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Correlation between ambulatory function and clinical factors in hemiplegic patients with intact single lateral corticospinal tract

A pilot study

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Abstract

To define the relationship between the complete destruction of 1 lateral corticospinal tract (CST), as demonstrated by diffusion tensor imaging (DTI) tractography, and ambulatory function 6 months following stroke.

Twenty-six adults (17 male, 9 female) with poststroke hemiplegia who were transferred to the physical medicine and rehabilitation department. Participants underwent DTI tractography, which showed that 1 lateral CST had been clearly destroyed.

Functional ambulation classification (FAC) scores at admission, discharge, and 6 months after discharge were used to evaluate the patients' ability to walk. The National Institutes of Health Stroke Scale (NIHSS) and the Korean version of the modified Barthel index (K-MBI) at admission, discharge, and 6 months after discharge were used to evaluate the degree of functional recovery.

Of the 26 patients, 18 were nonambulatory (FAC level 1–3), and 8 were able to walk without support (FAC level 4–6). The type of stroke (infarction or hemorrhage), site of the lesion, spasticity of lower extremities, cranioplasty, and the time taken from onset to MRI were not statistically significantly correlated with the ability to walk. However, statistically significant correlations were found in relation to age, K-MBI scores, and initial NIHSS scores.

Despite the complete damage to the lesion site and the preservation of 1 unilateral CST, as shown by DTI, good outcomes can be predicted on the basis of younger age, low NIHSS scores, and high MBI scores at onset.

Abbreviations: ADL = activity of daily living, CST = corticospinal tract, DTI = diffusion tensor imaging, FAC = functional ambulation classification, K-MBI = Korean version of the modified Barthel index, NIHSS = National Institutes of Health Stroke Scale.

Keywords: cerebrovascular stroke, corticospinal tracts, diffusion tensor imaging

1. Introduction

The corticospinal tract (CST) is a major neuronal pathway that mediates voluntary skilled movements. The CST is generally divided into the lateral CST and anterior CST. The lateral CST is larger than the anterior CST and is formed as the result of the decussation of 75% to 90% of CST fibers at the medulla.[1–3] However, the anterior CST does not cross at the medulla. The main function of the lateral CST is to control distal musculature, especially those muscles used for fine movement of the contralateral limb. In contrast, the anterior CST primarily innervates the ipsilateral musculature of the neck, trunk, and proximal upper extremities.[1–7] Larger-sized lesions involving the internal capsule or lesions that overlap into the pyramidal tract lead to atrophy of the CST, which in turn affects upper extremity functions.[8] Thus, patients recovering from a stroke often have difficulty performing fine motor activities after complete injury to the lateral CST.[1–3]

Although much research has been conducted, the exact mechanism accounting for ambulation after a stroke remains unclear. Previous animal studies indicate that there are several motor pathways that could be responsible for a patient's ability to walk, one of which is the crossing motor pathway from the lateral CST of the intact hemisphere.[1–3,9]

Diffusion tensor imaging (DTI) is a noninvasive magnetic resonance imaging (MRI) technique that can be used to assess the structural integrity of the CST. Significant attention has been given to the association between DTI tractography and the motor outcomes of poststroke patients.[10–12] Several studies have examined this relationship, reporting that patients with unilaterally intact CSTs could recover function and the ability to walk after rehabilitation, even after complete destruction of the other CTS.[13,14] In this study, we attempted to identify the correlating factors associated with improvement in ambulatory function after 6 months of rehabilitation in poststroke patients in which the single lateral CST was destroyed.

2. Methods

2.1. Subjects

A total of 135 patients who had been transferred to our department from March 2011 to July 2013 were reviewed. DTI tractography was performed on only 65 of the 135 potential subjects. Of the patients who underwent DTI tractography, 31

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displayed bilateral CSTs, while 6 experienced complete destruction of both CSTs. Subjects were excluded based on the following criteria: a prior history of stroke (n=27), concurrent serious medical complications such as pneumonia or cardiac disease between onset and follow-ups, traumatic intracranial hemorrhage or spontaneous subarachnoid hemorrhage as a result of stroke and paralysis (n=5), prior history of central nervous system disease (n=5), refusal of the patients or their caregivers to provide consent (n=33), and discontinuation of rehabilitation therapy within 6 months after discharge. A total of 28 patients were observed to have a single intact CST, and after excluding 2 who did not attend follow-ups, a total of 26 subjects were enrolled in this study (Fig. 1). Subjects were categorized into either the nonambulatory group or the ambulatory group, according to the degree of support they needed from others or their independency, as measured by their initial Functional Ambulation Category (FAC) scores on the day of transfer.

All the patients were transferred from neurology or neurosurgery departments and were discharged from the hospital after 1 month of treatment. After discharge, all the patients continued to receive rehabilitation treatment from other hospitals. Some of the subjects continued to receive treatment at other hospitals 6 months after discharge, while the rest were readmitted to our hospital 6 months after initial discharge.

2.2. Clinical evaluation

This study design was reviewed and approved by the Institutional Review Board of the National Health Insurance Service Ilsan Hospital, Republic of Korea. Written informed consent for DTI tractography was received from 65 patients.

A single physician (JSH) measured the patients' clinical outcomes on the day of transfer, on the day of discharge, and at the 6-month follow-up after initial discharge. All patients' medical records were retrospectively surveyed. All the subjects were examined in accordance with the hospital's standardized document forms, which assessed the subjects' age, gender, location of lesions, neglect, aphasia, history of decompressive craniectomy, type of stroke (ischemic or hemorrhagic), manual muscle test (MMT) results, range of motion (ROM) test results, FAC scores, National Institutes of Health Stroke Scale (NIHSS) scores, Korean version of the modified Barthel index (K-MBI) scores, and lower extremity spasticity assessment results.

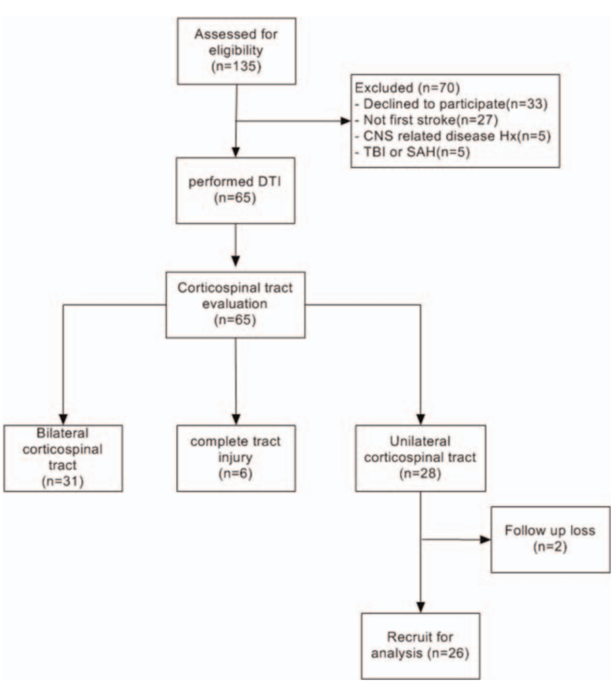

Figure 1. Flow of the participant recruitment process. CNS=central nervous system, DTI=diffusion tensor imaging, SAH=subarachnoid hemorrhage, TBI=traumatic brain injury.

Both the line bisection test (LBT) and the star cancelation test (SCT) were used to assess neglect.[15] These tests were conducted by an occupational therapist (MWJ) who was not involved in the treatment of and had no knowledge of the patients' condition. In the LBT, the line measuring the deviation between the point and the patient thought was the center of a line and the actual center point was divided in half, and the mean was obtained by summing up the percentage figures. Deviations of above 10% indicated evidence of neglect.[16] The SCT is a valid and sensitive test[17] that requires the patient to cross out all the small stars in an array of larger stars and other items. A score of less than 51 out of 54 indicated neglect.

The Korean version of the Western Aphasia Battery was performed on all patients.[18] The aphasia quotient (AQ) was calculated to diagnose aphasia.[19] Patients with an AQ score of 92.3 or above were presumed to be normal, while those with an AQ score of less than 92.3 were diagnosed with aphasia.[20]

The FAC score was used to assess the patients' ability to walk.[21] The FAC test was designed to examine the level of assistance required during a 15-minute walk. The scores are as follows: 1 (nonambulatory), 2 (needs continuous support from 1 person), 3 (needs intermittent support from 1 person), 4 (needs only verbal supervision), 5 (needs help on stairs and uneven surfaces), and 6 (can walk independently anywhere). Patients with FAC scores of 1, 2, and 3 were bound and categorized into the nonambulatory group, and patients with scores of 4, 5, and 6 were categorized into the ambulatory group. The reliability and validity of the FAC test have been well established.[21]

NIHSS is a graded neurological examination that assesses speech, language cognition, inattention, visual field abnormalities, motor and sensory impairments, and ataxia. The scale was developed for and has been evaluated for use in acute stroke therapy, and it is widely used as a standard part of assessments in clinical trials.[22,23]

The K-MBI consists of 10 individual items regarding activities of daily living (ADLs), with zero indicating complete dependence and with the highest score in each subitem signifying complete independence. The total score is either 20 points or 100 points. The values assigned to each item are weighted according to the amount of physical assistance required if the patient cannot perform the activity independently. The ADL items assessed on the K-MBI include: bowel control, bladder control, personal hygiene, toilet transfer, bathtub transfer, feeding, dressing, wheelchair transfer to and from bed, walking (wheelchair management if the patient is not ambulatory), and ascending and descending stairs.[24] The reliability and validity of the K-MBI are well established.[25]

Spasticity was assessed using the modified Ashworth scale.[26] In the present study, we tested knee flexors and extensors as well as plantar flexors in patients in a supine position. Patients with grades of 1 to 4 were classified as having spasticity.

2.3. Diffusion tensor imaging

MRI data consisting of a T1-weighted anatomical scan and DTI data were acquired using the 3.0T System with a 32-channel

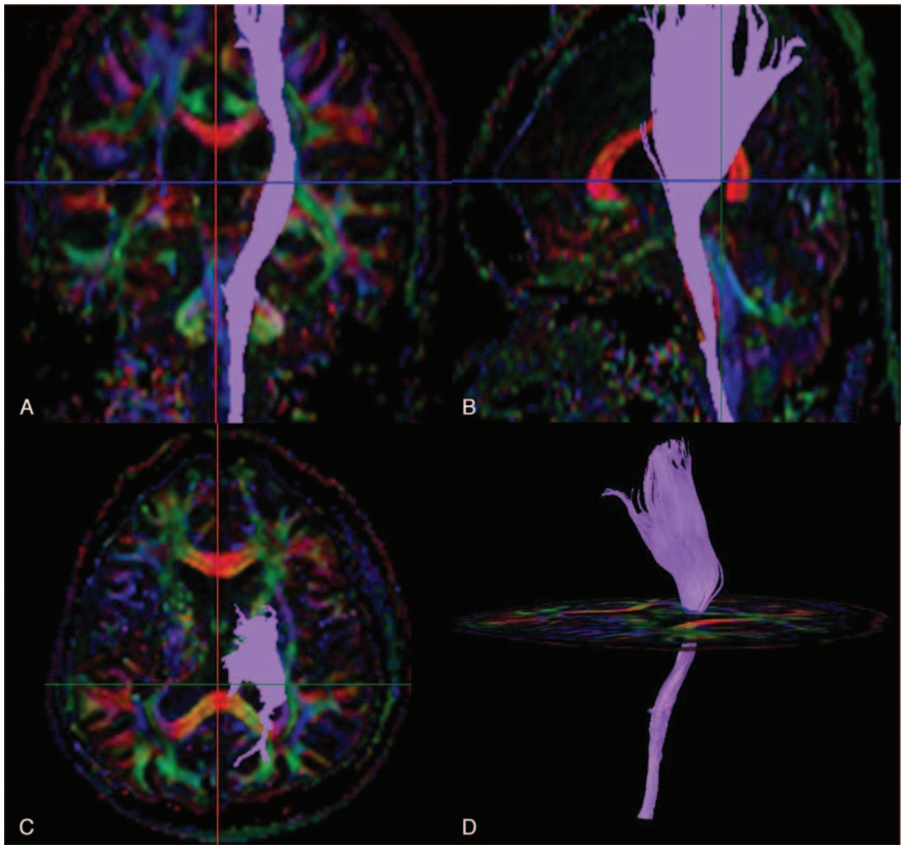

Figure 2. Example of a single lateral corticospinal tract. (A) Coronal view. (B) Sagittal view. (C) Axial view. (D) Three-dimensional imaging.

sensitivity-encoding (SENSE) head coil[1]. Diffusion-weighted imaging was performed using single-shot spin-echo echo-planar imaging with navigator echo-phase correction. The DTI technical parameters were as follows: a data matrix of 96 over a 220×220 mm^2 field of view, zero-filled to a 128×128 matrix; a 2.3-mm section thickness without a 45-direction gap; an echo time (TE) of 76 ms; a repetition time (TR) of 6599 to 8280 ms; a parallel imaging reduction (SENSE) factor of 2; 2 acquisitions; and a b-value set to 600 s/mm^2 with a nondiffusion weighted baseline image ($b=0$). The total imaging time was less than 20 minutes, with an echo planar imaging factor of 49 and a number of excitations score of 1.

2.4. Data processing and region of interest

Diffusion registration was implemented as a preprocessing step. This process can be used to correct for the patient movement that can occur during a dynamic scan. Thus, diffusion registration improves image quality in calculated diffusion images. The DTI datasets and anatomic MRI scans were analyzed with FiberTrak software for diffusion tensor analysis and fiber tracking from the MRI Workspace (Philips Healthcare)[1]. The parameters for the tractography were as follows: a minimum fractional anisotropy (FA) level of 0.15, a maximum angle change of 27°, and a minimum fiber length of 10 mm. The principle directions of diffusion, which represent the vector of the fiber axis, are color-coded in blue for the rostral-caudal axis, red for the left-right axis, and green for the ventral-dorsal axis. Two regions of interest (ROI) were selected to reconstruct the CST. One ROI was placed on the CST portion of the anterior lower pons, and the other was placed on the CST portion of the posterior limbs in the internal capsule.[27,28] Fiber tracts passing through both ROIs were designated as the final tracts of interest (Fig. 2). All data processing and CST reconstruction tasks were performed by a single physician (JSH) who was unaware of the patients' clinical data.

2.5. Statistical analysis

Independent *t* tests were used to analyze continuous data (age, onset time) and the Chi-square test or Fisher exact test was used to analyze categorical data (sex, injury type, neglect, aphasia, spasticity, and craniectomy).

Repeated K-MBI and NIHSS scores of ambulatory patients who did not need support and nonambulatory patients who needed support were compared using a linear mixed model. Participants were treated as a random effect, and all other effects were fixed. We assumed that the model had a compound symmetry variance-covariance structure. After adjusting for age, a multiple linear mixed-effects model was used to compare ambulatory patients who did not need support and ambulatory patients who needed support.

All statistical analyses were performed using SAS Software Version 9.2[2] and were tested for significance at an alpha level of

[1] Supplier: Philips Medical Systems International B.V., Veenpluis 4-6, 5684 PC Best, Netherlands.

[2] Supplier: SAS Institute, 100 SAS Campus Dr, Cary, NC 27513-2414.

0.05. Data were recorded as means ± SD for continuous variables and as counts for categorical variables.

3. Results

Of the 65 patients who received CST evaluations using DTI, 39 were excluded from the study. Bilateral CST was observed in 31 patients, both CSTs were destroyed in 6 patients, and 2 patients did not attend follow-ups (Fig. 1). The remaining patients were categorized into a nonambulatory group (n = 18) or an ambulatory group (n = 8) depending on their initial FAC scores, as assessed on the day of transfer. There were no statistically significant differences with regard to sex or the site of injury. Regarding the type of stroke, 16 patients had hemorrhages and 10 had infarctions, and there were no statistically significant differences between these 2 groups ($P > 0.05$). The ambulatory group showed a statistically significant lower age distribution, with a mean age of 42.8 years ($P = 0.0053$). Moreover, the mean onset time, which refers to the time between a patient's injury and their tractography evaluation, was 4.02 ± 3.7 months for the ambulatory group and 2.84 ± 2.4 months for the nonambulatory group, although this difference was statistically insignificant ($P = 0.3429$). Five patients could not be evaluated for neglect due to impaired cooperation, while 3 patients demonstrated clinical neglect. Of the 9 patients with aphasia, only 1 was in the ambulatory group while the other 8 were classified into the nonambulatory group. Nine patients did not have spasticity in the lower limbs. Three patients had a history of decompressive craniectomy. Clinical factors such as the presence of neglect, aphasia, spasticity of the affected limb, and cranioplasty were not significantly different between the 2 groups (Table 1).

The K-MBI and NIHSS parameters measured on the day of transfer, the day of discharge, and during the 6-month follow-up are listed in Tables 2 and 3. For all data collection periods, the ambulatory group (FAC 4–6) showed higher K-MBI and lower NIHSS scores than the nonambulatory group (FAC 1–3). All results were statistically significant except for the 6-month follow-up parameters. When adjusted for age, the average K-MBI scores of the ambulatory group were 78.5, 90.3, and 93.1 for the days of transfer, discharge, and 6 months after discharge, respectively, while the corresponding scores of the nonambulatory group were 32.2, 44.7, and 50.7. Similarly, the average NIHSS scores of the ambulatory group were 4.0, 2.6, and 1.8 compared to 11.2, 9.6, and 8.1 of the nonambulatory group. The difference between the groups decreased from 7.2 to 7 and, finally, to 6.2 (Tables 2 and 3 and Fig. 3). Figure 4 illustrates that both the mean differences and confidence intervals of K-MBI increased, and NIHSS scores decreased at each data collection period as rehabilitation was implemented. However, the interaction effect, which represents intergroup differences regarding time, was not statistically significant (data not shown).

4. Discussion

The results of our study indicate that the patients capable of ambulation without assistance were statistically significantly younger. When adjusted for age, the ambulatory group still achieved higher K-MBI scores with statistical significance on the days of transfer, discharge, and at the 6-month follow-up compared to the nonambulatory group. On the other hand, NIHSS scores showed different results: the score differences were statistically significant at the days of transfer and discharge but not at the 6-month follow-up (Table 3). There were no statistically significant differences in gender, injury type, or location of lesion ($P > 0.05$).

Most quantitative DTI studies of stroke patients with damage to regions of the CST reported better motor outcomes when the

Table 1

Baseline demographic characteristic for patients.

Characteristic	Ambulatory group	Nonambulatory group	P
Number	8	18	
Age	42.8 ± 13.6	58.9 ± 11.7	0.0053
Sex			
Male	6 (75.0)	11 (61.1)	0.6673
Female	2 (25.0)	7 (38.9)	
Onset time, months	4.02 ± 3.7	2.84 ± 2.4	0.3429
Location of lesion			
Left	3 (37.5)	9 (50.0)	0.6828
Right	5 (62.5)	9 (50.0)	
Injury type			
Infarction	4 (50.0)	12 (66.7)	0.6645
Hemorrhage	4 (50.0)	6 (33.3)	0.5292
Aphasia	1 (12.5)	8 (44.5)	0.1902
Cranioplasty	0	3	0.5292
Affected lower ex spasticity*	6 (75.0)	11 (61.1)	0.4300
Neglect (LBT)			
None	8 (100)	10 (55.6)	0.0852
Yes	0	3 (16.7)	
Uncheckable	0	5 (27.7)	
Neglect (SCT)			
None	8 (100)	11 (61.1)	0.1540
Yes	0	2 (11.1)	
Uncheckable	0	5 (27.8)	

Values are mean ± SD or n (%). LBT = line bisection test, MAS = modified Ashworth scale, SCT = star cancellation test.

* MAS grade 1 to 4.

Table 2

K-MBI analysis of linear mixed-effects model.

Variables	K-MBI mean ± SD*	MD (95% CI)	DF	F-value	P
Transfer					
Ambulatory group	78.5 ± 17.66	−46.2 (−63.3, −29.1)	48	9.49	0.0035†
Nonambulatory group	32.2 ± 21.84				
Discharge					
Ambulatory group	90.3 ± 6.48	−45.6 (−65.2, −26.0)	48	9.15	0.0040†
Nonambulatory group	44.7 ± 26.18				
6 m f/u					
Ambulatory group	93.1 ± 6.51	−42.3 (−59.8, −24.9)	48	6.91	0.0116†
Nonambulatory group	50.7 ± 32.96				

Values are mean ± SD. CI = confidence interval, DF = degree of freedom, K-MBI = Korean version of the modified Bathel index, MD = mean difference, SD = standard deviation.
* Values for each group.
† Significant difference comparison to the groups with age-adjusted.

CST was preserved; however, the number of subjects with only a single completely destroyed CST were limited compared to our study.[14,29–32]

Kim et al[14] conducted a uniform study of 37 patients with large middle cerebral artery (MCA) territory infarctions, but only 12 of these patients had a single completely destroyed CST. Similarly, Jang et al[29] also included 12 patients with a single completely destroyed CST in their study of the outcome of CST disruption in patients with pontine infarctions. Schaechter et al,[32] Parmar et al,[31] and Lie et al[30] included 10, 11, and 15 such patients, respectively.

One common theme underlying these studies is that they all predicted motor outcomes based on CST preservation and fractional anisotropy (FA) values rather than on the patients' clinical factors (e.g., age, sex, and location of lesion). In contrast, our study enrolled a relatively large number of patients with an intact lateral CST and complete disruption of the contralateral side, irrespective of the type of stroke the patient suffered (hemorrhagic or ischemic). Moreover, our study is the first to consider clinical factors related to functional outcomes by categorizing hemiplegic patients with an intact lateral CST into FAC stage groups and then categorizing them further into either an ambulatory without support group or a nonambulatory group upon follow-up at 6 months.[19] We used the K-MBI to determine functional outcomes, and our results were in line with studies that used the original MBI. By combining our results with the results of previous studies,[14,29] we suggest that there are better functional outcomes for stroke patients with the CST intact and extending to the cortex, compared to those with some of the CST intact but not extending to the cortex or those with none of the CST intact. Moreover, even with none of the CST intact on the lesion side, younger patients with low NIHSS scores and high K-MBI scores at initial evaluation are more likely to have ambulation and independence in their ADLs at 6 months after discharge. Adjusting for age, identical ambulation ability could be expected if NIHSS scores at the 6-month follow-up were excluded (Table 3).

4.1. Study limitations

The main limitation of our study is that it was a retrospective study with a relatively small sample size (only 26 patients), although the number of subjects was larger than in previous studies. This was due to the medical policies in Korea and the socioeconomic status of the patients, which made it difficult to perform DTI tractographies and to obtain the patients' consent, respectively. We prospectively examined completely and partially destroyed CSTs using DTI tractography, and we are reporting the effect of the severity of CST injuries on the recovery of ambulation. Although we initially performed DTI tractographies on 65 patients, 39 were dropped during follow-ups, resulting in a potential selection bias. Furthermore, the gender ratio was uneven. However, if we can recruit more patients in the future, we cannot only reduce bias but also obtain a reasonable cut-off value

Table 3

NIHSS analysis of linear mixed-effects model.

Variables	NIHSS mean ± SD*	MD (95% CI)	DF	F-value	P
Transfer					
Ambulatory group	4.0 ± 2.0	7.2 (2.9, 11.6)	48	4.49	0.0393†
Nonambulatory group	11.2 ± 5.74				
Discharge					
Ambulatory group	2.6 ± 2.26	7.0 (3.6, 10.4)	48	4.07	0.0492†
Nonambulatory group	9.6 ± 6.06				
6 m f/u					
Ambulatory group	1.8 ± 1.96	6.2 (3.2, 9.3)	48	2.88	0.0961
Nonambulatory group	8.1 ± 5.46				

Values are mean ± SD. CI = confidence interval, DF = degree of freedom, MD = mean difference, NIHSS = National Institutes of Health Stroke Scale, SD = standard deviation.
* Values for each group.
† Significant difference comparison to the groups with age-adjusted.

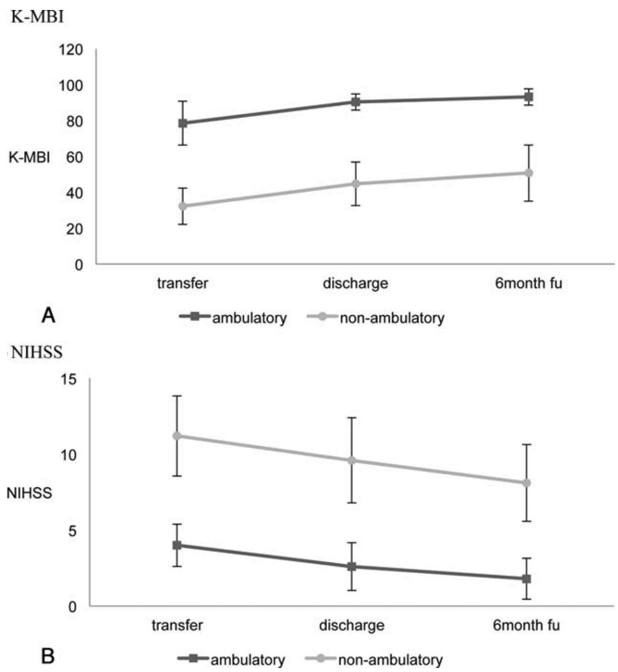

Figure 3. Comparison of K-MBI and NIHSS between the 2 groups. K-MBI = Korean version of the modified Bathel index, NIHSS = national institute of health stroke scale.

for independent gait predictions. Therefore, future prospective studies with larger numbers of recruits are necessary.

In addition, musculoskeletal and other medical comorbidities that could influence the ambulatory function of the subjects were not taken into account, and follow-up examinations were

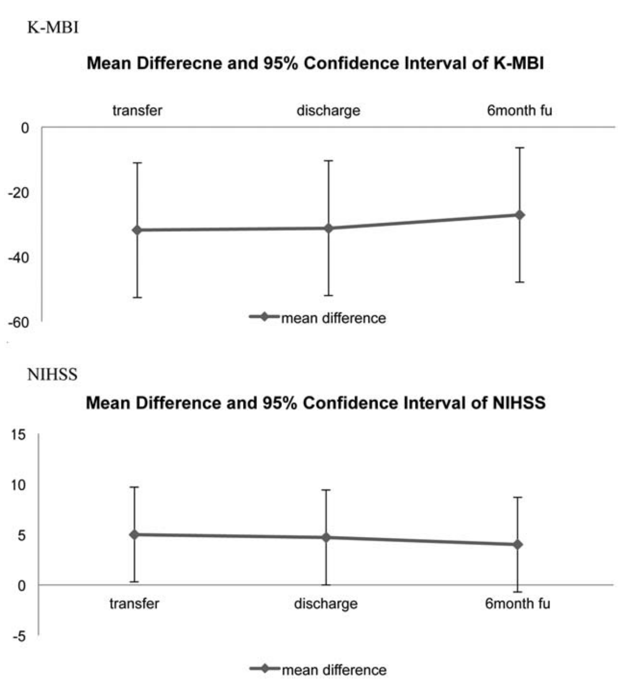

Figure 4. Mean difference and CI between groups of K-MBI and NIHSS with age-adjusted using linear mixed model. CI = confidence interval, K-MBI = Korean version of the modified Bathel index, NIHSS = national institute of health stroke scale.

restricted to 6 months after discharge, limiting the assessment of long-term outcomes.[33–35] Moreover, our study was limited to patients who had undergone rehabilitation for 6 months and thus is not applicable to those who have not undergone rehabilitation.

Excluding several cases in which the initial medical treatment of the patient was noted, all patients received standard rehabilitation treatment for 6 months. Studying patients who have not undergone rehabilitation treatment could confound our research results.

Finally, we have not considered the effect of other tracts that affect a patient's ambulation or gait besides the CST.

5. Conclusion

Through this study, we determined that complete destruction of 1 CST might not be a definite predictor of ambulatory function. We also found that that lower age along with good initial NIHSS and K-MBI scores could be important predictors of independent gait when a single CST is preserved. Thus, it can be concluded that independent gait can be achieved despite the complete loss of a single CST in DTI tractography through sufficient and consecutive rehabilitation therapy.

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