ORIGINAL ARTICLE

Balance Function Required for Bathing Independence in Patients with Stroke and Hip Fracture

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Objectives: Little attention has been paid to the relationship between balance function and bathing independence. This research aimed to determine the degree of balance function needed by patients with stroke and patients with hip fracture (hereinafter referred to as patients with stroke and hip fracture) to bathe independently. **Methods:** Retrospective data analysis was performed on 59 patients with hip fracture and 201 patients with stroke. Logistic regression was performed to determine whether bathing independence was associated with the Berg Balance Scale (BBS) in patients with stroke and hip fracture. A receiver operating characteristic curve was generated to calculate cutoff values. **Results:** The BBS was significantly associated with bathing independence in patients with stroke and hip fracture. The calculated BBS cutoff value was 48 points for those with stroke (sensitivity, 84.7%; specificity, 79.1%) and 43 points for those with hip fracture (sensitivity, 81.3%; specificity, 77.8%). **Conclusions:** Balance function was independently associated with bathing independence. The level of balance function required for bathing independence may be lower for patients with hip fracture than for those with stroke. This could be a simple and useful indicator for rehabilitation professionals to interpret BBS results when conducting bathing interventions.

Key Words : balance; bathing; hip fracture; rehabilitation; stroke

INTRODUCTION

Stroke and hip fracture are two of the major diseases that require rehabilitation. In 2019, 12.2 million incident cases of stroke and 14.2 million cases of hip fracture were reported.[1,2] These numbers are unlikely to decline in the foreseeable future as the global population continues to age. Stroke and hip fractures have a substantial impact on the medium- to long-term disabilities of affected patients.[3,4] For these individuals, rehabilitation is crucial to regaining the capacity to perform activities of daily living (ADLs).

Bathing is one of the most difficult ADLs to perform independently.[5] Patients with stroke and those with hip fracture (hereinafter collectively referred to as patients with stroke and hip fracture) have difficulty with independent bathing even after rehabilitation.[6,7] However, bathing is an important ADL that maintains physical cleanliness and relaxes the body and mind. Bathing has also been reported to improve subjective health and sleep quality, reduce the risk of cardiovascular disease, and decrease blood glucose and obesity.[8–10] Bathing is a popular and often habitual pastime that is part of the Japanese culture.[8]

Balance function has been closely associated with independence in ADL among patients with stroke and hip fracture.[11,12] Reports have shown that around 83% of patients with stroke suffer from balance impairment, and good balance is a prerequisite for regaining the ability to perform ADLs independently.[13] Balance impairment is the primary risk factor for falls in the elderly population, and falls are the most common cause of age-related hip fractures.[14,15]

Therefore, improving balance function is a key component of rehabilitation for patients with stroke and hip fracture.[16,17]

Generally, little attention has been paid to the relationship between balance function and bathing independence. In particular, the level of balance function necessary for bathing independence has not been investigated to date and remains unclear. Clarifying the level of balance function required for bathing independence in patients with stroke and hip fracture will provide useful information for rehabilitation planning. This study aimed to determine the level of balance function required for bathing independence in patients with stroke and hip fracture. The results of this research are expected to be used to interpret balance assessment data and to guide balance training.

MATERIALS AND METHODS

A retrospective observational research design was used for this study. The participants included 260 inpatients (201 with stroke and 59 with hip fracture) who were admitted to a convalescent rehabilitation ward in Japan and satisfied the following criteria. The inclusion criteria for patients with stroke were as follows: (1) those aged 20 years or older, (2) those with unilateral supratentorial lesions, (3) those diagnosed with a cerebral hemorrhage or infarction for the first time, (4) those admitted or discharged between April 2011 and December 2017. The inclusion criteria for patients with hip fracture were as follows (1) those admitted or discharged between April 2015 and March 2018, (2) those diagnosed with a femoral neck or trochanteric fracture, (3) those without a history of stroke, and (4) those aged 20 years or older. Patients with missing data were excluded. This study was approved by the Kita-Fukushima Medical Center and Fukushima Medical University's ethics review committee (No. 94, general 2020–236). Because the design of our study was retrospective without intervention, the opt-out method was used instead of informed consent.

Instruments for Data Collection

Information on age, gender, independence in bathing (including showering), and physical and mental functions (including balance function at discharge) were collected from the medical charts of the participants. Bathing was assessed using the Barthel Index,[18] and a score of 5 points was defined as "independent" in this study. Assessment using the Barthel Index was performed by occupational therapists. The Berg Balance Scale (BBS)[19] was used as an index of balance function. This scale evaluates balance function based

on 14 tasks, with higher scores indicating a higher balance function. Other important functional assessments included the Stroke Impairment Assessment Set (SIAS)[20] for patients with stroke and knee extension strength for patients with hip fracture. The SIAS comprehensively assesses functions commonly affected by stroke, which include motor function, sensory function, muscle tone, range of motion, non-affected side function, language and visuospatial perception, and pain. Knee extension strength was measured using a hand-held dynamometer (Tas F1; Anima, Tokyo, Japan) in the sitting position. The sensor was placed on the front of the distal lower leg and fixed with a belt and the therapist's hand. To standardize the knee extension strength, the result was calculated as the average value for the left and right sides and was normalized relative to body weight and lower leg length. The Revised Hasegawa's Dementia Scale (HDS-R) was used as an indicator of cognitive performance.[21]

Data Analysis

To determine whether bathing independence was correlated with balance function in patients with stroke and hip fracture, logistic regression was used, with bathing independence and the BBS being considered as the dependent and independent variables, respectively (crude model). In addition, logistic regression adjusting for age, gender, HDS-R, and SIAS in patients with stroke or knee extension strength in patients with hip fracture was also performed to adjust for confounders (adjusted model). Thereafter, we determined cutoff values using the receiver operating characteristic (ROC) curve. Accordingly, cutoff values were determined using the Youden Index when the area under the ROC curve (AUC) was greater than 0.7 (moderate accuracy).[22] All statistical analyses were performed using SPSS Statistics for Windows Version 25.0 (IBM, Armonk, NY, USA) with the significance level set at less than 5%.

RESULTS

Patients with stroke had a mean age of 73.2±13.7 years, with men accounting for 57.7% of the cohort, whereas those with hip fracture had a mean age of 82.3±7.4 years, with men accounting for 18.6% of the cohort (**Table 1**). Of the 201 patients with stroke and the 59 patients with hip fracture, 72 (35.8%) and 32 (54.2%) were capable of independent bathing, respectively. The BBS scores were 39.0±17.5 and 40.5±14.5 for patients with stroke and those with hip fracture, respectively. The HDS-R scores were 22.5±7.3 and 21.5±7.6 for patients with stroke and those with hip fracture, respectively.

Table 1. Characteristics of study participants

Variable	Stroke (n=201)	Hip fracture (n=59)
Age, years	73.2 (13.7)	82.3 (7.4)
Male, %	57.7	18.6
Right-side affected, %	50.7	50.8
Post-onset period at admission, days	28.3 (11.0)	24.4 (7.8)
Length of hospital stay, days	77.8 (34.7)	56.6 (22.1)
Bathing item of Barthel Index at discharge	0 (0–5)	5 (0–5)
Bathing independence at discharge, %	35.8	54.2
Berg Balance Scale	39.0 (17.5)	40.5 (14.5)
HDS-R	22.5 (7.3)	21.5 (7.6)
SIAS	59.3 (14.4)	
Knee extension strength, Nm/kg		0.79 (0.31)

Data given as mean (standard deviation), percentage, or median (interquartile range).

Table 2. Logistic regression with bathing independence as dependent variable in stroke patients

	Crude model		Adjusted model	
	Odds ratio (95% CI)	P value	Odds ratio (95% CI)	P value
Berg Balance Scale	1.28 (1.18–1.38)	<0.01	1.21 (1.10–1.32)	<0.01
Age			0.98 (0.95–1.03)	0.44
Gender (Women:1)			0.72 (0.31–1.67)	0.44
HDS-R			1.03 (0.95–1.11)	0.53
SIAS			1.07 (1.00–1.14)	<0.05

Table 3. Logistic regression with bathing independence as dependent variable in hip fracture patients

	Crude model		Adjusted model	
	Odds ratio (95% CI)	P value	Odds ratio (95% CI)	P value
Berg Balance Scale	1.18 (1.08–1.29)	<0.01	1.17 (1.02–1.33)	<0.05
Age			1.08 (0.96–1.22)	0.20
Gender (Women:1)			5.48 (0.69–43.3)	0.11
HDS-R			1.15 (0.99–1.33)	0.07
Knee extension strength			1.43 (0.02–91.04)	0.87

Logistic regression showed that in the crude model (univariate analysis), BBS was significantly associated with bathing independence in patients with stroke and hip fracture (P<0.01; **Table 2, 3**). In the adjusted model (multivariate analysis), the BBS remained significantly associated with bathing independence. ROC curve analysis showed that patients with hip fracture had an AUC of 0.88 [95% confidence interval (CI): 0.79–0.96, P<0.01] and those with stroke had an AUC of 0.90 (95% CI: 0.85–0.94, P<0.01) for independence of bathing based on the BBS. The calculated cutoff values for the BBS were 48 points for patients with stroke (sensitivity, 84.7%; specificity, 79.1%) and 43 points for patients with hip fracture (sensitivity, 81.3%; specificity, 77.8%).

DISCUSSION

The current study investigated the relationship between bathing, the most difficult ADL to perform independently, and balance function for patients with stroke and hip fracture. The strengths of this study were as follows: (1) our

inclusion of two major groups of patients requiring rehabilitation, namely those with stroke and hip fracture and (2) our examination of not only the relationship between bathing and balance function but also the level required for independence. The results of this study revealed cutoff values associated with bathing independence as measured by the BBS in patients with stroke and hip fracture.

An extensive survey of previous studies[23,24] reported that the mean age at stroke onset was 74.3 years with men accounting for 46.1% of patients, whereas the mean age upon sustaining a hip fracture was 84.5 years with men accounting for 22.1% of patients. In our study population, patients with stroke had a mean age of 73.2 years (57.7% men), whereas those with hip fracture had a mean age of 82.3 years (18.6% men), a finding consistent with those presented in previous studies. Regarding the BBS score in previous studies that included patients similar to those included herein (i.e., those admitted to Japanese rehabilitation hospital wards), Tamura et al.[25] found that patients with stroke had a median BBS score of 39.5, whereas Takeda et al.[26] reported that patients with hip fracture had a mean BBS score of 39.7. These values are close to those obtained in the current study. Therefore, the participants of the current study do not appear to constitute a significantly biased sample.

The outcomes of logistic regression in this study revealed a relationship between bathing independence and balance function in patients with stroke and hip fracture. Age,[27] gender,[28] cognitive function,[29] and the SIAS[30] have been reported to be associated with ADL independence in patients with stroke. However, age,[31] cognitive function,[31] and knee extension muscle strength[32] have also been reported to be associated with ADL independence in patients with hip fracture. In this study, bathing independence remained significantly associated with balance function after adjusting for these factors, suggesting that balance function is independently associated with bathing. The calculated odds ratios for BBS were 1.21 and 1.17 in patients with stroke and hip fracture, respectively, which were higher than those for age, gender, and other functions. Furthermore, considering that the BBS is a multistep scale ranging from 0 to 56 points, the odds ratio value of this study suggests that the influence of balance on bathing independence is large.

The BBS cutoff values associated with bathing independence calculated in this study were 48 points for patients with stroke and 43 points for patients with hip fracture. This could be a simple and useful indicator that could help rehabilitation professionals interpret the results of the BBS when conducting bathing interventions. In previous studies, several BBS

cutoff values associated with ADL independence in patients with stroke have been reported: 39–43 points for toileting,[33] 41–44 points for dressing,[33,34] and 49–54 points for climbing stairs.[33,35] Considering that bathing is one of the most difficult ADLs in patients with stroke[36] and the values of other ADLs mentioned above, the calculated cutoff values for bathing in patients with stroke are considered reasonable. However, there was a 5-point difference in BBS cutoff values between patients with stroke and those with hip fracture. The minimal clinically important difference (MCID) for the BBS has been reported to be 4–5 points in patients with stroke,[25] 3 points in those with multiple sclerosis,[37] and 5 points in those with chronic obstructive pulmonary disease.[38] Therefore, it is possible that the 5-point difference in the cutoff value between patients with stroke and those with hip fracture is beyond the margin of error. In fact, patients with hip fracture can compensate for balance function by grasping a support with both hands, which allows them to move and transfer more easily than patients with stroke hemiplegia. Therefore, the required balance function for bathing independence may have been lower for patients with hip fracture than for those with stroke. However, a score of 11.5 points for BBS was reported for MCID in patients with hip fracture,[39] suggesting the need for further study.

One of the major limitations of this study is that it was conducted in a hospital setting. The hospital bathrooms are well equipped when compared with an average home; for example, handrails are installed, there are no steps at the toilet entrance, and shower chairs are available if necessary. Therefore, generalization of the results of this study would be restricted to hospitalized patients. Another limitation of the current study is that we also considered patients who were able to shower independently as being capable of independent bathing. This is because showering is easier than bathing in a bathtub. Therefore, bathing, which involves getting in and out of the bathtub, may require a balance function higher than the cutoff value established in the current study. Moreover, the sample size of patients with hip fracture was quite small for this study, suggesting the need for further studies with a larger sample size to confirm our findings.

CONFLICTS OF INTEREST

ACKNOWLEDGMENTS

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The authors declare that there are no conflict of interests.

REFERENCES

1. GBD 2019 Stroke Collaborators: Global, regional, and national burden of stroke and its risk factors, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet Neurol 2021;20:795–820. https://doi.org/10.1016/S1474-4422(21)00252-0, PMID:34487721

2. GBD 2019 Fracture Collaborators: Global, regional, and national burden of bone fractures in 204 countries and territories, 1990–2019: a systematic analysis from the Global Burden of Disease Study 2019. Lancet Healthy Longev 2021;2:e580–e592. https://doi.org/10.1016/S2666-7568(21)00172-0, PMID:34723233

3. Adamson J, Beswick A, Ebrahim S: Is stroke the most common cause of disability? J Stroke Cerebrovasc Dis 2004;13:171–177. https://doi.org/10.1016/j.jstrokecerebrovasdis.2004.06.003, PMID:17903971

4. Dyer SM, Crotty M, Fairhall N, Magaziner J, Beaupre LA, Cameron ID, Sherrington C, Fragility Fracture Network (FFN) Rehabilitation Research Special Interest Group: A critical review of the long-term disability outcomes following hip fracture. BMC Geriatr 2016;16:158. https://doi.org/10.1186/s12877-016-0332-0, PMID:27590604

5. Gerrard P: The hierarchy of the activities of daily living in the Katz index in residents of skilled nursing facilities. J Geriatr Phys Ther 2013;36:87–91. https://doi.org/10.1519/JPT.0b013e318268da23, PMID:22894986

6. Melo LP, Oliveira DC, Dantas AA, Silva Júnior RA, Ribeiro TS, Campos TF: Predictive factors of functional independence in basic activities of daily living during hospitalization and after discharge of stroke patients. Brain Inj 2021;35:26–31. https://doi.org/10.1080/02699052.2020.1861649, PMID:33369484

7. Alarcón T, González-Montalvo JI, Gotor P, Madero R, Otero A: Activities of daily living after hip fracture: profile and rate of recovery during 2 years of follow-up. Osteoporos Int 2011;22:1609–1613. https://doi.org/10.1007/s00198-010-1314-2, PMID:20521027

8. Hayasaka S, Shibata Y, Goto Y, Noda T, Ojima T: Bathing in a bathtub and health status: a cross-sectional study. Complement Ther Clin Pract 2010;16:219–221. https://doi.org/10.1016/j.ctcp.2010.05.002, PMID:20920807

9. Ukai T, Iso H, Yamagishi K, Saito I, Kokubo Y, Yatsuya H, Muraki I, Eshak ES, Sawada N, Tsugane S: Habitual tub bathing and risks of incident coronary heart disease and stroke. Heart 2020;106:732–737. https://doi.org/10.1136/heartjnl-2019-315752, PMID:32209614

10. Katsuyama H, Hakoshima M, Adachi H, Masui Y, Sako A, Inokuma S, Yanai H: Habitual hot-tub bathing and cardiovascular risk factors in patients with type 2 diabetes mellitus: a cross-sectional study. Cardiol Res 2022;13:144–153. https://doi.org/10.14740/cr1371, PMID:35836731

11. Khan F, Chevidikunnan MF: Prevalence of balance impairment and factors associated with balance among patients with stroke. A cross sectional retrospective case control study. Healthcare (Basel) 2021;9:320. https://doi.org/10.3390/healthcare9030320, PMID:33805643

12. Gialanella B, Santoro R, Prometti P, Bertolinelli M, Monguzzi V, Grioni G: Predictors of balance in older hip fracture patients undergoing standard motor rehabilitation. Eur Geriatr Med 2021;12:69–77. https://doi.org/10.1007/s41999-020-00402-2, PMID:32974887

13. Li J, Zhong D, Ye J, He M, Liu X, Zheng H, Jin R, Zhang S: Rehabilitation for balance impairment in patients after stroke: a protocol of a systematic review and network meta-analysis. BMJ Open 2019;9:e026844. https://doi.org/10.1136/bmjopen-2018-026844, PMID:31326927

14. Mitchell R, Harvey L, Brodaty H, Draper B, Close J: Hip fracture and the influence of dementia on health outcomes and access to hospital-based rehabilitation for older individuals. Disabil Rehabil 2016;38:2286–2295. https://doi.org/10.3109/09638288.2015.1123306, PMID:26765956

15. Lee SY, Jung SH, Lee SU, Ha YC, Lim JY: Effect of balance training after hip fracture surgery: a systematic review and meta-analysis of randomized controlled studies. J Gerontol A Biol Sci Med Sci 2019;74:1679–1685. https://doi.org/10.1093/gerona/gly271, PMID:30517613

16. Kim JH, Park EY: Balance self-efficacy in relation to balance and activities of daily living in community residents with stroke. Disabil Rehabil 2014;36:295–299. https://doi.org/10.3109/09638288.2013.790488, PMID:23651185

17. Dyer SM, Perracini MR, Smith T, Fairhall NJ, Cameron ID, Sherrington C, Crotty M: Rehabilitation following hip fracture. In: Falaschi P, Marsh D, editors. Orthogeriatrics: the management of older patients with fragility fractures [Internet]. 2nd edition. Cham (CH): Springer; 2021. Chapter 12.

18. Mahoney FI, Barthel DW: Functional evaluation: the Barthel Index. Md State Med J 1965;14:61–65. PMID:14258950

19. Berg K, Wood-Dauphinee S, Williams JI: The Balance Scale: reliability assessment with elderly residents and patients with an acute stroke. Scand J Rehabil Med 1995;27:27–36. PMID:7792547

20. Chino N, Sonoda S, Domen K, Saitoh E, Kimura A: Stroke Impairment Assessment Set (SIAS). A new evaluation instrument for stroke patients. Jpn J Rehabil Med 1994;31:119–125. https://doi.org/10.2490/jjrm1963.31.119

21. Imai Y, Hasegawa K: The revised Hasegawa's dementia scale (HDS-R): evaluation of its usefulness as a screening test for dementia. J Hong Kong Coll Psychiatr 1994;4:20–24.

22. Akobeng AK: Understanding diagnostic tests 3: receiver operating characteristic curves. Acta Paediatr 2007;96:644–647. https://doi.org/10.1111/j.1651-2227.2006.00178.x, PMID:17376185

23. Akyea RK, Vinogradova Y, Qureshi N, Patel RS, Kontopantelis E, Ntaios G, Asselbergs FW, Kai J, Weng SF: Sex, age, and socioeconomic differences in nonfatal stroke incidence and subsequent major adverse outcomes. Stroke 2021;52:396–405. https://doi.org/10.1161/STROKEAHA.120.031659, PMID:33493066

24. Guzon-Illescas O, Perez Fernandez E, Crespí Villarias N, Quirós Donate FJ, Peña M, Alonso-Blas C, García-Vadillo A, Mazzucchelli R: Mortality after osteoporotic hip fracture: incidence, trends, and associated factors. J Orthop Surg Res 2019;14:203. https://doi.org/10.1186/s13018-019-1226-6, PMID:31272470

25. Tamura S, Miyata K, Kobayashi S, Takeda R, Iwamoto H: The minimal clinically important difference in Berg Balance Scale scores among patients with early subacute stroke: a multicenter, retrospective, observational study. Top Stroke Rehabil 2022;29:423–429. https://doi.org/10.1080/10749357.2021.1943800, PMID:34169808

26. Takeda R, Miyata K, Tamura S, Kobayashi S, Iwamoto H: Item distribution of the Berg Balance Scale in older adults with hip fracture: a Rasch analysis. Physiother Theory Pract 2022;5:1–8. https://doi.org/10.1080/09593985.2022.2109541, PMID:35930439

27. Bagg S, Pombo AP, Hopman W: Effect of age on functional outcomes after stroke rehabilitation. Stroke 2002;33:179–185. https://doi.org/10.1161/hs0102.101224, PMID:11779908

28. Appelros P, Stegmayr B, Terént A: A review on sex differences in stroke treatment and outcome. Acta Neurol Scand 2010;121:359–369. https://doi.org/10.1111/j.1600-0404.2009.01258.x, PMID:20002005

29. Irfani Fitri F, Fithrie A, S Rambe A: Association between working memory impairment and activities of daily living in post-stroke patients. Med Glas 2020;17:433–438. PMID:32489085

30. Liu M, Chino N, Tuji T, Masakado Y, Hase K, Kimura A: Psychometric properties of the stroke impairment assessment set (SIAS). Neurorehabil Neural Repair 2002;16:339–351. https://doi.org/10.1177/0888439002239279, PMID:12462765

31. Ouellet JA, Ouellet GM, Romegialli AM, Hirsch M, Berardi L, Ramsey CM, Cooney LM Jr, Walke LM: Functional outcomes after hip fracture in independent community-dwelling patients. J Am Geriatr Soc 2019;67:1386–1392. https://doi.org/10.1111/jgs.15870, PMID:30964203

32. Fujita H, Shiomi T, Arahata K, Ishibashi H: Relationship between activity of daily living and motor function in the community-dwelling elderly after hip fracture [in Japanese]. Jpn J Geriatr 2006;43:241–245. https://doi.org/10.3143/geriatrics.43.241, PMID:16683660

33. Fujita T, Kisara Y, Iokawa K, Sone T, Yamane K, Yamamoto Y, Ohira Y, Otsuki K: Relationship between post stroke duration and balance function necessary for performing activities of daily living independently in stroke patients on the convalescence. J Allied Health Sci 2021;12:24–30. https://doi.org/10.15563/jalliedhealthsci.12.24

34. Fujita T, Sato A, Yamamoto Y, Otsuki K, Tsuchiya K, Tozato F: Motor function cut-off values for independent dressing in stroke patients. Am J Occup Ther 2016;70:7003290010p1–7. https://doi.org/10.5014/ajot.2016.018945, PMID:29334332

35. Fujita T, Sato A, Ohashi Y, Nishiyama K, Ohashi T, Yamane K, Yamamoto Y, Tsuchiya K, Otsuki K, Tozato F: Amount of balance necessary for the independence of transfer and stair-climbing in stroke inpatients. Disabil Rehabil 2018;40:1142–1145. https://doi.org/10.1080/09638288.2017.1289254, PMID:28637145

36. Iwai N, Aoyagi Y, Tokuhisa K, Yamamoto J, Shimada T: The gaps between capability ADL and performance ADL of stroke patients in a convalescent rehabilitation ward—based on the functional independence measure. J Phys Ther Sci 2011;23:333–338. https://doi.org/10.1589/jpts.23.333

37. Gervasoni E, Jonsdottir J, Montesano A, Cattaneo D: Minimal clinically important difference of Berg balance scale in people with multiple sclerosis. Arch Phys Med Rehabil 2017;98:337–340. https://doi.org/10.1016/j.apmr.2016.09.128, PMID:27789239

38. Beauchamp MK, Harrison SL, Goldstein RS, Brooks D: Interpretability of change scores in measures of balance in people with COPD. Chest 2016;149:696–703. https://doi.org/10.1378/chest.15-0717, PMID:26203790

39. Tamura S, Miyata K, Kobayashi S, Takeda R, Iwamoto H: Minimal clinically important difference of the Berg Balance Scale score in older adults with hip fractures. Disabil Rehabil 2022;44:6432–6437. https://doi.org/10.1080/09638288.2021.1962993, PMID:34410873