J. Phys. Ther. Sci. 36: 167–174, 2024

The Journal of Physical Therapy Science

Original Article

Factors associated with independent ambulation at 3 months after putaminal hemorrhage: an observational study

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Abstract. [Purpose] This study was aimed at evaluating the clinical indicators for predicting ambulation at 3 months after putaminal hemorrhage. [Participants and Methods] The participants were 84 inpatients with putaminal hemorrhage. The patients' background characteristics and computed tomography findings at the time of the onset of putaminal hemorrhage were obtained from their medical records. Impaired consciousness, severity of hemiplegia, higher brain dysfunction, sensory impairment, activities of daily living, and ambulatory ability were evaluated. Logistic regression analysis was performed to identify factors associated with ambulation at 3 months, and receiver operating characteristic curve analysis was conducted to determine the predictive value of the identified factors and the optimal cut-off values. [Results] Ventricular rupture, severity of hemiplegia (determined using the 12-grade hemiplegia function test), and Functional Independence Measure cognitive score were found to be independent predictors of prognosis. Severity of hemiplegia was the strongest predictor of ambulation, with a sensitivity of 80.4% and specificity of 100% when the cut-off was set at grade 6 (the ability for coordinated movement of the extensor and flexor muscles of the hip joint). [Conclusion] The severity of hemiplegia, Functional Independence Measure cognitive score, and ventricular rupture were independently associated with ambulation in patients with putaminal hemorrhage. The ability of the hip joint movement is one of the most important factors in ambulation prognosis.
Key words: Ambulation, Prognosis, Putaminal hemorrhage

(This article was submitted Nov. 14, 2023, and was accepted Dec. 30, 2023)

INTRODUCTION

Stroke can cause sequelae that have major impacts on activities of daily living (ADL) and quality of life (QOL). In particular, ambulatory impairment is a major problem. Whether a stroke patient can ambulate again is a major concern for patients and their families, and rehabilitation plays an important role in this respect.

There are an estimated 1,115,000 patients with cerebrovascular disease in Japan[1)]. The incidence of cerebrovascular disease is similar to or lower than in Western countries, but the incidence of intracerebral hemorrhage is two to three times higher than in Western countries[2)].

Intracerebral hemorrhage accounts for about 10–20% of all strokes and is a serious condition that leads to more severe disability and death than ischemic stroke[3–6)]. The putamen is a common site of hypertensive cerebral hemorrhage and is reported

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to be more common in younger patients[7–9]. Important neural fibers densely surround the putamen; in putaminal hemorrhage (PH), direct damage to the neurons is caused by the hematoma; surrounding tissues may also be damaged by ischemia[7]. The size of the PH directly affects the degree of motor dysfunction, sensory impairment and higher brain dysfunction, which often result in gait disturbance[10]. The nature of the hematoma progression also affects the prognosis. A hematoma that affects the anterior limb of the internal capsule generally results in milder paresis. Severe hemiplegia can result from a hematoma that extends into the posterior limb[11].

Ambulation in stroke patients is associated with ambulatory ability and the severity of hemiplegia during the early after onset and these physical functions are used to predict prognosis[12, 13]. Ambulation prognosis in patients with PH has been reported to be associated with hematoma volume and progression on computed tomography (CT) images, as well as impaired consciousness and age[14–16]. However, few studies have evaluated the ambulation prognosis of patients with PH using these physical functions. Because PH is common in younger people who need to return to their home and work duties, early and accurate ambulatory prognosis is desirable for patients and their families. This information is also useful to health care providers in advancing rehabilitation.

This study aims to identify factors associated with ambulation 3 months after the onset of PH, including indicators used in physical function, and to evaluate the utility of these factors for predicting ambulation prognosis.

PARTICIPANTS AND METHODS

This study used a single-center, retrospective observational design. The participants were patients admitted to the Kanazawa Medical University Hospital from March 2010 to December 2020, who were requested by the Department of Neurosurgery after the onset of PH and underwent rehabilitation. Patients who met the following criteria were excluded from the study: peripheral neurological disease, including intracerebral hemorrhage; a significant psychiatric, bone or joint disease; deceased patients; patients who underwent surgery during their hospital stay for another disease; patients who were transferred from the acute care ward; patients with missing data; and patients who could not undergo active rehabilitation for any other reason. Rehabilitation included 2–3 weeks in the acute care ward, followed by rehabilitation for up to 6 months in the rehabilitation ward for physiotherapy and occupational therapy (40–80 min per day, 6 days per week in the acute care ward, 120 min per day, 7 days per week in the rehabilitation ward.).

The participant selection process is shown in Fig. 1. Of 145 PH patients prescribed rehabilitation during the study period, 61 were excluded (4 due to death, 20 due to complications associated with central and peripheral neurological disorders, 8 with significant mental, bone or joint disease, 4 who underwent surgery for another disease during their hospital stay, 6 who were unable to undergo continuous rehabilitation for other reasons, 17 who were discharged from the acute care ward, and 2 with incomplete data); thus, 84 participants were included in the analysis.

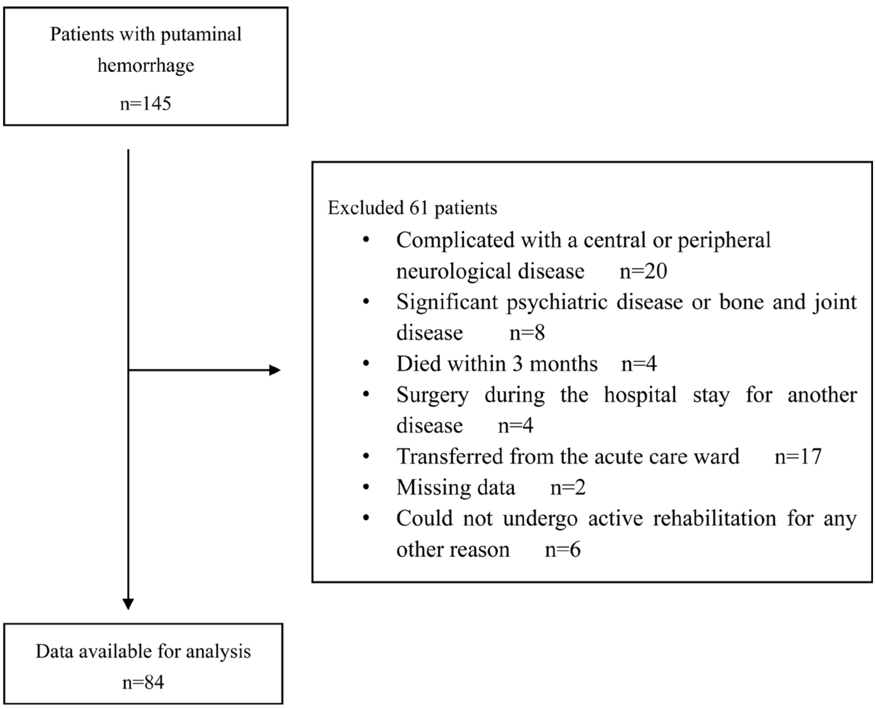

Fig. 1. Flowchart of participant inclusion.

The following data were extracted from the patients' medical records: age, gender, affected side, hematoma volume, presence of ventricular rupture, hematoma progression based on CT images, time to start rehabilitation after PH, time to start standing after PH, the length of hospital stay, and outcome. Hematoma progression was categorized into five classes according to Kanaya's classification: I, extracapsular; II, extending to the anterior limb of the internal capsule; III, extending to the posterior limb of the internal capsule; IV, extending to the anterior and posterior limbs of the internal capsule; and V, extending to the thalamus or subthalamus[17].

Severity of hemiplegia, ADL, aphasia, impaired consciousness, superficial sensory impairment, unilateral spatial neglect, and ambulatory ability were assessed at the start of rehabilitation. Impaired consciousness was classified based the Japan Coma Scale (JCS), as follows: 0, alert; I, awake without stimulation; II, awake with stimulation but asleep when stimulation stops; and III, does not wake with any stimulation[18]. The severity of hemiplegia was evaluated according to Ueda's 12-grade hemiplegia function test[19]. This test grades hemiplegia from 0–12, as follows: grade 0, inadequate associated reactions; grade 1, adequate associated reactions; grade 2, adequate voluntary contractions; grades 3–6, conjugate movement of extensor muscles, and unilateral or bilateral adequacy of conjugate movements of the flexor muscles; grades 7–8, adequacy in 1–2 of the following movements: lower limb extension, knee flexion, or ankle dorsiflexion; grades 9–11, adequacy in 1–3 of the following movements: ankle dorsiflexion with knee extension, ankle dorsiflexion with hip and knee extension, or hip medial rotation; grade 12, able to perform all movements in grade 11, and good performance on a speed test. The ADL was assessed with the Functional Independence Measure (FIM) which consists of 13 motor subscale items (1–7 points per item, maximum of 91 points) and 5 cognitive subscale items (1–7 points per item, maximum of 35 points)[20].

Ambulatory ability was evaluated at 3 months after the onset of PH and at discharge. Ambulatory ability was assessed with the Functional Ambulation Categories (FAC), as follows: 0, non-functional ambulator; 1, ambulator, dependent on physical assistance−level I (a patient who requires continuous manual contact to support their body weight, as well as to maintain balance or to assist coordination); 2, ambulator, dependent on physical assistance−level II (a patient who requires intermittent or continuous light touch to assist balance or coordination); 3, ambulator, dependent on supervision; 4, ambulator, independent on level surface only; 5, ambulator, independent[21]. Patients with a FAC ≥4 were defined as ambulators, and patients with a FAC ≤3 as non-ambulators.

The percentages of ambulators, 3 months after the onset of PH and at discharge, were calculated and the clinical backgrounds of ambulators and non-ambulators were compared. Continuous variables with normal distributions were compared with Student's t-test, and variables with non-normal distributions were compared using the Mann–Whitney U test. For Normality, we used the Shapiro–Wilk test. Percentages were compared using the χ^2 test or Fisher's exact test. Logistic regression analysis was used to identify factors associated with ambulation at 3 months after the onset of PH; all such factors in the univariate analysis were included as independent variables in the logistic regression, which used the stepwise entry method. Receiver operating characteristic (ROC) curves were drawn, and area under the curve (AUC) values were calculated. Optimal cut-off values were determined by the Youden index. Data are expressed as median (interquartile range [IQR]) or mean (standard deviation [SD]). The IBM SPSS statistical package (ver. 27.0; IBM Corp., Armonk, NY, USA) was used for all statistical analyses, and $p<0.05$ was taken to indicate statistical significance.

Ethical considerations were taken into account in conducting this study in strict adherence to the ethical principles of the Declaration of Helsinki. This study was conducted with strict adherence to the ethical principles of the Declaration of Helsinki. The research plan was approved by the Research Ethics Review Committee of Kanazawa Medical University (approval no. H265). All participants provided written informed consent before participating in the study.

RESULTS

Among the participants, 60.7% (FAC ≥4) were ambulatory 3 months after PH, 29.8% had FAC ≤3, and 9.5% had FAC 0. The median duration of hospitalization was 165 (IQR: 149–175) days, and the percentage of ambulators at discharge was 70.2% (FAC ≥4), 21.5% had FAC ≤3, and 8.3% had FAC 0. The time between PH to ambulation was ≤2 weeks, 2 weeks–3 months, and >3 months in 29.8%, 30.9% and 9.5% of patients, respectively.

The characteristics of the participants according to their ambulatory status 3 months after PH are shown in Table 1. No significant differences in gender or age were found between ambulators and non-ambulators. The median hematoma volume, as determined by CT, in the acute stage after PH was 12.0 (IQR: 6.5–19.0) mL in ambulators and 28.0 (IQR: 21.0–46.0) mL in non-ambulators ($p<0.001$). CT images of hematoma progression were classified as IV (extension to the anterior and posterior limbs of the internal capsule) or V (extension to the thalamus or subthalamus) in a higher percentage of non-ambulators than ambulators ($p<0.001$). Ventricular rupture and a requirement for surgery were also more common among non-ambulators ($p<0.001$ for both). The median length of hospitalization was 53.0 (IQR: 22.0–97.5) days in ambulators and 165.0 (IQR: 149.0–175.0) days in non-ambulators ($p<0.001$), and ambulators were discharged significantly more often than non-ambulators ($p<0.001$). There were no significant group differences in the time to start rehabilitation after PH, the time to start standing after PH, and the affected side.

Table 2 shows the results of physical function assessments performed at the start of rehabilitation according to the patient's ambulatory ability 3 months after PH. Ambulators had an FAC 2–3 ($p<0.001$), and a higher likelihood of unimpaired or only mildly impaired consciousness (JCS 0, I) ($p<0.001$). Fewer ambulators had unilateral spatial neglect ($p=0.003$) or superficial sensory impairment (p=0.01); they also had a significantly higher hemiplegia function grade, as well as higher FIM motor and FIM cognitive (p<0.001 for all). There was no significant association between ambulatory ability and aphasia.

Among the baseline characteristics and physical function assessments, hematoma volume, CT classification of hematoma progression, ventricular rupture, surgery, FAC, JCS, unilateral spatial neglect, sensory impairment, hemiplegia function grade, and FIM motor and cognitive were associated with ambulation 3 months after PH. Stepwise logistic regression analysis identified three factors independently associated with ambulation: ventricular rupture, hemiplegia function grade and FIM cognitive. The odds ratio (95% confidence interval [CI]) of ambulation at 3 months was 0.018 (CI: 0.001–0.640) in patients with ventricular rupture. The odds ratio increased by 2.32 (CI: 1.36–3.95) per grade, and 1.11 (CI: 1.01–1.22) per 1-point increase in the FIM cognitive (Table 3).

Next, the predictive value of the various factors associated with ambulation 3 months after PH was evaluated. Absence of ventricular rupture predicted ambulation with 77.8% sensitivity and 90.4% specificity (Table 4). ROC analysis of hemiplegia function grade (Fig. 2A) and FIM cognitive (Fig. 2B) was performed; the AUC values were 0.933 and 0.881, respectively. The optimal cut-off value was obtained via Youden index analysis (Table 4). Hemiplegia function grade predicted ambulation 3 months after PH with 80.4% sensitivity and 100% specificity, at a cut-off grade of 6. The FIM cognitive predicted ambulation with 76.5% sensitivity and 87.9% specificity when the cut-off value was set at 18 points.

DISCUSSION

Previously reported rates of ambulatory independence after the onset of PH ranging from 54.1% to 74.6%[15, 16, 22]. In our study, 70.2% of the patients were ambulating at discharge, a high percentage. Approximately 60% of our patients were ambulatory at 3 months after the onset of PH. However, improvement thereafter was observed in only 10% of patients. Jorgensen

Table 1. Patient characteristics according to ambulatory ability 3 months after putaminal hemorrhage (PH)

	Total N=84	Ambulators n=51	Non-ambulators n=33	p-value
Age (years)	60.7 ± 10.0	59.7 ± 9.6	62.1 ± 10.5	
Gender (male/female)	51/33	33/18	18/15	
Affected side (right/left)	42/42	26/25	16/17	
Hematoma volume (mL)	17.0 (10.0–29.0)	12.0 (6.5–19.0)	28.0 (21.0–46.0)	**
Hematoma progression (I/II/III/IV/V)	23/13/27/15/6	22/11/14/3/1	1/2/13/12/5	**
Operation (yes/no)	11/73	0/51	11/22	**
Ventricular rupture (yes/no)	21/63	2/49	19/14	**
Time to start rehabilitation after PH (days)	3.0 (2.0–4.0)	3.0 (2.0–4.5)	2.0 (2.0–4.0)	
Time to start standing after PH (days)	4.0 (2.0–6.0)	4.0 (2.0–5.0)	4.0 (3.0–7.0)	
Length of hospitalization (days)	100.0 (32.5–165.0)	53.0 (22.0–97.5)	165.0 (149.0–175.0)	**
Outcome (return to home/other)	67/17	48/3	19/14	**

Data are expressed as mean ± standard deviation or median (interquartile range).
*p<0.05, **p<0.01.

Table 2. Physical function assessment variables at the start of rehabilitation according to ambulatory ability 3 months after putaminal hemorrhage (PH)

	Ambulators n=51	Non-ambulators n=33	p-value
FAC (0/1/2/3)	20/0/13/18	32/1/0/0	**
JCS (0/1/2/3)	27/17/7/0	2/13/13/5	**
Aphasia (yes/no)	9/42	12/21	
Unilateral spatial neglect (yes/no)	8/43	15/18	**
Sensory impairment (yes/no)	14/37	18/15	*
12-grade hemiplegia function test (0–12)	11.0 (7.5–11.0)	1.0 (0–2.0)	**
FIM motor score	29.0 (16.5–57.5)	13.0 (13.0–13.0)	**
FIM cognitive score	34.0 (19.5–35.0)	8.0 (5.0–14.0)	**

Data are n, or median (interquartile range).
*p<0.05, **p<0.01.
FAC: functional ambulation categories; JCS: Japan come scale; FIM: functional independence measure.

et al. classified stroke patients by the severity of hemiplegia and investigated the time to achieve maximum ambulatory ability[12]. They reported that 95% of patients with mild, moderate and severe hemiplegia became ambulatory within 4, 6 and 11 weeks, respectively. Other studies reported improved ambulation within 3 months after stroke; improvement thereafter was observed in only 5% of patients[23–25]. In our results, it was suggested that it would be useful to analyze the ambulation prognosis, delimited by 3 months after the onset of PH. The percentage of ambulation at 3 months or more after PH was 10%, which was higher than in other studies. The participants in this study were young, with an average age of 60 years, and it was thought that recovery of ambulatory ability was possible with appropriate rehabilitation, even if hemiplegia was severe.

The ambulation prognosis for stroke patients has been based on indicators of physical function, such as the ambulatory ability and severity of hemiplegia in the early stage after stroke[12, 23, 24, 26, 27]. In the ambulation prognosis of PH, the volume and progression of hematoma on CT imaging impaired consciousness and age have been reported as prognostic factors[14–16]. Previously reported thresholds for hematoma volume leading to non-ambulation after PH include 30–40 mL[28, 29]. Our study found that the median hematoma volume was 12.0 (IQR: 6.5–19.0) mL for ambulators and 28.0 (IQR: 21.0–48.0) mL for

Table 3. Factors associated with ambulation 3 months after putaminal hemorrhage (PH): results of multiple logistic regression analysis

	Partial regression coefficients	p-value	Odds ratio (95% confidence interval)
Ventricular rupture	−4.021	*	0.018 (0.001–0.640)
12-grade hemiplegia function (/1 grade)	0.841	**	2.32 (1.36–3.95)
FIM_ cognitive score (/1 point)	0.103	*	1.11 (1.01–1.22)

*p<0.05, **p<0.01.
FIM: functional independence measure.

Table 4. Optimal cut-off, sensitivity, and specificity values for the prediction of ambulation 3 months after putaminal hemorrhage (PH): results of receiver operating characteristic (ROC) curve analysis

	Cut-off value	Sensitivity (%)	Specificity (%)
12-grade hemiplegia function	6	80.4	100
FIM cognitive score	18	76.5	87.9
Ventricular rupture	No	77.8	90.4

Optimal cut-off value was determined by the Youden index.
FIM: functional independence measure.

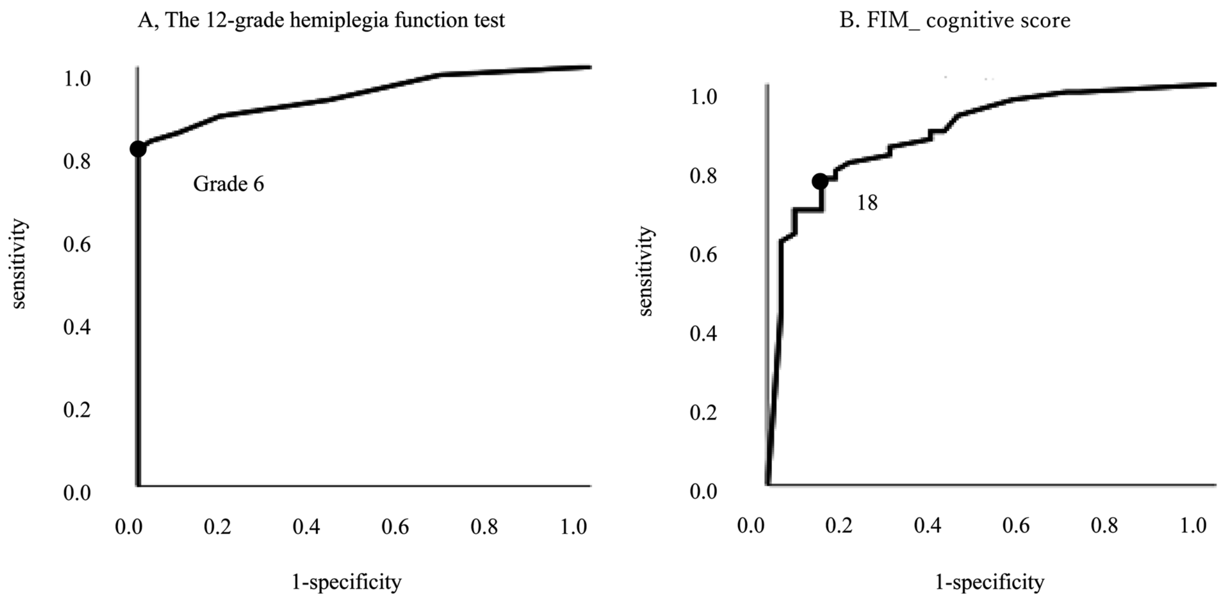

Fig. 2. Predictive performance of ambulation variables 3 months after putaminal hemorrhage (PH).
ROC curves of the 12-grade hemiplegia function test (A) and FIM cognitive score (B) are shown. The AUC was 0.933 (CI: 0.880–0.986) for the 12-grade hemiplegia function test and 0.881 (CI: 0.807–0.955) for the FIM cognitive score.
ROC: receiver operating characteristic; AUC: area under the curve; FIM: Functional Independence Measure; CI: confidence interval.

non-ambulators, comparable to previous reports. Hematoma progression classes with relatively good prognosis are I–III; IV and V have poor prognosis[14, 15, 22]. Ventricular rupture in PH causes severe brain damage and is an important factor in poor functional prognosis[30]. Furthermore, a study evaluating ambulation prognosis based on hematoma progression and presence of ventricular rupture found significant differences between classes III–V. Those with no ventricular rupture and less hematoma progression had a better prognosis[16]. These findings were replicated in our study.

Surgery in PH patients is associated with lower mortality but a poorer functional prognosis[31]. After endoscopic surgery, the percentage of patients with mRS (modified Rankin Scale) ≥3 was higher than for other procedures, indicating efficacy[32]. However, the rate of ambulatory independence in these patients was low. Our study also revealed that patients who underwent surgery had a poor prognosis for ambulation. Since the indication for surgery is determined by the hematoma volume, it is possible that the high hematoma volume was the cause of the poor prognosis in patients who underwent surgery. Indeed, logistic regression analysis showed no significant association between surgery and ambulation.

Age has also been reported to influence the ambulation prognosis of PH patients[14, 16, 22]. However, in our study, we found no significant relationship with age. The majority of patients in this study were young, with an average age of 60 years; only about 20% of patients were over 70 years old, with half in the independent and half in the non-independent group, suggesting that age had no effect. In addition, previous reports investigated factors affecting ambulation prognosis at 6 months after the onset of PH and at discharge from hospital. Our study investigated factors affecting ambulation prognosis at 3 months onset, and this difference in timing of ambulation prognosis may have resulted in this outcome.

In the physical function assessment, ambulation 3 months after the onset of PH was associated with FAC and consciousness impairment at the time of starting rehabilitation; these results are consistent with previous studies[12–14, 32]. Unilateral spatial neglect, which was seen more often in non-ambulators, is involved in posture control in the seated and standing positions, as well as in ambulation[26, 27, 33]. There were fewer patients with sensory impairments in the ambulator than non-ambulator group. Sensory impairment affects ambulation control. Hemiplegia function grade, and FIM motor and cognitive, were higher in ambulators, consistent with previous studies; this suggests that these are important ambulation prognosis factors[34, 35].

Stepwise logistic regression analysis was performed to investigate which of the factors associated with ambulation 3 months after the onset of PH independently predicted prognosis; the presence of ventricular rupture, hemiplegia function grade, and FIM cognitive were identified. Previous reports have identified the amount and progression of hematomas as important factors in the ambulation prognosis of patients with PH[14–16]. These appear to be closely related to the degree of hemiplegia and ventricular rupture.

The ROC analysis revealed AUC values of 0.933 and 0.881 for hemiplegia function grade and the FIM cognitive, respectively, confirming their utility for predicting ambulation 3 months after the onset of PH. Youden index analysis revealed optimal cut-off values to predict ambulation of 6 for hemiplegia function grade and 18 for FIM cognitive. A hemiplegia function ≥grade 6, FIM cognitive ≥18 points, and absence of ventricular rupture had 75–80% sensitivity and 88–100% specificity for predicting ambulation. Of these three indicators, hemiplegia function grade ≥6 had the highest AUC, sensitivity and specificity values in the ROC analysis, demonstrating its superiority as a predictor of ambulation prognosis.

A grade of 6 on the 12-grade hemiplegia function test was an effective cut-off value for predicting ambulation. The basal ganglia, including the putamen, receive input from all areas of the cortex and project primarily via the thalamus to the premotor and frontal association areas (cortico-basal ganglia loop). It also projects to the brainstem via the mesencephalic tegmentum (basal ganglia-brainstem loop). Corticospinal tract control refined movements of the upper and lower limbs. The corticoreticular tract and the basal ganglia-brainstem system control the medial descending tract of the brainstem and are involved in postural reflexes, muscle tone, walking, and activity of the neck and trunk muscles and proximal muscles of the lower limbs[36]. Similarly, the corticospinal and corticoreticular tract play important roles in motor function and are located near the putamen.

Previous studies reported that the degree of damage to the corticospinal tract is significantly associated with hemiplegia and ambulation[37, 38]. Damage to only the corticospinal tract due to PH is associated with only mild loss of ambulatory ability, damage to only the corticoreticular tract is associated with moderate loss, and damage to both is associated with severe motor dysfunction and substantial loss of ambulatory ability[39]. Taken together, these studies suggest that ambulation prognosis after the onset of PH is affected by damage to the corticospinal and corticoreticular tract, and by the degree of hemiplegia. Furthermore, the proximal muscles of the lower extremity on the Stroke Impairment Assessment Set (SIAS) are more accurate and valid predictors of ambulation in stroke hemiplegic patients than diffusion-weighted imaging parameters[40]. These studies suggest that a cutoff value of 6 for hemiplegic functional grade, which indicates the ability to coordinate hip extensors and flexors, may be physiologically valid.

If the proximal muscles of the lower extremity are preserved and hip motion is possible, standing balance and ambulation practice may be adequate if only peripheral organs are controlled. The basic neural mechanisms for ambulation reside in the brainstem and spinal cord, with the brainstem reticular formation receiving input from the cerebral cortex, basal ganglia, limbic system, and cerebellum. These are transmitted via the brainstem reticular formation to the spinal cord, where they are said to contribute to posture and muscle tone regulation and ambulation control. The spinal cord is involved in the formation of ambulation rhythm and ambulation patterns, and the ambulation pattern generation mechanism is believed to exist as this neural mechanism[41]. Inserting more stimuli from the periphery that increase motor output is effective in rehabilitation and leads to ambulatory independence.

In this study, FIM cognition was associated with ambulation, with scores of 18 or higher predicting ambulation with high sensitivity and specificity. Brain edema immediately after stroke results in impaired consciousness, decreased spontaneity, and ultimately decreased activity. In addition, attention, comprehension, and judgment also affect cognitive function. Decreased cognitive function is likely to have a negative impact on ambulatory independence because motor learning is difficult to obtain.

The main strength of this study was the continuous assessment of ambulation ability during rehabilitation, from the acute to chronic phases, in a single facility. This study also had several limitations. First, the data were obtained from a single university hospital, such that the results may not apply to the general population. Second, our functional assessments did not evaluate trunk stability or balance; assessment of these parameters in future studies is important for a more multi-faceted analysis. Finally, this study investigated factors predicting ambulation 3 months after the onset of PH. However, a mild number of patients who became ambulatory after 3 months were also observed, indicating the need for long-term follow-up.

This study investigated factors associated with ambulation in patients with PH. Three months after PH, 60% of the patients were ambulatory, and the severity of hemiplegia, FIM cognitive score, and presence of ventricular rupture were independent predictors of the ambulation prognosis. The 12-grade hemiplegia function test and FIM are convenient and commonly used indicators of gait prognosis in physiotherapy settings. The 12-grade hemiplegia function test had 80% sensitivity and 100% specificity when grade 6, which indicates the ability for coordinated movement of the extensor and flexor muscles of the hip joint, was set as the cut-off. The ability of the hip joint movement would be one of the important factors for the ambulation prognosis.

Funding

This study was funded by the Kanazawa Medical University Hospital Research Grant-in-Aid for Allied Hearth Professionals (H2022-12).

Conflict of interest

The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

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