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Original Article

Predictive factors for walking in acute stroke patients: a multicenter study using classification and regression tree analysis

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Abstract. [Purpose] Walking ability should be predicted as early as possible in acute stroke patients. The purpose is to construct a prediction model for independent walking from bedside assessments using classification and regression tree analysis. [Participants and Methods] We conducted a multicenter case-control study with 240 stroke patients. Survey items included age, gender, injured hemisphere, the National Institute of Health Stroke Scale, the Brunnstrom Recovery Stage for lower extremities, and "turn over from a supine position" from the Ability for Basic Movement Scale. The National Institute of Health Stroke Scale items, such as language, extinction, and inattention, were grouped under higher brain dysfunction. We used the Functional Ambulation Categories to classify patients into independent (four or more the Functional Ambulation Categories; n=120) and dependent (three or fewer the Functional Ambulation Categories; n=120) walking groups. A classification and regression tree analysis was used to create a model to predict independent walking. [Results] The Brunnstrom Recovery Stage for lower extremities, "turn over from a supine position" from the Ability for Basic Movement Scale, and higher brain dysfunction were the splitting criteria for classifying patients into four categories: Category 1 (0%), severe motor paresis; Category 2 (10.0%), mild motor paresis and could not turn over; Category 3 (52.5%), with mild motor paresis, could turn over, and had higher brain dysfunction; and Category 4 (82.5%), with mild motor paresis, could turn over, and no higher brain dysfunction. [Conclusion] We constructed a useful prediction model for independent walking based on the three criteria.

Key words: Acute stroke, Classification and regression tree, Multicenter study

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INTRODUCTION

In stroke rehabilitation, it is important to predict the prognosis of motor function and activities of daily living (ADL) ability as early as possible and consider intervention methods based on the prediction. Although previous studies[1–10] have reported predictive factors for ADL, walking ability, and length of stay, it is especially important to predict walking ability accurately. The predictive factors for walking in patients in acute and recovery phases are early-onset lower extremity function, trunk function, ADL ability, and higher brain dysfunction (HBD).

Many reports used logistic regression analysis to construct prognostic equations[5, 6, 8, 10]. The odds ratio is calculated as the weighting of the independent variables, and it is possible to compare the strength of the impact of each independent variable on the dependent variable. In recent years, there have been several predictive studies using Classification and Regression Tree (CART) analysis, which is an easy-to-understand prediction[11–13]. CART analysis is one of the methods of data mining; it is often used in marketing, machine learning, etc. Since it is possible to create a prediction model in the form of a flowchart using this method, it is easy for non-experts to understand the contents and it has the added advantage of being easily applied in clinical practice. In CART analysis, a vertex node, a set of all data, is divided based on a certain criterion until a predetermined end condition is reached, and a model is constructed for the relationship between the dependent and independent variables[14]. However, there is a risk that clinically unimportant variables may be incorporated into the model due to mechanical computation. Therefore, it is necessary to consider the input variables carefully in clinical applications. Although some studies have used CART analysis to create prediction models for walking and ADL ability, these are cross-sectional studies and cannot be applied to prognosis prediction. In addition, these prediction models incorporate assessments that require comprehensive evaluation batteries and instrumental measurements in the splitting criteria, while acute clinical situations require a simpler prognostic model.

Moreover, most of the prediction studies collected data from a single institution. In a single-institution study, there is a possibility that the characteristics and data may be biased. On the contrary, a multicenter study has the advantage of less bias in the characteristics and data[15]. This may help predict factors that are valid and more accurate. We collected data from five emergency hospitals to clarify the predictive factors for walking ability from the initial bedside assessment, and aimed to clarify the predictive factors for independent walking using CART analysis at acute hospital discharge.

PARTICIPANTS AND METHODS

In this multicenter case-control study, data were collected from five acute care hospitals. This study was conducted after obtaining approval from the Ethics Committee of the International Medical Center of Saitama Medical University and the participating institutions.

Of 564 patients with cerebral infarction or cerebral hemorrhage admitted to the five facilities and undergoing physical therapy from January to June 2017, 240 were included in the analysis. These patients were classified into an independent walking group (n=120) and a non-independent walking group (n=120) at discharge. The criteria for exclusion were patients: (a) with a modified Ranking Scale ≥3 before admission; (b) with subtentorial lesions; (c) with bilateral lesions; (d) suffering recurrent strokes; (e) who died; (f) without motor paralysis; and (g) who did not assess FAC at discharge (Fig. 1).

The survey items included age; gender; lesion side; hemisphere of injury; type of disease; length of hospital stay; National Institute of Health Stroke Scale (NIHSS) on rehabilitation start date (2.57 ± 2.10 days); and lower items such as consciousness, questions, commands, gaze, visual fields, ataxia, sensory, language, extinction/inattention, Brunnstrom Recovery Stage for lower extremity (BRS-LE) on rehabilitation start date (2.57 ± 2.10 days), and Ability for Basic Movement Scale II (ABMSII)[16] on the first day out of bed after admission (4.21 ± 3.68 days). ABMS is an index that evaluates five items ("turn over from the supine position", "sit up", "remain sitting", "stand up", and "remain standing"). The "turn over from the supine position" item (ABMS-T) was used for analysis in our study. For statistical analysis, the NIHSS subitems, BRS-LE and ABMS-T, were transformed from ordinal scales to dummy data.

The NIHSS subitems were categorized into two groups: 0 (asymptomatic) and 1–3 (symptomatic) (dummy variable: subitem 0 point: 0, subitem 1–3 points: 1). Those who did not show language or extinction/inattention were categorized as having no higher brain dysfunction (HBD). Those who showed language or extinction/inattention were categorized as having HBD (dummy variables: no HBD: 0, with HBD: 1). BRS-LE was categorized as I–III for severe motor paralysis and IV–VI for mild motor paralysis (dummy variables: IV–VI: 0, I–III: 1). The ABMS-T was categorized based on whether movement was possible, with a score of 1 to 3 (prohibited to light assistance) and a score of 4 to 6 (monitored to completely independent) (dummy data: 4 to 6 points: 0, 1 to 3 points: 1). Functional ambulation categories (FAC) were used to determine whether the patients could walk at the time of discharge from the hospital, and categories 4 and 5 (independent to independent walking on level ground) were classified as the independent walking group, and categories 0 to 3 (unable to walk to monitored walking) were classified as the non-independent walking group.

For statistical analysis, the patients were classified into two groups based on the level of walking independence at the time of discharge. The categorical scales of gender, disease type, damaged hemisphere, and NIHSS subitems of consciousness,

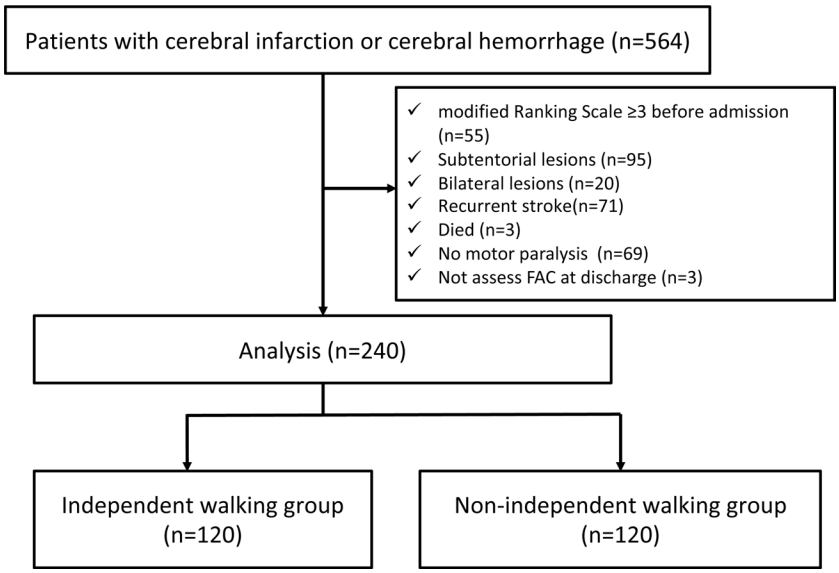

Fig. 1. Flow diagram of the study.

questions, commands, gaze, visual fields, ataxia, sensory, language, extinction/inattention, HBD (language and extinction/inattention), BRS-LE, and ABMS-T were subjected to a χ^2 test. An unpaired t-test was applied on age, date of first intervention, and length of hospital stay.

The growth method of the CART analysis was Chi-squared automatic interaction detection. The dependent variable was the degree of walking independence, and the independent variables were items with significant differences among the above survey items. At each node, a cross table was created in which the dependent and independent variables were combined, and the combination of dependent and independent variables with the smallest p-value was selected from the results of the χ^2 test. The maximum depth of the tree was set to 3, the minimum case of the parent node was set to 10, and the minimum case of the child node was set to 3. To verify the external validity of the obtained prediction model, a 10-fold split cross-validation was conducted[14], a method in which the model was built using 90% of the data divided randomly into 10 equal parts. The model was then validated using the remaining 10% of the data and the process was repeated 10 times. SPSS version 23 (IBM SPSS Corp., Chicago, IL, USA) was used for statistical analysis, and the significance level was set at 5%.

RESULTS

Of the 240 patients included in the analysis (Fig. 1), 120 (50.0%) were ambulatory and independent at discharge. The group differences are shown in Table 1. There were no significant differences in age, gender, hemisphere of injury, or date of first intervention between the two groups. There were significant differences in the type of disease ($\chi^2(1)=25.7$, $p<0.001$), length of hospital stay ($t_{(238)}=6.63$, $p<0.001$), NIHSS subitems of consciousness ($\chi^2(1)=30.1$, $p<0.001$), questions ($\chi^2(1)=38.4$, $p<0.001$), commands ($\chi^2(1)=25.6$, $p<0.001$), gaze ($\chi^2(1)=31.4$, $p<0.001$), visual fields ($\chi^2(1)=13.2$, $p<0.001$), sensory ($\chi^2(1)=32.5$, $p<0.001$), language ($\chi^2(1)=25.8$, $p<0.001$), extinction/inattention ($\chi^2(1)=54.6$, $p<0.001$), HBD ($\chi^2(1)=54.8$, $p<0.001$), BRS-LE ($\chi^2(1)=80.0$, $p<0.001$), and ABMS-T ($\chi^2(1)=78.5$, $p<0.001$) between the two groups.

The flowchart created by the CART is as shown in Fig. 2. The splitting criteria in the prediction model of walking independence at discharge were BRS-LE, ABMS-T, and the presence of HBD. In the first stratum of the model, BRS-LE was selected as the partitioning criterion. The probability of walking independence for cases with BRS-LE I–III was 0% (Category 1), and for cases with BRS-LE IV–VI was 66.7%. In the second stratum, ABMS-T was selected as a splitting criterion. The probability of walking independence in cases with BRS-LE of IV to VI and ABMS-T of 1 to 3 points was 10.0% (Category 2), and in patients with ABMS-T of 4 to 6 points was 73.8%. In the third stratum, the presence or absence of HBD was selected as the splitting criterion. The probability of walking independence in cases with HBD with BRS-LE IV–VI and ABMS-T of 4 to 6 points was 52.2% (Category 3), and 82.5% in cases without HBD (Category 4). The model showed a positive classification rate of 81.7%, a sensitivity of 98.3%, a specificity of 65.0%, a positive predictive value of 73.8%, and a negative predictive value of 97.5%. The relative risk estimate by cross-validation was 0.22, whereas the relative risk by the reassignment method was 0.18.

Table 1. Comparison between the independent and non-independent walking groups

	Independent (FAC ≥4) n=120	Non-independent (FAC ≤3) n=120
Age (years)	69.0 ± 10.8	69.9 ± 13.4
Gender (male/ female)	86 (71.7)/ 34 (28.3)	80 (66.7)/ 40 (33.3)
Hemisphere of injury (right/ left)	62 (51.7)/ 58 (48.3)	57 (47.5)/ 63 (52.5)
Types of disease (infarction/ hemorrhage)	102 (85.0)/ 18 (15.0) ***	66 (55.0)/ 54 (45.0) ***
Length of hospital stay (days)	18.6 ± 12.7***	30.8 ± 15.7***
National Institutes of Health Stroke Scale (points)		
Consciousness (0/ 1/ 2/ 3)	108 (90.0)/ 11 (9.2)/ 1 (0.8)/ 0 (0.0)	71 (59.2)/ 39 (32.5)/ 7 (5.8)/ 3 (2.5)
Dummy variable (0/ 1)	108 (90.0)/ 12 (10.0) ***	71 (59.2)/ 49 (40.8) ***
Questions (0/ 1/ 2)	106 (88.3)/ 8 (6.7)/ 6 (5.0)	62 (51.7)/ 26 (21.7)/ 32 (26.7)
Dummy variable (0/ 1)	106 (88.3)/ 14 (11.7) ***	62 (51.7)/ 58 (48.3) ***
Commands (0/ 1/ 2)	116 (96.7)/ 2 (1.7)/ 2 (1.7)	88 (73.3)/ 17 (14.2)/ 15 (12.5)
Dummy variable (0/ 1)	116 (96.7)/ 4 (3.3) ***	88 (73.3)/ 32 (26.7) ***
Gaze (0/ 1/ 2)	108 (90.0)/ 12 (10.0)/ 0 (0.0)	70 (58.3)/ 36 (30.0)/ 14 (11.7)
Dummy variable (0/ 1)	108 (90.0)/ 12 (10.0) ***	70 (58.3)/ 50 (41.7) ***
Visual fields (0/ 1/ 2/ 3)	106 (88.3)/ 12 (10.0) / 1 (0.8)/ 1 (0.8)	83 (69.2)/ 23 (19.2)/ 8 (6.7)/ 6 (5.0)
Dummy variable (0/ 1)	106 (88.3)/ 14 (11.7) ***	83 (69.2)/ 37 (30.8) ***
Ataxia (0/ 1/ 2)	112 (93.3)/ 2 (1.7)/ 6 (5.0)	114 (95.0)/ 3 (2.5)/ 3 (2.5)
Dummy variable (0/ 1)	112 (93.3)/ 8 (6.7) ***	114 (95.0)/ 6 (5.0) ***
Sensory (0/ 1/ 2)	68 (56.7)/ 48 (40.0)/ 4 (3.3)	25 (20.8)/ 54 (45.0)/ 41 (34.2)
Dummy variable (0/ 1)	68 (56.7)/ 52 (43.3) ***	25 (20.8)/ 95 (79.2) ***
Language (0/ 1/ 2/ 3)	105 (87.5)/ 8 (6.7)/ 7 (5.9)/ 0 (0.0)	70 (58.3)/ 19 (15.8)/ 15 (12.5)/ 16 (13.3)
Dummy variable (0/ 1)	105 (87.5)/ 15 (12.5) ***	70 (58.3)/ 50 (41.7) ***
Extinction/ Inattention (0/ 1/ 2)	106 (88.3)/ 11 (9.2)/ 3 (2.5)	52 (43.3)/ 32 (26.7)/ 36 (30.0)
Dummy variable (0/ 1)	106 (88.3)/ 14 (11.7) ***	52 (43.3)/ 68 (56.7) ***
Higher brain dysfunction (0/ 1)	95 (79.2)/ 25 (20.9) ***	38 (31.7)/ 82 (68.3) ***
Brunnstrom Recovery Stage for lower extremity		
Stage (I/ II/ III/ IV/ V/ VI)	0 (0.0)/ 0 (0.0)/ 0 (0.0)/ 9 (7.5)/ 33 (27.5)/ 78 (65.0)	12 (10.0)/ 26 (21.7)/ 22 18.3)/ 22 (18.3)/ 25 (20.8)/ 13 (10.8)
Dummy variable (0/ 1)	0 (0.0)/ 120 (100.0) ***	60 (50.0)/ 60 (50.0) ***
Ability for Basic Movement Scale (points)		
Turn over from the supine position (1/2/3/4/5/6)	0 (0.0)/ 0 (0.0)/ 2 (1.7)/ 7 (5.8)/ 13 (10.8)/ 98 (81.7)	1 (0.8)/ 33 (27.5)/ 29 (24.2)/ 19 (15.8)/ 17 (14.2)/ 21 (17.5)
Dummy variable (0/ 1)	2 (1.7)/ 118 (98.3) ***	63 (52.5)/ 57 (47.5) ***

***p<0.001.
Continuous data are presented as the mean and range. Categorical data are presented as n (%).
FAC: functional ambulation categories.

DISCUSSION

This was a multicenter study conducted with data on acute stroke patients to predict their outcome in terms of walking ability at discharge from the hospital based on bedside assessments. The splitting criteria for the model created by CART analysis were BRS-LE, ABMS-T, and the presence of HBD. This is the first study to develop a simple and accurate model that can predict walking ability at hospital discharge using only three simple criteria assessed at bedside, without comprehensive evaluation batteries and instrumental measurements for the criteria.

In the first stratum, BRS-LE was extracted as the splitting criterion. BRS can be classified into six categories ranging from I to VI, and the degree of motor dysfunction was evaluated based on spasticity and synergistic movements. The probability of walking independence at the time of hospital discharge was 0% if the patient had BRS-LE I–III at the early stage of onset and 66.7% if the patient had BRS-LE IV–VI. It has been reported that severe motor paralysis leads to muscle weakness and loss of support, resulting in decreased walking ability[1, 4, 9]. Mercer et al.[9] showed that the Fugel–Meyer score of the lower extremity at early onset was a predictor of the ability to load the paretic leg during standing and self-select gait speed. A systematic review by Hendricks et al.[4] argued that the recovery period in patients with severe motor paresis was twice as

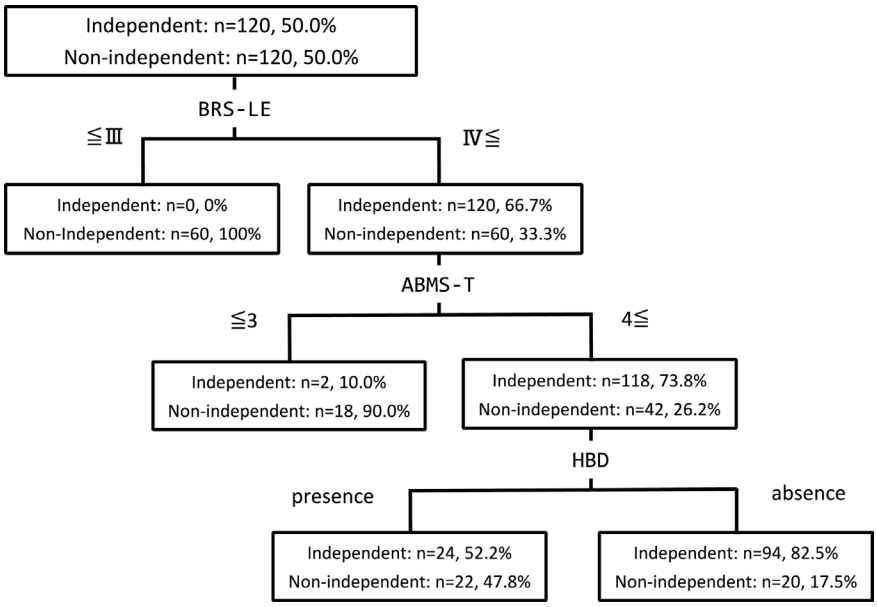

Fig. 2. The flowchart created by the Classification and Regression Tree (CART) analysis.

long as in patients with mild motor paresis. The initial degree of motor paresis and motor-evoked potentials were strong predictors. The study by Jorgensen et al.[1)] of 804 acute stroke patients found that the time course and degree of the recovery of gait function were related to the initial impairment of gait function and the severity of LE paresis. They reported that 21% of patients with severe paresis on admission gained independent walking function by the end of rehabilitation (35 ± 41 days). A higher percentage of walking independence compared to the present study (0%) considered different criteria for the degree of motor paresis. While the previous study used the Scandinavian Stroke Scale to assess the severity of motor paralysis based only on muscle strength, our study used the BRS to assess spasticity and synergistic movements. Thus, the probability of walking independence seems lower when using the BRS, which assesses both quantity and quality of movement.

In the second stratum, ABMS-T was extracted as a splitting criterion. In this model, the probability of walking independence was 10.0% when the BRS-LE IV–VI and ABMS-T was 0 to 3 points, and 73.8% when it was 4 to 6 points. Impaired trunk mobility in stroke patients is caused by abnormal muscle tone and lack of coordination of the limbs and trunk, resulting in decreased displacement center of pressure and increased movement time[17)]. Many reports predict the prognosis of walking ability based on the ability to sit up and maintain sitting, and it has been agreed that trunk function plays an important role[1, 4–8, 10, 17, 18)]. Therefore, trunk function in the early stage of the disease is as important as lower limb function. Even if motor paralysis of the lower extremities is not too bad, patients in Category 2 who have difficulty in turning over may not be able to walk independently at the time of discharge from the hospital.

In the third stratum, the presence or absence of HBD consisting of NIHSS language and extinction/inattention were extracted as the splitting criterion. In this model, the probability of walking independence at the time of discharge was 52.2% in patients with HBD and 82.5% in patients without higher brain dysfunction, among patients who had BRS-LE IV to VI and could turn over from the supine position. Lazar et al.[19)] reported that aphasia in the acute phase has been found to contribute to increased length of stay, inpatient complications, overall neurological disability, and mortality, which may alter discharge disposition. Furthermore, in the sub-acute and chronic stroke phase, aphasia is associated with lower functional independence measures (FIM) scores, longer stays in rehabilitation settings, poorer function in ADL, and mortality. Gillen et al.[20)] noted that patients with unilateral spatial neglect (USN) in the acute phase stayed in the rehabilitation hospital almost 11 days longer than patients without USN and showed lower FIM scores, especially in activities like grooming, bathing, toileting, bladder control, and walking. These cases belonging to Category 3 should be carefully monitored for the course of symptoms before determining whether they can be discharged home.

The model has a positive classification rate of 81.6%, a sensitivity of 98.0%, a specificity of 65.0%, a positive predictive value of 73.8%, and a negative predictive value of 97.5%, indicating that the flowchart obtained in this study can discriminate among 240 patients to indicate those with a high probability of walking independence. The relative risk estimated by the reassignment method was 0.18, while the relative risk estimated by cross-validation was 0.22, which are almost the same, indicating that this model can be generalized to predict walking independence in acute stroke patients.

The limitation of our study is that we did not evaluate follow-up after discharge. To confirm the usefulness of this model, a further study of long-term walking prognosis should be conducted. Another limitation is that we did not conduct any additional research. Further studies to prove the validity of this model would be of value to the field of walking prognosis.

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Conflict of interest

There are no conflicts of interest to disclose in this study.

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