Can the Amount of Interventions during the Convalescent Phase Predict the Achievement of Independence in Activities of Daily Living in Patients with Stroke? A Retrospective Cohort Study

Takuya Umehara, RPT, MS,* Ryo Tanaka, RPT, PhD,† Miwako Tsunematsu, RN, PhD,* Katsunori Sugihara, MD, PhD,‡ Yasuyuki Moriuchi, RPT, MS,‡ Kaori Yata, OTR, MS,‡ Kurumi Muranaka, RN,§ Junko Inoue, HIM,‖ Tatsuo Kohriyama, MD, PhD,¶ and Masayuki Kakehashi, PhD, DSc*

Background: This study aimed to evaluate the diagnostic performance of the amount of physical, occupational, and speech therapy intervention and optimal timing necessary for activities of daily living (ADL) independence in patients with stroke. *Method:* Patients (N = 441) with stroke admitted to the convalescent rehabilitation ward were classified into an early intervention or a nonearly intervention group on the basis of the duration from the date of onset to date of hospital admission. Logistic regression model was used to identify factors influencing independence in ADL in both groups. Cutoff point, likelihood ratio, and posterior probabilities for ADL independence were calculated, and diagnostic accuracy was evaluated for extracted factors. *Results:* Results of logistic regression analysis revealed that age and physical and occupational therapy intervention amount provided during convalescent phase and Functional Independent Measure (FIM) motor score at admission significantly influenced independence in ADL at discharge from the hospital in the early intervention group (hospitalization date was 30 days or less). The cutoff point was 168 hours; positive likelihood ratio was 1.74; negative likelihood ratio was .78; and the posterior probability for the time spent by the therapist was 81.0%. FIM motor score at admission was the only factor extracted for the nonearly intervention group (hospitalization date was 31 days or more). *Conclusion:* The ADL independence in patients with stroke admitted to convalescent rehabilitation ward during their convalescent phase cannot be determined simply on the basis of the amount of physical and occupational therapy they receive. **Key Words:** Stroke—independence in ADL—diagnostic performance—intervention.

© 2018 National Stroke Association. Published by Elsevier Inc. All rights reserved.

From the *Department of Health Informatics, Graduate School of Biomedical and Health Sciences; †Department of Graduate School of Integrated Arts and Sciences, Hiroshima University, Hiroshima, Japan; ‡Department of Rehabilitation; §Department of Nursing; ‖Department of Medical Division; and ¶Department of Neurology, Hiroshima City Rehabilitation Hospital, Hiroshima, Japan.

Received December 16, 2017; revision received April 17, 2018; accepted April 28, 2018.

Address correspondence to Takuya Umehara, RPT, MS, Department of Health Informatics, Graduate School of Biomedical and Health Sciences, Hiroshima University, Hiroshima, 737–0821, Japan. E–mail: start.ume0421@gmail.com.

1052–3057/$ - see front matter

© 2018 National Stroke Association. Published by Elsevier Inc. All rights reserved.

https://doi.org/10.1016/j.jstrokecerebrovasdis.2018.04.038

Introduction

Stroke is a leading cause of death and disability in many countries[1–3] and generally results in motor function restriction. Almost two thirds of stroke survivors have initial mobility deficits,[4,5] and 6 months after a stroke, more than 30% of the survivors still cannot independently walk.[4,6,7] Patients with stroke without independence in their activities of daily living (ADL) suffer from a decline in the quality of life,[8,9] and their expenditure may increase due to subsequent medical treatments.[10] Therefore, health–care providers are required to promptly recover the ADL of patients with stroke. Exercise and speech therapies designed by therapists are effective for recovering functions and ADL after stroke.[11,12] In patients with stroke, ADL ability is improved after 3 months of onset by increasing intervention amount per day early after the onset.[13,14] In addition, for patients with stroke within 14 days after admission, the Functional Independent Measure (FIM) motor score at discharge has been reported to be significantly higher in the group treated 7 days a week than that in the group treated 5 days a week.[15] Results of the previous studies suggest that the amount and frequency of interventions are related to ADL improvement in patients with stroke. However, the diagnostic performance of factors influencing ADL independence at discharge from the convalescent rehabilitation ward has not been clarified. If these are identified, a standard regimen to improve ADL ability can be developed. Therefore, the purpose of this study was to evaluate the diagnostic performance of the amount of physical, occupational, and speech therapy intervention and optimal timing necessary for the recovery of ADL in patients with stroke.

Methods

This was a retrospective cohort study. Medical records of hospitalized patients between April 2013 and March 2016 were collected. Inclusion criteria were patients who had experienced cerebral infarction or hemorrhage as recorded in an accumulated patient database. Exclusion criteria were patients who were transferred to an acute hospital due to complications, patients with modified Rankin Scale (mRS) 2 or more at admission (as patients with mRS 2 or more at admission are already independent in their ADL), and patients who experienced subarachnoid hemorrhage, which generally has a poorer prognosis than cerebral infarction and hemorrhage because subarachnoid lesions are outside the brain parenchyma unlike those in cerebral hemorrhage and cerebral infarction that are within the brain parenchyma.[16] In this study, we defined early and nonearly intervention groups on the basis of the number of days from admission to the acute hospital to the point of transfer earlier or later than the median value for the entire study group, respectively. The reasons for dividing the subjects into 2 groups were as follows. First, previous studies suggested the possibility that the amount of intervention influences the degree of independence of ADL only if the intervention is started at an early stage.[17] Second, there has been no evidence whether the amount of intervention has had any influence in the nonearly stage. To clarify the influence in early and nonearly stages separately, we divided the subjects into early and nonearly intervention groups. This study was approved by the Ethics Review Committee of Hiroshima University (approval number: E–692–1).

In this study, physical, occupational, and speech therapy were tailored for each case and conducted under the direction of a doctor. Speech therapy involved the evaluation of eating or swallowing disorders, aphasia, higher brain dysfunction, and hearing impairment for those with communication disorders. Elements of physical therapy intervention included the range of motion exercises, muscular strength development centering on the lower limbs and trunk, ADL exercises, and sitting or standing balance and walking exercises. Elements of occupational therapy intervention included durability improvement, balance exercises, muscular strength development centering on the upper limbs, ADL exercises, higher brain function exercises, instrumental ADL exercises, and guidance on environment adjustment, such as house renovations and welfare equipment adaptation. Elements of speech therapy intervention included language function and swallowing function training exercises. In addition, the number of hours spent in each department was examined by the attending doctor and therapist–in–charge at the conference. Finally, the doctor determined the patient's level of ADL independence and presence or absence of higher brain dysfunction.

The study used basic medical information, intervention by each therapist, and the degree of ADL capability. Basic medical information included sex, age, period until admission, length of stay, disease for which the patient was hospitalized, presence or absence of higher brain dysfunction, and body mass index (BMI). Intervention amount of each therapist was included as the hours of physical, occupational, and speech therapy received by each patient. ADL capabilities were measured using mRS and FIM scores at admission and discharge. All these factors were extracted from patients' clinical records. Age was assumed to be at the time of admission. The period until admission was calculated from the day of diagnosis at the acute hospital to the day of transfer to Hiroshima City Rehabilitation Hospital. The length of hospital stay was set as the period between the admission and discharge dates. The presence or absence of higher brain dysfunction was assessed by a doctor and the clinical report of the acute hospital was extracted from the medical records. Higher brain dysfunction was not associated with the degree of disability or content. In this study, on the basis of International Classification of Diseases 10, aphasia, asthma, blindness, memory disorder, attention disorder, performance impairment, and social behavior disorder were addressed as higher cortical dysfunction. Thus, memory disturbance, attention disturbance, and ignorance are included in higher cortical dysfunction. The amount of physical, occupational, and speech therapy intervention hours of each therapist was also extracted. The mRS scores of the patients are calculated on the basis of the perception of functioning within the context of their own lives and have a potential to offer a meaningful assessment for evaluating global poststroke functional recovery, in which each grade describes patients' status.[18,19] The mRS defines 6 levels of disability with the score of 6 for death[18]: 0 = no symptom at all; 1 = no significant disability despite symptoms, able to carry out all usual duties and activities; 2 = slight disability, unable to carry out all previous activities but able to look after own affairs without assistance; 3 = moderate disability, requires some help but able to walk without assistance; 4 = moderately severe disability, unable to walk without assistance and unable to attend to own bodily needs without assistance; 5 = severe disability, bedridden, incontinent, and requiring constant nursing care and attention; and 6 = dead. mRS 6 is not considered in this analysis because the present study focuses on the disability outcomes among stroke survivors. Individual scores in the mRS describe clinically distinct functional states of the patients. FIM evaluates motor and cognitive scores[20] and allows the evaluation of actual ADL capability. All 18 items in the instrument are evaluated in 7 stages depending on the degree of assistance required. The highest attainable score is 126 points and the lowest is 18 points. After consultation, FIM score at admission and discharge were determined by 2 nurses–in–charge for each patient.

Logistic regression analysis was performed to explore the predictors of ADL independence. In this study, patients with an mRS 2 or lower were considered ADL independent, whereas those with mRS 3 or higher were considered ADL dependent.[21] Further, logistic regression analysis was performed to explore the association between the desired outcome of mRS less than 2 points (scored as 1) and mRS 3 points or lower (scored 0). To account for multicollinearity, the threshold of the correlation coefficient between independent factors was set to .8, leaving the measured variables clinically important. For higher correlation coefficients, only the intervention amount of the therapist was considered. This was a newly added variable. For example, when the correlation coefficient between physical and occupational therapy intervention exceeded .8, the amount of physical and occupational therapy intervention was considered as a combination variable. To comprehensively examine the extracted variables, the logit transformed value of the *P* value obtained from the regression analysis was defined as the score. The score was given as a summary of the effects of the intervention amount in the form of a linear expression, and this score can appropriately correspond to the probability value by inverse transformation of the logit transformed value. The score can be used to appropriately estimate the mutual association (tradeoff) between each intervention amount considering the main effect leading to independence in ADL. After logistic regression analysis, the receiver operating characteristic (ROC) curve was calculated for the significant predictors to assess the cutoff point for ADL independence.[21] A cutoff value that maximizes the likelihood ratio was specified, and sensitivity, specificity, predictive value, likelihood ratio, and area under the curve (AUC) were calculated.[22] Sensitivity, specificity, positive predictive value, and negative predictive value were determined to be good at .8 or higher. Generally, the criterion value recognized as excellent diagnostic performance is 5 or higher for the positive likelihood ratio and is .2 or lower for the negative likelihood ratio.[23,24] The AUC could distinguish between nonpredictive (AUC < .5), less predictive (.5 < AUC < .7), moderately predictive (.7 < AUC < .9), highly predictive (.9 < AUC < 1), and perfect prediction (AUC = 1).[25,26] Further, to predict ADL independence, prior probability was calculated on the basis of Bayes' theorem to calculate the posterior probability for each variable. All statistical analyses were performed using SPSS version 22.0 for Macintosh (IBM Corp., Armonk, NY), and the significance level was set at $P < .05$.

Result

The flow chart of the measurement of patient characteristics is shown in Figure 1. Of the 441 patients, 35 patients who were transferred to acute hospitals, 36 patients who developed subarachnoid hemorrhage, and 89 patients who had mRS of 2 or higher before onset were excluded. Finally, 281 patients (165 men, 116 women) with a mean age of 67.4 ± 13.6 years were included in this study (Table 1). In total, 178 patients suffered from cerebral infarction (63.3%) and 103 patients suffered from intracranial hemorrhage (36.7%). The median period until admission was 31 days. There were 136 patients in the early intervention group (<30 days) and 145 in the nonearly intervention group (≥31) as measured by the time period until admission.

The ADL of 97 patients were at independent level (Fig 1). Correlation analysis between the 2 groups revealed sex, age, presence of cerebral infarction or hemorrhage, presence or absence of higher brain dysfunction, the amount of physical, occupational, and speech therapy intervention, BMI, FIM motor score, and cognitive score as variables in the logistic regression model. The amount of physical and occupational therapy intervention were highly correlated; therefore, these physical and occupational therapy intervention amounts were used as a combined variable in the further analysis. The results of logistic regression analysis revealed that age ($P < .05$), amount of

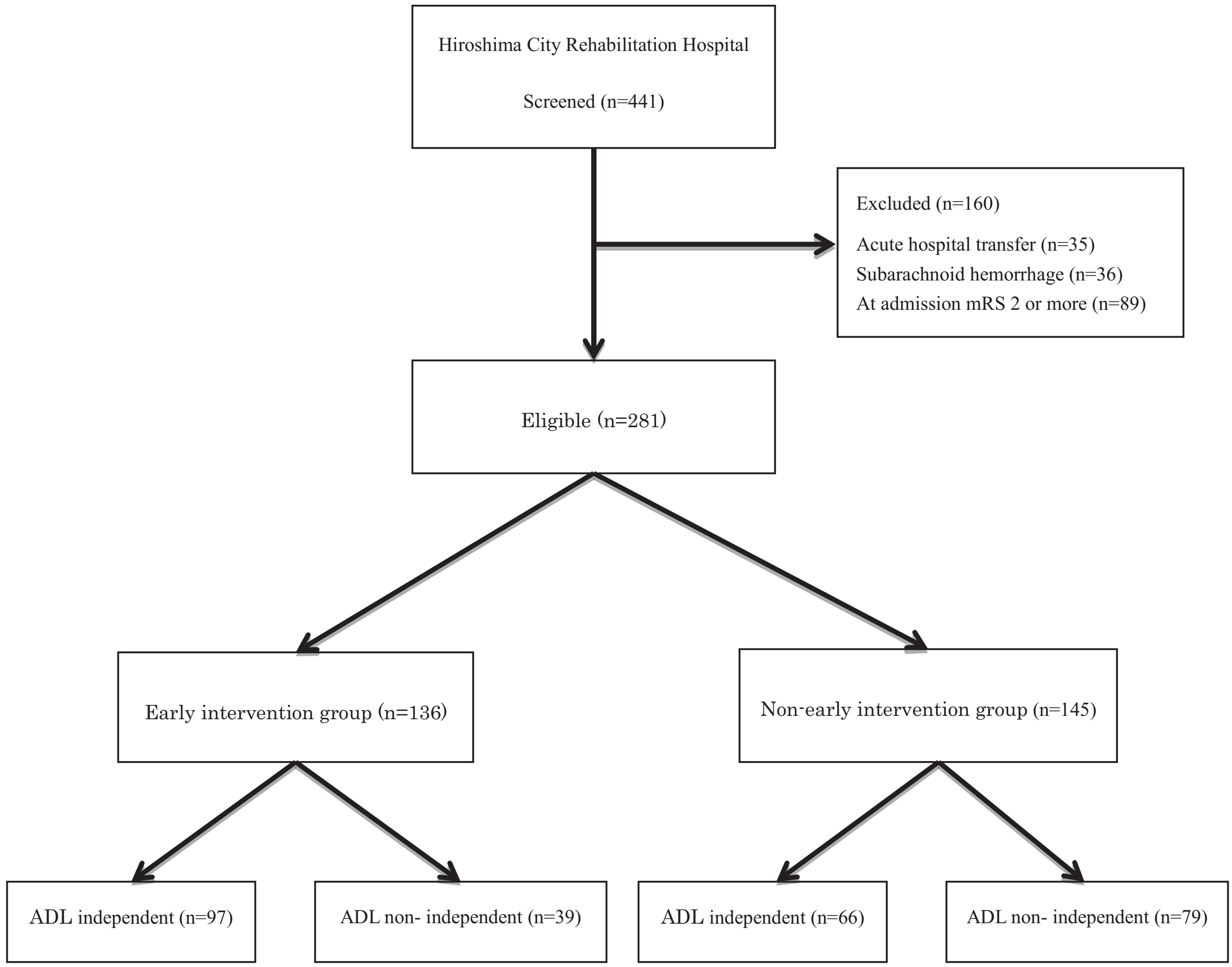

Figure 1. *Flow chart of patients with stroke. Abbreviations: ADL, activities of daily living; mRS, modified Rankin Scale.*

physical and occupational therapy interventions ($P < .05$), and FIM motor score at admission ($P < .05$) were significant predictors of ADL independence (Table 2). The diagnostic performance of the predictive variables for ADL independence is shown in Table 3. The element extracted using the number of hours spent by the therapist was considered as the amount of physical and occupational therapy intervention. The results of ROC analysis revealed that the cutoff value of the amount of physical and occupational therapy intervention was 168 points, and the sensitivity, specificity, and likelihood ratios were .40, .77, and 1.74, respectively. The prior probability of ADL independence was 71.0%, and the posterior probability was 81.0%. The results of ROC analysis revealed that the cutoff value of score was .75 points, and the sensitivity, specificity, and likelihood ratios were .80, .80, and 3.92, respectively. The posterior probability was 91.0%. The score prediction formula is shown in Figure 2.

The ADL of 66 patients were at independent level (Fig 1). Correlation analysis between the 2 groups revealed that sex, age, presence of cerebral infarction or cerebral hemorrhage, presence or absence of higher brain dysfunction, the amount of physical, occupational, and speech therapy intervention, and BMI, FIM motor score, and cognitive scores were included as variables in the logistic regression model. The amount of physical and occupational therapy intervention were highly correlated; therefore, these physical and occupational therapy intervention amounts were used as a combined variable in the further analysis. The results of logistic regression analysis revealed that FIM motor score at admission was a significant predictor of ADL independence (Table 2). The diagnostic performance of the predictive variables for independence of ADL is shown in Table 3. No factor was extracted using the number of hours spent by the therapist.

Discussion

This study examined the factors that influence the independence in ADL at discharge from hospital admission in patients with stroke who were admitted to a rehabilitation ward during their convalescent phase. The patients

Table 1. *Basic attributes, medical attributes, and ADL of subjects in early and nonearly intervention groups*

	Early intervention group	Nonearly intervention group
Gender	Male: 78, female: 58	Male: 87, female: 58
Age, years	67.7 ± 12.9	67.2 ± 14.4
Period until admission, days	22.9 ± 4.8	43.7 ± 10.5
Length of stay, days	109.5 ± 46.5	122.1 ± 40.6
BMI, kg/m^2	22.8 ± 4.2	21.7 ± 3.1
Left and right disorder of the brain	Left: 65 (47.8%), right: 71 (52.2%)	Left: 80 (55.1%), right: 65 (44.9%)
Stroke subtype	Cerebral infarction: 99 (72.8%) Cerebral hemorrhage: 37 (27.2%)	Cerebral infarction: 79 (54.5%) Cerebral hemorrhage: 66 (45.5%)
Cerebral infarction subtype	Lacunar infarction: 18 (18.2%) Atherothrombotic infarction: 48 (48.5%) Cardioembolic infarction: 19 (19.2%) Others: 14 (14.1%)	Lacunar infarction: 12 (15.2%) Atherothrombotic infarction: 33 (41.2%) Cardioembolic infarction: 18 (22.8%) Others: 16 (20.8%)
Cerebral hemorrhage subtype	Putaminal: 13 (35.1%) Thalamic: 9 (24.3%) Pontine: 1 (2.7%) Cerebellum: 3 (8.0%) Subcortical: 11 (29.9%)	Putaminal: 31 (47.0%) Thalamic: 12 (18.2%) Pontine: 1 (1.5%) Cerebellum: 1 (1.5%) Subcortical: 21 (31.8%)
Presence or absence of higher brain dysfunction	Presence: 35 (25.7%) Absence: 101 (74.3%)	Presence: 55 (37.9%) Absence: 90 (62.1%)
mRS before onset	.4 ± .7	.4 ± .7
mRS at admission	3.7 ± .6	3.9 ± .7
mRS at discharge	2.2 ± .9	2.7 ± 1.1
FIM motor score at admission	53.5 ± 17.9	43.5 ± 22.2
FIM cognitive score at admission	26.2 ± 7.1	21.7 ± 8.7
FIM motor score at discharge	78.2 ± 14.0	66.6 ± 22.2
FIM cognitive score at discharge	30.7 ± 4.9	26.2 ± 8.0
Amount of physical therapy intervention, hours	113.5 ± 54.2	118.8 ± 45.2
Amount of occupational therapy intervention, hours	103.0 ± 46.7	112.2 ± 40.0
Amount of speech therapy intervention, hours	69.7 ± 44.6	91.4 ± 44.8
Amount of physical and occupational therapy intervention, hours	216.5 ± 98.0	230.9 ± 83.2
Amount of 1 day physical therapy intervention, hours	1.1 ± .3	1.0 ± .2
Amount of 1 day occupational therapy intervention, hours	1.0 ± .2	1.0 ± .1
Amount of 1 day speech therapy intervention, hours	.6 ± .4	.7 ± .3
Amount of 1 day physical and occupational therapy intervention, hours	2.1 ± .5	2.0 ± .3

Abbreviations: BMI, body mass index; FIM, Functional Independence Measure; mRS, modified Rankin Scale.

were classified into the early intervention or the nonearly intervention group on the basis of the duration from the date of stroke onset to date of hospital admission. For the early intervention group, logistic regression model revealed that the significant predictors of independent ADL capability were age, the amount of physical and occupational therapy intervention received during hospitalization, and the FIM motor score at admission. The cutoff value, the positive likelihood ratio, the negative likelihood ratio, and the posterior probability of the amount of physical and occupational therapy intervention were 168 hours or more, 1.74, .78, 81.0%, respectively. Only FIM motor score at admission was extracted as a factor in the nonearly intervention group.

Among the factors associated with the intervention amount considered in this study, factor affecting ADL independence in the early intervention group included the amount of physical and occupational therapy intervention. For patients with stroke in the acute stage, ADL abilities reportedly improved by increasing the amount

Table 2. *Logistic regression analysis results of the variable in the hospital that affected the ADL independence*

		Partial regression coefficient	*P* value	Odds ratio	95% confidence interval (lower limit–upper limit)
Early intervention group*	Age, years	−.055	.008	.946	.909–.986
	Amount of physical and occupational therapy intervention, hours	.008	.021	1.008	1.001–1.016
	At admission FIM motor score	.097	.000	1.102	1.056–1.149
	Constant	−1.942	.402		
Nonearly intervention group†	At admission FIM motor score	.075	.000	1.078	1.052–1.104
	Constant	−3.435	.000		

Abbreviations: FIM, Functional Independence Measure.
*$\chi 2$ test: $P < .01$, discrimination rate: 73.4%.
†$\chi 2$ test: $P < .01$, discrimination rate: 61.1%.

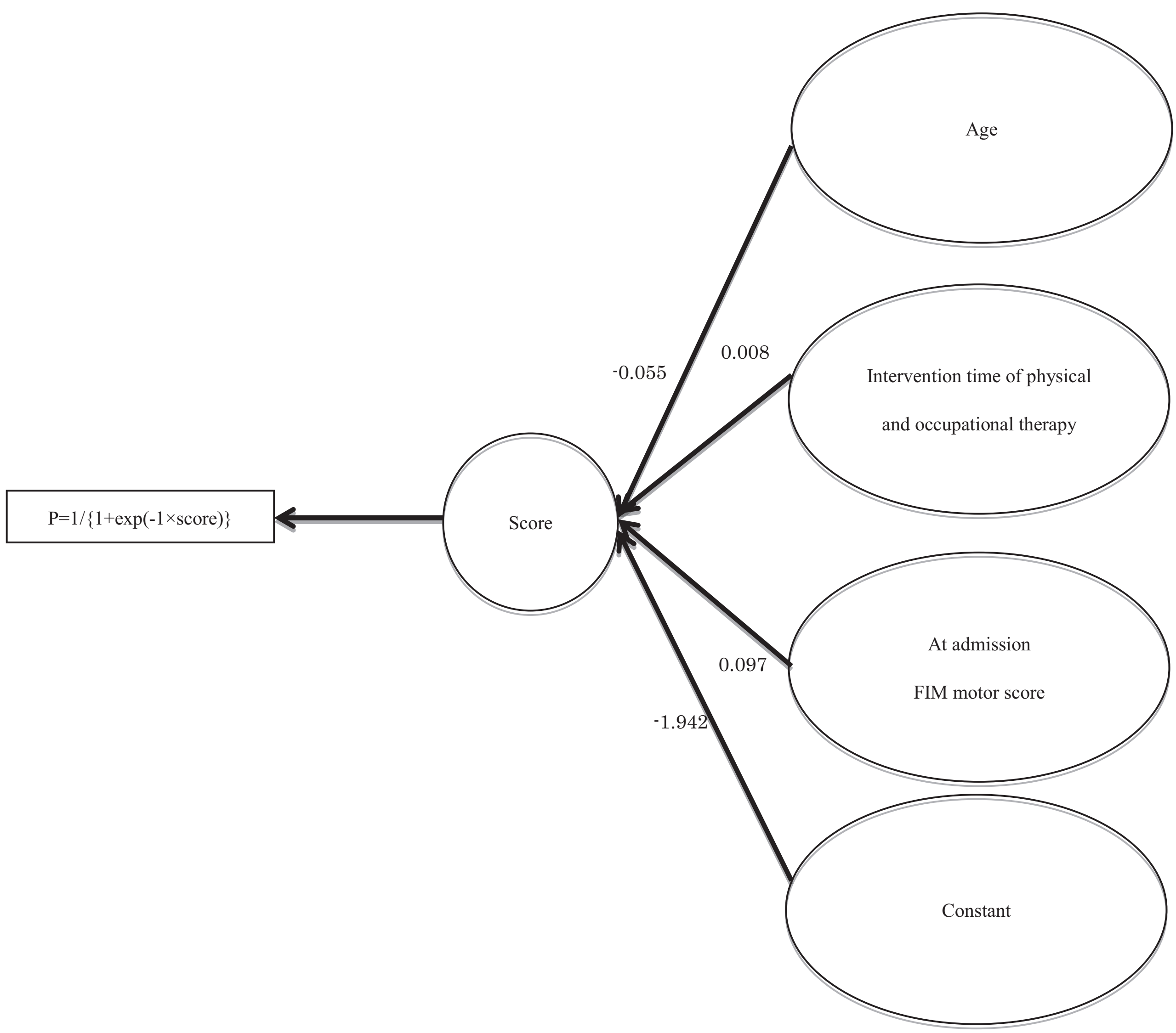

Figure 2. *Prediction formula for the probability of ADL independence. Abbreviations: ADL, activities of daily living; FIM, Functional Independent Measure.*

Table 3. *Diagnostic performance of the variable in the hospital that affected the ADL independent*

	Cutoff value	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Positive likelihood ratio	Negative likelihood ratio	AUC	Posterior probability
Early intervention group									
Age, years	76 or less	.84	.51	.57	.80	1.71	.32	.64	.81
Amount of physical and occupational therapy intervention, hours	168 or more	.40	.77	.57	.63	1.74	.78	.64	.81
At admission FIM motor score	56 or more	.60	.85	.75	.73	3.88	.48	.64	.91
Score	.75 or more	.80	.80	.75	.84	3.92	.25	.78	.91
Nonearly intervention group									
At admission FIM motor score	50 or more	.73	.84	.77	.80	4.41	.33	.64	.79

Abbreviations; AUC, area under the curve; FIM, Functional Independence Measure.

of such intervention at the early stage.[15,27,28] ADL capability in patients with stroke with moderate or higher dysfunction reportedly improved after 3 months by increasing the intervention amount per day early after onset.[13,14] Similar outcomes have been observed in our systematic review.[29] Results of this study are consistent with the previous results. In addition, this study stratified the patients on the basis of the duration from the date of stroke onset to date of hospital admission. Only, in patients who started therapy in convalescent rehabilitation hospital within 30 days after onset, the amount of physical and occupational therapy intervention influenced the achievement of ADL independence. To the best of our knowledge, this finding has not been reported to date. Furthermore, the cutoff value was calculated and diagnostic performance was evaluated in this study, which revealed that the number of physical and occupational therapy intervention sessions required to achieve ADL independence of ADL above 168 hours. However, the positive and negative likelihood ratios were 1.74 and .78, respectively. The amount of physical and occupational therapy intervention observed in this study did not meet these criteria. Therapists cannot predict the possibility of the achievement of ADL independence even if they increase the amount of physical and occupational therapy intervention. The results of this study demonstrate that it is more productive to use age and the FIM motor score measured at admission when predicting whether ADL independence can be achieved. However, our results suggest that ADL independence may be achieved by increasing the amount of physical and occupational therapy intervention in younger patients with stroke with high motor function, who are hospitalized early in the convalescent rehabilitation hospital. The factor necessary for ADL independent was FIM motor score measured at admission in the nonearly intervention group, which was a common factor between the 2 groups. Several studies suggest that for patients with stroke, the degree of ADL independence at admission affects the independence of ADL later.[30,31] The results of our investigation are consistent with the results of these studies. Furthermore, the cutoff value and diagnostic performance of FIM motor score measured at admission were calculated in this study. The FIM motor score measured at admission showed the highest diagnostic performance among the extracted factors. The positive likelihood ratio of the FIM motor score measured at admission was 3.88 in the early intervention group, and the prediction probability increased from 71% to 91%. The positive likelihood ratio was 4.41 in the nonearly intervention group, and the prediction probability increased from 71% to 79%. To the best of our knowledge, no previous study has reported the cutoff value and diagnostic performance. Therefore, this study reports novel findings regarding the prognostic prediction of ADL in patients with stroke. Another factors influencing ADL independence was the age in the early intervention group.[32–34]

Although there are previous studies showing the influence of age on the recovery of ADL capabilities after stroke, we observed the association between age and ADL in early intervention group only. This discrepancy of results between the 2 groups may be attributed to the differences in disease condition and disorders. In general, patients were observed to have significantly lower FIM motor and cognitive scores at admission than patients with cerebral infarction.[35,36] In addition, regarding differences in disorders, many higher brain dysfunctions are known to interfere with ADL capability and walking.[37] Furthermore, a left–brain injury disorder has been known to produce lower ADL performance than a right brain injury.[38] Therefore, these studies indicate that ADL independence tends to be lower in patients with higher brain dysfunction and left cerebral hemorrhage. In fact, our results demonstrate that the nonearly intervention group tends to have greater left cerebral hemorrhage and higher brain dysfunction than the early intervention group. In other words, the association between age and ADL independence is considered to be involved in the left cerebral hemorrhage and the presence or absence of the higher brain dysfunction.

The diagnostic performance and clinical usefulness suggested from this study are as follows. This study evaluated the diagnostic performance of the scores including the age, amount of physical and occupational therapy interventions, and FIM motor score at admission to predict the ADL independence. The AUC of the scores was less than the optimum value (<.9), but showed moderate accuracy (>.7). Additionally, the negative predictive value was higher than positive predictive value. Therefore, the information of the age, amount of physical and occupational therapy interventions, and FIM motor score at admission of this study is clinically useful as an index to predict the possibility of ADL nonidependence rather than of ADL independence.

The limitations of this study are as follows. First, the data used were collected from only 1 hospital, and further investigation should be undertaken in cooperation with other hospitals for a wider application of our findings. Second, the intervention program and proportion performed during the convalescent phase differed for each patient. In actual clinical practice, the therapist customized the intervention program and proportion depending on the condition of the patient with stroke.

The proportion of total time spent on physical, occupational, and speech therapies performed within this study was on average 1:1:.6, respectively, although the proportion was not necessarily the same in all patients. In the future, it will be necessary to take into account the influence of treatment modalities on the recovery of ADL. Third, the detailed characteristics of our patients with stroke, such as sites of cerebral blood vessel infarction, hemorrhage, supratentorial or subtentorial, and details of physical functions and higher brain dysfunction were not registered in the database used in this study. The fact that details of patient condition were not considered in the analysis may be 1 reason why we could not develop a model with higher diagnostic performance. Future researchers should specify the detailed characteristics of patients who increased their ADL independence by increasing the amount of therapy intervention.

Conclusion

The ADL independence in patients with stroke admitted to a rehabilitation ward during their convalescent phase cannot be determined simply on the basis of the amount of physical and occupational therapy they receive. Nonetheless, with the amount of interventions, ADL independence may be achieved only in younger (age < 75) patients with stroke with high motor function who could start intervention at an early stage in the convalescent rehabilitation ward.

References

1. Fisher A, Martin J, Srikusalanukul W, et al. Trends in stroke survival incidence rates in older Australians in the new millennium and forecasts into the future. J Stroke Cerebrovasc Dis 2013;23:759–770.
2. Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. PLoS Med 2006;3:e442.
3. Ovbiagele B, Nguyen–Huynh MN. Stroke epidemiology: advancing our understanding of disease mechanism and therapy. Neurother 2011;8:319–329.
4. Jorgensen HS, Nakayama H, Raaschou HO, et al. Recovery of walking function in stroke patients: the Copenhagen Stroke Study. Arch Phys Med Rehabil 1995;76:27–32.
5. Shaughnessy M, Michael KM, Sorkin JD, et al. Steps after stroke: capturing ambulatory recovery. Stroke 2005;36:1305–1307.
6. Mayo NE, Wood–Dauphinee S, Cote R, et al. Activity, participation, and quality of life 6 months poststroke. Arch Phys Med Rehabil 2002;83:1035–1042.
7. Petel AT, Duncan PW, Lai SM, et al. The relation between impairments and functional outcomes poststroke. Arch Phys Med Rehabil 2000;81:1357–1363.
8. Takemasa S, Nakagoshi R, Murakami M, et al. Factors affecting quality of life of the homebound elderly hemiparetic stroke patients. J Phys Ther Sci 2014;26:301–303.
9. Choi–Kwon S, Choi JM, Kwon SU, et al. Factors that affect the quality of life at 3 years post–stroke. J Clin Neurol 2006;2:34–41.
10. Johansen I, Lindbak M, Stanghelle JK, et al. Independence, institutionalization, death and treatment costs 18 months after rehabilitation of older people in two different primary health care settings. BMC Health Serv Res 2012;14:400.
11. Pollock A, Gray C, Culham E, et al. Interventions for improving sit–to–stand ability following stroke. Cochrane Database Syst Rev 2014;(26):CD007232.
12. Cicerone KD, Dahlberg C, Malec JF, et al. Evidence–based cognitive rehabilitation: updated review of the literature 1998 through 2002. Arch Phys Med Rehabil 2005;86:1681–1692.

13. Langhorne P, Wagenaar R, Partridge C. Physiotherapy after stroke: more is better? Physiother Res Int 1996;1:75–88.
14. Kwakkel G, Wagenaar RC, Twisk JW, et al. Intensity of leg and arm training after primary middle–cerebral–artery stroke: a randomized trial. Lancet 1999;354:191–196.
15. Sonoda S, Saitoh E, Nagai S, et al. Full–time integrated treatment program, a new system for stroke rehabilitation in Japan: comparison with conventional rehabilitation. Am J Phys Med Rehabil 2004;83:88–93.
16. Yoshimoto Y, Kwak S. Age–related multifactorial causes of neurological deterioration after early surgery for aneurysmal subarachnoid hemorrhage. J Neurosurg 1995;83:984–988.
17. Chippala P, Sharma R. Effect of very early mobilisation on functional status in patients with acute stroke: a single–blind, randomized controlled trail. Clin Rehabil 2016;30:669–675.
18. van Swieten JC, Koudstaal PJ, Visser MC, et al. Interobserver agreement for the assessment of handicap in stroke patients. Stroke 1988;19:604–607.
19. Bonita R, Beaglehole R. Recovery of motor function after stroke. Stroke 1988;19:1497–1500.
20. Mosselman MJ, Kruitwagen CL, Schuurmans MJ, et al. Malnutrition and risk of malnutrition in patients with stroke: prevalence during hospital stay. J Neurosci Nurs 2013;45:194–204.
21. Weisscher N, Vermeulen M, Roos YB, et al. What should be defined as good outcome in stroke trial; a modified Rankin score of 0–1 or 0–2? J Neurol 2008;255:867–874.
22. Akobeng AK. Understanding diagnostic tests 3: receiver operating characteristic curves. Acta Paediatr 2007;96:644–647.
23. Swets JA. Measuring the accuracy of diagnostic systems. Science 1988;240:1285–1293.
24. Greiner M, Pfeiffer D, Smith RD. Principles and practical application of the receiver–operating characteristic analysis for diagnostic tests. Prev Vet Med 2000;45:23–41.
25. Hee L. Likelihood rations for the prediction of preterm delivery with biomarkers. Acta Obstet Gynecol Scand 2011;90:1189–1199.
26. Ruiz–González A, Utrillo L, Bielsa S, et al. The diagnostic value of serum C–reactive protein for identifying pneumonia in hospitalized patients with acute respiratory. J Biomark 2016;2016:2198745.
27. Studenski S, Duncan PW, Perera S, et al. Daily functioning and quality of life in a randomized controlled trial of therapeutic exercise for subacute stroke survivors. Stroke 2005;36:1764–1770.
28. Galvin R, Murphy B, Cusack T, et al. The impact of increased duration of exercise therapy on functional recovery following stroke—what is the evidence? Top Stroke Rehabil 2008;15:365–377.
29. Kwakkel G, van Peppen R, Wagnenaar RC, et al. Effects of augmented exercise therapy time after stroke: a meta–analysis. Stroke 2004;35:2529–2539.
30. Jongbloed L. Prediction of function after stroke: a critical review. Stroke 1986;17:765–776.
31. Granger CV, Dewis LS, Peters NC, et al. Stroke rehabilitation: analysis of repeated Barthel index measures. Arch Phys Med Rehabil 1979;60:14–17.
32. Veerbeek JM, Kwakkel G, van Wegen EE, et al. Early prediction of outcome of activities of daily living after stroke: a systematic review. Stroke 2011;42:1482–1488.
33. Kugler C, Altenhoner T, Lochner P, et al. Does age influence early recovery from ischemic stroke? A study from the Hessian Stroke Data Bank. J Neurol 2003;250:676–681.
34. Nakayama H, Jorgensen HS, Raaschou HO, et al. The influence of age on stroke outcome. The Copenhagen Stroke Study. Stroke 1994;25:808–813.
35. Katrak PH, Black D, Peeva V. Do stroke patients with intracerebral hemorrhage have a better functional outcome than patients with cerebral infarction? PM R 2009;1:427–433.
36. Kelly PJ, Furie KL, Shafqat S, et al. Functional recovery following rehabilitation after hemorrhagic and ischemic stroke. Arch Phys Med Rehabil 2003;84:968–972.
37. Takahashi J, Takami A, Wakayama S. Clinical reasoning of physical therapists regarding in–hospital walking independence of patients with hemiplegia. J Phys Ther Sci 2014;26:771–775.
38. Gardarsdottir S, Kaplan S. Validity of the Arnadottir OT–ADL Neurobehavioral Evaluation (A–ONE): performance in activities of daily living and neurobehavioral impairments of persons with left and right hemisphere damage. Am J Occup Ther 2002;56:499–508.