participants. In addition, observer bias cannot be excluded because the same therapists implemented both training and assessment. Furthermore, spatiotemporal gait parameters could not be evaluated during walking. Finally, because randomization was conducted without allocation factors, there were differences in baseline characteristics, such as age. At this time, the indication patients, when to start HAL treatment, the mechanism for improving motor control, the optimal intervention frequency and cost-effectiveness, etc., are unknown, and further research is needed to investigate these parameters. We will attempt to answer these questions in our future study.

In conclusion, in this study, the characteristics of MWS and 6MWD methods in the stroke rehabilitation field were evaluated using clinical data on HAL treatment compared with conventional training. Our data suggest that 6MWD may be a good assessment parameter for stroke rehabilitation, particularly recovery of physiological walking ability.

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**Conflict of interest**

There are no conflicts of interest.

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