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Preexisting brain lesions in patients with post stroke pusher behavior and their association with the recovery period: A one year retrospective cohort study in a rehabilitation setting

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ABSTRACT

The presence of preexisting brain lesions due to previous stroke and cerebral small vessel disease has been reported to influence stroke related disability or rehabilitation outcomes. However, there is no data about the impact of such lesions on the recovery period after pusher behavior (PB). This retrospective cohort study aimed to determine the influence of preexisting brain lesions on PB recovery time. Nineteen patients who were suffering from PB were included in the study. The presence of preexisting brain lesions, including previous stroke, silent brain infarcts, microbleed, white matter hyperintensity, and enlarged perivascular spaces were assessed using medical history reports, radiological reports, and magnetic resonance imaging data. The lesion score, ranging from 0 to 5, was calculated based on each preexisting brain lesion. The time to recovery from PB was assessed using the Scale for Contraversive Pushing. Based on the median value of the lesion score, we divided patients into those with a lesion score < 2 and those with a lesion score ≥ 2. A Kaplan Meier survival analysis was performed between these two groups. A multivariable Cox proportional hazards analysis was also performed using the side with hemiparesis and the score of preexisting brain lesions as covariates to determine the hazard ratio. The results showed that the group with a lesion score ≥ 2 had significantly delayed recovery from PB and the hazard ratio of preexisting brain lesions score was 0.458 (95% confidence interval: 0.221, 0.949), while the side of hemiparesis was not identified a significant covariate. Our results indicated that patients with PB having higher score of preexisting brain abnormalities might require a longer time to recover, and this might be useful in planning inpatient rehabilitation and treatment goals for patients with PB.

1. Introduction

Stroke survivors sometimes exhibit postural tilt toward the side with hemiparesis and actively push to this side by using their unaffected limbs. This symptom is called pusher behavior (PB) [1] and is considered as one of the causes of balance and gait disorders [2]. PB has often been observed during the acute phase of stroke and this symptom is reported to gradually disappear over time from stroke onset [3,4]. However, prolonged PB limits the activities of daily living (ADL) and influences the length of hospital stay [4,5]. Therefore, predicting recovery from PB is important for planning the programs and goals of rehabilitation. Some studies have investigated the demographic or disease factors that influence recovery from PB [6–9]. The side of hemiparesis is one of the most frequently reported factors affecting the recovery period in many studies. Abe et al. [6] revealed that right sided brain damage is a negative factor for recovery from PB in the acute phase. Other studies have also indicated that right sided brain damage influences recovery from PB in rehabilitation settings [7,8].

Stroke is widely known to have a high rate of recurrence [10]. Nevertheless, the 5-year recurrence rate decreased from 18% in the late 1990s to 12% in the early 2000s, and has remained the same since [11]. There is conflicting evidence regarding the impact of stroke recurrence

Abbreviations: ADL, activities of daily living; cSVD, cerebral small vessel diseases; MRI, magnetic resonance imaging; CT, computed tomography; FIM, functional independence measure; FLAIR, fluid attenuated inversion recovery; PB, pusher behavior; SBIs, silent brain infarcts; SCP, scale for contraversive pushing; SIAS, stroke impairment assessment set; WMH, white matter hyperintensity.

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on functional outcomes [12,13]. Therefore, further studies are necessary to understand the impact of recurrent stroke on functional recovery and impairment, including postural abnormalities. Cerebral small vessel diseases (cSVD), such as silent brain infarctions (SBIs), white matter hyperintensity (WMH), microbleeds, and enlarged perivascular spaces (EPS) [14], should not be ignored. Most of cSVD are related to stroke onset and cognitive impairment [14]. Moreover, most cSVDs or the total burden of cSVD at the time of stroke onset were reportedly associated with poor functional outcomes or disability [15–19].

A large sample cohort study that investigated recovery from PB [6] excluded cases with multiple or bilateral lesions or other brain abnormalities. In most studies about recovery from PB, the association with a prior stroke and coexisting brain lesions such as cSVD has not been reported [3,7,9]. Although cSVD or a history of stroke has been reported to influence stroke related outcomes, no data are available on whether these preexisting lesions influence the recovery time from PB. The purpose of this study was to reveal the association between preexisting brain lesions and the time to recover from PB, using survival analyses.

2. Materials and methods

2.1. Study design and statement of ethics

This retrospective cohort study was conducted in accordance with the Declaration of Helsinki and approved by the Medical Ethics Committee of Kakeyu Hospital (approval number: 2020011). Informed consent could not be obtained because of the retrospective study design.

2.2. Patients

This study included patients with stroke, admitted to the Kakeyu Misayama Rehabilitation Center Kakeyu Hospital from December 2013 and December 2014. In all, 435 patients who underwent inpatient rehabilitation were screened. The patients underwent up to 3 h of standard physiotherapy, occupational therapy, and speech and language therapy per day to regain the ability to perform basic ADL. The inclusion criteria were as follows: 1) age over 20 years, 2) PB at the time of admission to the rehabilitation hospital, 3) independent living before the symptomatic stroke that induced PB, 4) no history of psychological diseases or dementia, and 5) available magnetic resonance imaging (MRI) data.

2.3. The assessment of preexisting brain lesions

The presence of cSVD is usually evaluated by MRI while the severity of cSVD is assessed by burden score, which combines the above-mentioned lesion presence. A high score represents increasing manifestations of abnormal signs on brain MRI [20,21]. In this study, we incorporated a history of stroke in the ordinal score because it was considered one of the risk factors for stroke recurrence and severity of disability, as in cSVD [22]. Each sign of preexisting lesion was allocated 1 point (minimum score, 0; maximum, 5) and lesion score was composed. We defined “severe lesion” as having a composed score equal to or greater than the median value, as per a previous study [21].

The information about the history of stroke and cSVD was confirmed from the medical history and radiological reports. MRI and/or computed tomography (CT) scan images taken at the time of onset and admission to the rehabilitation hospital were confirmed by a clinician to identify and avoid overlooking the presence of prior stroke and cSVD, which were not described in the reports. The confirmed MRI images included T1 weighted images, T2 weighted images, Fluid Attenuated Inversion Recovery (FLAIR) images, and T2* weighted images.

The history of stroke was mainly confirmed by the medical history and radiological reports and checked using MRI and/or CT images. Stroke data, including type and location of the lesion, was allocated one point if the medical history and brain images matched. SBIs were assessed by comparing the T1 weighted, T2 weighted, and FLAIR images [23]. Regardless of the number of SBIs, if ≥ 1 lesion was confirmed, it was allocated one point. WMH was assessed using the Fazekas visual scale [24]. If periventricular hyperintensity of grade 3 and/or deep and subcortical WMH of a grade more than 2 was seen, it was allocated one point. T2* weighted images were used to assess the presence of microbleeds. Fake signals, such as flow voids in sulcal locations, bilateral calcifications in the basal ganglia and/or in the choroid plexus, the pineal gland, and partial volume artifacts from the bone, were excluded. One point was allocated if ≥ 1 microbleeds were seen. EPS, fluid filled spaces, linear, round, or ovoid lesions < 3 mm in diameter could be seen on T2 weighted images. They were evaluated using a category 3 ordinal scale [25], and moderate to extensive EPS in the basal ganglia was allocated one point [19,20].

2.4. Assessment of pusher behavior

The Scale for Contraversive Pushing (SCP) [3] was used to assess the presence and severity of PB by a physiotherapist at a fixed daily schedule. SCP consists of 3 subscales, including postural sway, abduction or extension of the unaffected limbs, and resistance to passive postural correction. This assessment was performed within the first 7 days of admission and every week subsequently. We calculated the time to recover from PB based on the modified criteria of the SCP which mean the presence of PB was confirmed when all subcategory scored >0 [26]. Patients who did not recover from PB at the time of discharge from the rehabilitation hospital were considered “censored.”

2.5. Assessment of stroke related impairments and activities of daily living

The Stroke Impairment Assessment Set (SIAS) [27] was used to assess the severity of impairment at the time of admission to the rehabilitation hospital. SIAS consists of 22 subcategories, including motor and sensory functions, muscle tone, range of motion, pain, trunk function, speech ability, visuospatial function, and muscle strength of the unaffected limbs. The summed subcategories score ranges from 0 to 76 points, with a low score indicating severe impairment. We used the total score of all the subcategories for analysis.

Occupational therapists evaluated the Functional Independence Measure (FIM) to assess the ADL.

2.6. Statistical analyses

Descriptive data of the patients’ characteristics were analyzed. The Kaplan Meier survival and multivariable Cox proportional hazards analyses, which can handle censored cases, were performed to determine the influence of preexisting brain lesions on the time to recovery from PB. We first divided the patients into two groups based on the median lesion score value. Then, two groups’ baseline characteristics at admission and discharge were compared using the *t*-test or Wilcoxon rank sum test and Fisher’s exact test. Second, a Kaplan Meier analysis was performed to describe survival curves. The survival distribution was then compared using the Log Rank test. Finally, because the hemiparesis side was identified as the factor influencing the incidence of PB and delayed recovery in many previous studies, a multivariable Cox proportional hazards analysis was performed using the hemiparesis side and the number of preexisting brain lesions as variables and the hazard ratio with 95% confidence interval was computed.

All data analyses were computed using SPSS statistics ver. 25 (IBM Corp., Armonk, NY, USA). Differences were considered statistically significant at P values<0.05.

3. Results

A total of 21 (4.83%) out of the 435 patients screened exhibited PB. Two patients were excluded from this study because their MRI data were

missing. Finally, 19 patients were eligible for the analysis. The descriptive data are shown in Table 1. A patient did not recover from PB by the time of discharge from the rehabilitation hospital. The percentages of patients with a history of stroke, SBIs, WMH, microbleeds, and ESP were 21.1%, 47.4%, 47.4%, 31.6%, and 0.0%, respectively. The median value for lesion score was 2 (range: 0–3), therefore we divided patients into two groups: a group with scores < 2 and another with scores ≥ 2. The median survival time of the < 2 and ≥ 2 lesion groups were 62.0 days (95% confidence interval [CI]: 56.2, 67.8) and 94.0 days (95% CI: 77.0, 111.1), respectively. Individual data regarding the recovery process from PB are presented in Table 2. No significant differences were found in the baseline characteristics between the two groups at admission and discharge; however, the log-rank test indicated that the group with a lesion score ≥ 2 showed significantly delayed recovery from PB compared to those with a score < 2 ($\chi^2 = 4.796$, $P = 0.029$) (Fig. 1). The results of the multivariable Cox proportional hazards analysis are presented in Table 3. While the side of hemiparesis had no significant effect on the time to recover from PB, the hazard ratio for the score of preexisting brain lesions was 0.458 (95 % CI: 0.221, 0.949) and significantly impacted the recovery time from PB.

Table 1
Descriptive and clinical characteristics of the patients with pusher behavior.

	Total	Lesion score < 2 group	Lesion score ≥ 2 group	P Value
Variables	(N = 19)	(N = 9)	(N = 10)	
Age, years	74.4 (±7.5)	75.7 (±9.1)	73.3 (±6.0)	0.507
Sex (Male/Female), no.	8/11	4/5	6/4	0.656
Stroke type (Hemorrhage/ Ischemia), no	12/7	5/4	3/7	0.370
Hemiparesis side (right/left), no	5/14	2/7	3/7	0.701
Admission at rehabilitation hospital from onset, days	41.7 (±11.9)	37.4 (±7.7)	45.6 (±14.0)	0.141
Preexisting brain lesions				
Past history of stroke, % (no)	21.1% (4/19)			
SBIs, % (no)	47.4% (9/19)			
WMH, % (no)	47.4% (4/19)			
Microbleeds, % (no)	31.6% (6/19)			
EVS, % (no)	0% (0/ 19)			
SCP at admission, points	4.1 (±1.3)	4.0 (±1.1)	4.3 (±1.5)	0.676
SIAS at admission, points	24.0 (±6.4)	22.2 (±4.9)	25.0 (±7.5)	0.358
At discharge, points	29.5 (±10.4)	30.8 (±12.1)	28.4 (±9.1)	0.631
FIM at admission				
Motor, points	19.4 (±5.3)	20.2 (±5.1)	18.7 (±5.6)	0.484
Cognition, points	17.4 (±6.3)	16.7 (±5.8)	18.1 (±7.0)	0.633
FIM at discharge				
Motor, points	37.6 (±14.6)	41.1 (±16.6)	34.5 (±12.5)	0.338
Cognition, points	21.0 (±7.0)	22.3 (±7.7)	19.8 (±7.0)	0.461
				Mean (±standard deviation)

SBIs, silent brain infarctions; WMH, white matter hyperintensity; EVS, enlarged perivascular spaces; SCP, scale for contraversive pushing; SIAS, stroke impairment assessment set; FIM, functional independence measure.

4. Discussion

The purpose of this study was to determine the association between preexisting brain lesions and recovery time from PB in post stroke patients in a rehabilitation setting by using survival analyses. The results of this study showed that patients with a lesion score of 2 or more had significantly delayed recovery from PB. In the results of the multivariable Cox proportional hazards analysis, the side of hemiparesis did not significantly affect the time to recover from PB, while the score for preexisting brain lesions significantly impacted recovery from PB. To the best of our knowledge, this is the first study to reveal the association of preexisting brain lesions with time to recover from PB.

In this study, some of the preexisting brain lesions were up to 47.4%. While there are no reports explicitly detailing how many patients with PB have preexisting brain lesions, this proportion is similar to a previous study that investigated cSVD prevalence in patients with stroke [28]. A more important finding in this study was the number of preexisting brain lesions associated with a prolonged recovery period from PB in patients with stroke. Although there have been reports that a history of stroke has a negative impact on rehabilitation [29,30] and the presence of cSVD at the time of symptomatic stroke onset is an independent variable of poor functional outcomes [15–19], most previous studies that investigated recovery from PB excluded patients with other brain lesions or signs of any other brain abnormality [6] or did not mention them in detail. Therefore, it was not clearly indicated whether preexisting brain abnormalities influence the PB recovery period. Our results might indicate that preexisting brain abnormalities had a negative impact on recovery from PB, similar to other functional outcomes after stroke. One possible reason that might explain our results is the influence of the brain volume before a symptomatic stroke. Brain volume has been reported to be a protective factor against the severity of stroke, and a prior stroke decreases the brain volume [31]. Therefore, brain volume, which was lower in those with a history of stroke or cSVD, might also have been an important factor that influenced the recovery period from PB. In fact, a recent study has revealed the association between lesion size and incidence of PB in patients with right hemiparesis stroke, although the association between the lesion site and incidence has not been confirmed [32]. Another possible reason is that patients with cSVD originally had poor balance. Some previous studies have reported that the presence of SBIs and microbleeds among the middle aged to elderly population [33], or the presence of severe WMH in patients with lacunar stroke [34] are associated with poor balancing ability. When people with inadequate reserve balance ability due to prior brain lesions develop stroke and lose postural control, it can be difficult to control postural abnormalities, which might lead to delayed recovery from PB.

Regardless of previous studies [6–8], our results showed that the side of hemiparesis was not associated with recovery from PB. Our results regarding the relationship between hemiparesis and recovery time may have been influenced by the small sample size and unequal distribution between patients with right and left hemiparesis. However, a previous study that included patients with and without a history of stroke reported no significant difference in the PB recovery periods between right and left hemiparesis [4], recovery periods might possibly be different between patients with or without previous stroke and/or cSVD.

The presence of preexisting brain lesions may have possibly negatively impacted outcomes other than PB, but we were unable to confirm any corresponding statistical differences in SIAS and FIM results at discharge. Thus, it is unclear whether our results are due to the number of preexisting brain lesions, PB itself, which is known to influence outcomes after stroke [4,35] or both. Further studies are needed to explore this relationship.

Although our findings may provide a new perspective regarding the recovery process from PB, this study has limitations, and the results should be interpreted with caution. First, the small sample size

Table 2
The individual characteristics of stroke type, preexisting brain lesion, and recovery process from pusher behavior

NO	Age	Etiology	Hemiparesis Side	Location of lesions	Presence of preexisting brain lesion(Yes/No)					SCP		Days to recover from PB
		(H/I)	(L/R)		Prior stroke	SBIs	WMH	Microbleeds	EPS	Initial	Final	
1	68	H	L	Striatum	No	Yes	No	Yes	No	6.0	4.25	Censored[#]
2	73	I	L	Striatum	No	No	Yes	No	No	4.25	0	62
3	82	H	R	Striatum	No	Yes	Yes	Yes	No	3.0	0.75	94
4	81	I	L	Frontal and temporal lobes	No	No	Yes	No	No	4.75	0.75	151
5	69	H	L	Striatum	No	Yes	Yes	No	No	2.25	1.25	64
6	64	H	L	Thalamus	Yes	No	Yes	No	No	2.75	1.25	85
7	74	H	L	Frontal subcortical area	Yes	No	No	No	No	2.25	1.25	57
8	87	I	R	Internal capsule and occipital lobe	No	Yes	No	No	No	4.25	1.25	83
9	71	H	R	Thalamus, Internal capsule	No	Yes	No	Yes	No	3.25	0.5	167
10	69	H	L	Striatum, Thalamus	Yes	No	No	Yes	No	5.0	1.25	191
11	81	I	L	Frontal, Temporal and Partial lobes	No	No	No	No	No	5.25	1.5	71
12	63	I	L	Temporal lobe	No	No	No	No	No	2.5	1.0	37
13	80	I	L	Temporal lobe	No	Yes	Yes	No	No	3.5	0.75	56
14	67	H	L	Striatum	No	No	No	Yes	No	5.0	1.25	63
15	79	I	R	Thalamus	No	Yes	Yes	No	No	4.5	0.75	54
16	67	H	L	Thalamus	No	Yes	No	No	No	4.25	1.5	42
17	74	H	L	Thalamus	No	No	Yes	Yes	No	6.0	0.75	96
18	77	H	L	Striatum	Yes	No	Yes	No	No	6.0	0.75	105
19	88	H	R	Thalamus	No	Yes	No	No	No	3.3	0.75	60

PB, pusher behavior; H, hemorrhage; I, ischemia; R, right; L, left; SBIs, silent brain infarctions; WMH, white matter hyperintensity; ESP, enlarged perivascular spaces; SCP, scale for contraversive pushing. [#]The final assessment of pusher behavior of a censored case was conducted at 220 days from stroke onset.

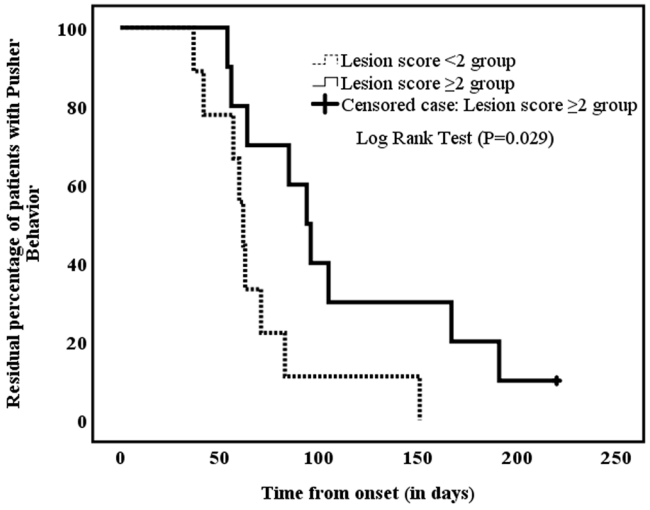

Fig. 1. A Kaplan Meier plot of time to recover from pusher behavior (in days). Censored case failed to recover from pusher behavior by the time of discharge from rehabilitation hospital.

Table 3
Hazard ratio for the time to recover from pusher behavior

Variables	Hazard ratio	95% CI		P Value
		Lower	Upper	
Hemiparesis side	0.669	0.227	1.976	0.467
The score of preexisting brain lesions	0.458	0.221	0.949	0.036

CI, confidence interval

prohibited the use of subgroup analysis between patients with and without prior brain lesions or patients with each type of lesion and limited the covariates used in the Cox proportional hazards analysis. To overcome this limitation, future studies with a longer duration and by multiple centers are necessary for the generalization of these results. Second, we counted the number of lesions based on the presence of each cSVD but did not consider the number of damages in the same lesions. Multiple SBIs or microbleeds have been reported to be associated with severe stroke or lower functional recovery 6 months after stroke onset [15,17]. Further studies based on the number of impairments caused by similar lesions and their influence on the PB recovery period are necessary.

5. Conclusions

Patients with a score of $\geq$ 2 for preexisting brain lesions showed delayed recovery from PB. The multivariable Cox proportional hazards analysis also showed that the score for preexisting brain lesions was a significant covariate for delayed recovery period from PS. Our results might be useful in planning rehabilitation and treatment goals for PB patients in a rehabilitation setting.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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