

*Original Article***Assessment of the effects of factors in stroke rehabilitation using eight multiple regression analyses—An analysis of the Japan Rehabilitation Database—**

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**ABSTRACT**

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**Objective:** The objective of the present study was to determine via multiple regression analysis what types of patient groups demonstrate large effects for factors in stroke rehabilitation.

**Methods:** The subjects were 1,465 stroke patients in *Kaifukuki* rehabilitation wards who were registered in the 2014 Japan Rehabilitation Database. The subjects were stratified into eight groups based on age, motor functional independence measure (FIM) score at hospital admission, and cognitive FIM score at admission; multiple regression analysis was then performed with motor FIM score at discharge as the dependent variable.

**Results:** Among the eight groups, the following independent variables were significant: motor FIM score at admission in seven groups, *Nichijo-seikatsukino-hyokahyo* at admission in five groups, age and post-onset duration of hospitalization in four groups, cognitive FIM score at admission in three groups, and pre-onset modified Rankin Scale in one group.

**Conclusion:** The creation of multiple predictive formulas in multiple regression analysis enables

identification of the types of patient groups which demonstrate large effects for factors in stroke rehabilitation.

**Key words:** multiple regression analysis, stroke, stratification, factors, Functional Independence Measure

**Introduction**

In our searches of existing literature, we found 12 reports which used multiple regression analysis to predict Functional Independence Measure (FIM) score at hospital discharge in stroke patients who were hospitalized in *Kaifukuki* rehabilitation wards [1–12]. Of those 12 reports, nine [1–9] created a single predictive formula which was applied to all patients. In contrast, Inouye [10] divided patients into five groups based on age and created five predictive formulas. Similarly, Hirano et al. [11] divided patients into three groups based on FIM score at admission and created three predictive formulas. In addition, Tokunaga et al. [12] divided patients into two groups based on age and three groups based on FIM score at admission, thus creating a total of six groups and six predictive formulas. The use of six predictive formulas rather than one yielded a greater correlation between actual values and predicted values, and thus a smaller residual of actual value minus predicted value.

The reason why multiple predictive formulas are preferable to a single predictive formula is the absence of a linear relationship between stroke rehabilitation factors and FIM improvement. Improvement in the total score for the 13 motor-related items of the FIM (motor FIM) is nearly constant in individuals aged  $\leq 69$  years, but declines in a nearly linear fashion in individuals aged  $\geq 70$  years [13, 14]. Motor FIM gain, when plotted on a graph, appears as a curve which peaks at a motor FIM score at admission of 25–30 [15] or 33–36 [16]. Multiple regression analysis assumes

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that independent variables and the dependent variable are linearly related; therefore, in the absence of a linear relationship between the independent variables and the dependent variable, the creation of multiple predictive formulas is considered to yield higher predictive accuracy.

Recently, Sonoda et al. [17] reported that “inhibitory factors in rehabilitation do not necessarily demonstrate uniform effects in all patient groups”. Their report described the results of motor FIM score at discharge as predicted by decision tree analysis. Among cognitive FIM items at admission, “memory” first appeared as a conditional branch at the sixth branch, in regard to patients with a motor FIM score at admission of 31–69 [17]. Following the decision tree to the fourteenth branch shows that age was involved in patients with a motor FIM score at admission of 13–30 [17]. Thus, if the effects of the factors affecting motor FIM at discharge differ according to the patient group, failing to create predictive formulas for each patient group in multiple regression analysis would make it impossible to assess accurately the effects of these factors. However, we could find no past reports in which multiple predictive formulas were created in multiple regression analysis to predict motor FIM score at discharge in order to assess which types of patients demonstrate large effects in the factors affecting motor FIM at discharge.

In the present study, we used data from stroke patients in *Kaifukuki* rehabilitation wards registered in the Japan Rehabilitation Database [18] in multiple regression analysis to predict motor FIM at discharge. The objective of the study was to stratify patients based on age, motor FIM score at admission, and cognitive FIM score at admission in order to create multiple predictive formulas to determine which types of patient groups demonstrate large effects for those factors.

### Subjects and Methods

We used patient data from the Japan Rehabilitation Database. The goal behind the creation of the Japan Association of Rehabilitation Database, which was established in September 2012, is to construct and use a rehabilitation database to help improve rehabilitation medicine and care [18]. The groups which comprise the Japan Rehabilitation Database Association are: the Japanese Association of Rehabilitation Medicine, the Japanese Physical Therapy Association, the Japanese Association of Occupational Therapists, and the Japanese Association of Speech-Language-Hearing Therapists. Data on patients who have suffered stroke, hip fracture, or spinal cord injury are collected from participating institutions throughout Japan.

The present epidemiologic study is a retrospective investigation. The number of patients registered in the May 2014 Japan Rehabilitation Database (stroke and

rehabilitation) was 4,949. After narrowing down these patients according to the conditions shown in Figure 1, we used 1,465 of these patients as subjects.

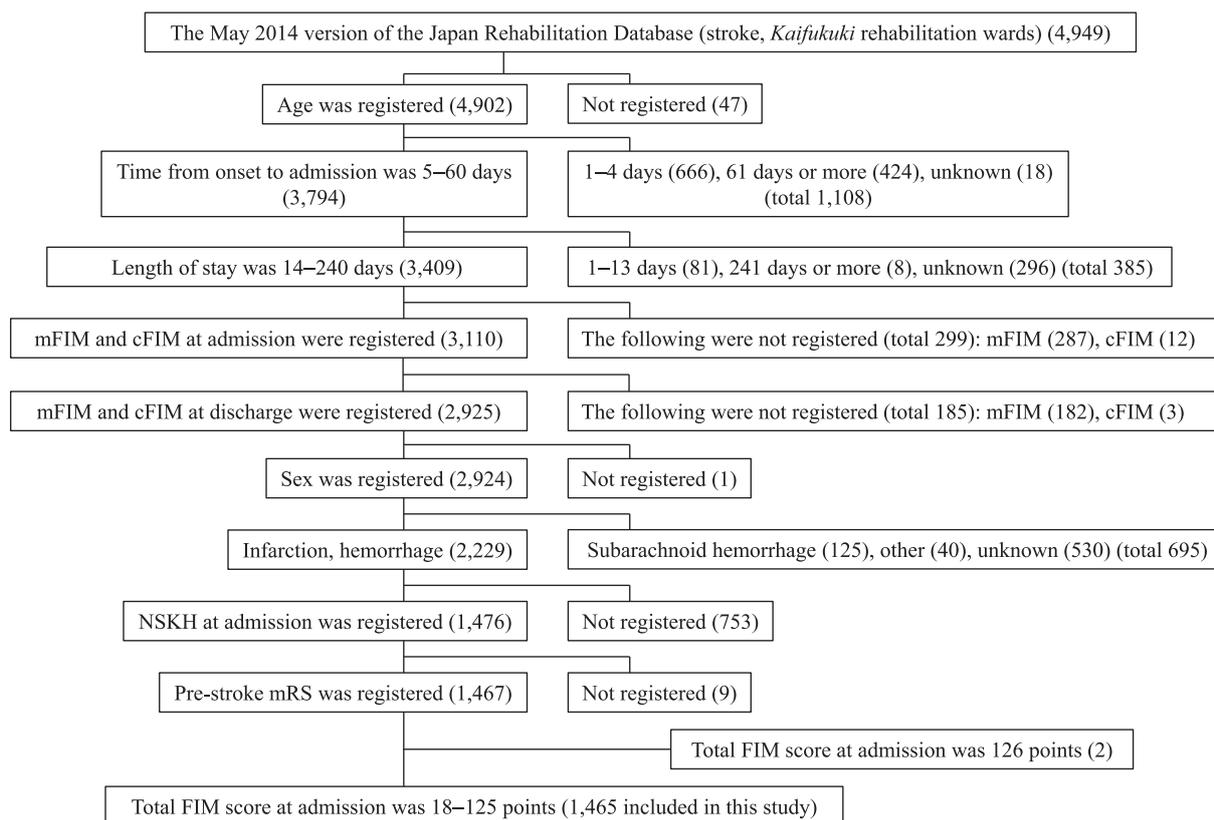
### 1. Stratification of patients into 12 groups based on age, motor FIM score at admission, and cognitive FIM score at admission

Based on a previous examination in which we found that motor FIM improvement declined beginning at age 70 [13, 14], we divided patients into an age  $\leq 69$  years group and an age  $\geq 70$  years group. Also, because motor FIM improvement declines when cognitive FIM score at admission is  $\leq 9$  [19], we divided patients into groups of those with cognitive FIM scores at admission of 5–9 (cFIM 5–9) and 10–35 (cFIM 10–35). Furthermore, motor FIM gain when plotted on a graph appears as a curve which peaks at a motor FIM score at admission of 25–30 [15] or 33–36 [16], while Sonoda et al. [17] reported that age and cognitive function exerted effects on patients with motor FIM scores at admission of 13–30 and 31–69; therefore, we divided patients into groups of those with motor FIM scores at admission of 13–30 (mFIM 13–30), 31–69 (mFIM 31–69), and 70–91 (mFIM 70–91). Thus, based on age, cognitive FIM score at admission, and motor FIM score at admission, we stratified patients into 12 groups (Table 1).

### 2. Multiple regression analysis with motor FIM score at discharge as the dependent variable

We performed multiple regression analysis with motor FIM score at discharge as the dependent variable. Drawing upon variables which previous studies had reported to be correlated with FIM at discharge, we used the following six items as independent variables: age, pre-onset modified Rankin Scale (mRS), post-onset duration of hospitalization, motor FIM score at admission, cognitive FIM score at admission, and *Nichijo-seikatsu-kino-hyokahyo* (NSKH) at admission. We initially elected to perform multiple regression analysis for each of the 12 groups and for all patients together. However, because four of the 12 groups had fewer than 10 patients (Table 1), we excluded those four groups and their 17 patients, therefore ultimately performing multiple regression analysis on eight groups comprising a total of 1,448 patients. In addition, we investigated which of the six independent variables (factors) were significant in which of the eight patient groups. Our creation of a single predictive formula for overall patients also excluded the above-mentioned 17 patients and thus involved a total of 1,448 patients. For multiple regression analysis with patients divided into eight groups and singular multiple regression analysis (for overall patients), we investigated the correlation between actual value and predicted value (Pearson product-moment correlation coefficient,  $p < 0.05$ ) and the residual of actual value minus predicted value.

In the Japan Rehabilitation Database, all personal



**Figure 1.** Inclusion and exclusion criteria.

FIM, Functional Independence Measure; mFIM, motor FIM; cFIM, cognitive FIM; NSKH, *Nichijo-seikatsu-kino-hyokahyo*; mRS, modified Rankin Scale; Numerical value, number of patients.

information is converted to data to prevent identification of individuals. The present epidemiologic study was conducted based on the regulations of the institutional review board of the hospital to which the authors belong and with the permission of an employee designated in advance by the institutional review board.

## Results

All eight of the multiple regression analyses were significant ( $p < 0.001$ ). Adjusted  $R^2$ , which demonstrates the extent to which independent variables can explain the dependent variable, ranged from 0.15 (Group F) to 0.56 (Group A) (Table 1). No correlations among the six independent variables were greater than 0.8, and no multicollinearity was observed. Motor FIM score at admission was a significant independent variable in seven groups (all except for Group D). Moreover, in comparison with the other five independent variables, motor FIM score at admission demonstrated the largest standardized partial regression coefficient (the relative strength of the association of an independent variable with the dependent variable) (Table 1). Cognitive FIM score at admission was a significant independent variable in three groups (Groups E, J, and L). Age, NSKH at admission, and post-onset duration of hospitalization were significant independent variables

in four groups, five groups, and four groups, respectively. However, pre-onset mRS was a significant independent variable only in one group (Group G).

When we created eight predictive formulas for the 1,448 patients, the actual value and the predicted value demonstrated a significant strong positive correlation ( $r = 0.885$ ,  $p < 0.001$ ) (Fig. 2a). The residual (actual value minus predicted value) was  $-0.01 \pm 10.87$  (median: 0.37).

When we created only a single predictive formula, the adjusted  $R^2$  was 0.72 (Table 2); all six of the independent variables were significant. The actual value and the predicted value demonstrated a significant strong positive correlation ( $r = 0.847$ ,  $p < 0.001$ ), while the residual (actual value minus predicted value) was  $-0.04 \pm 12.39$  (median:  $-0.58$ ) (Fig. 2b).

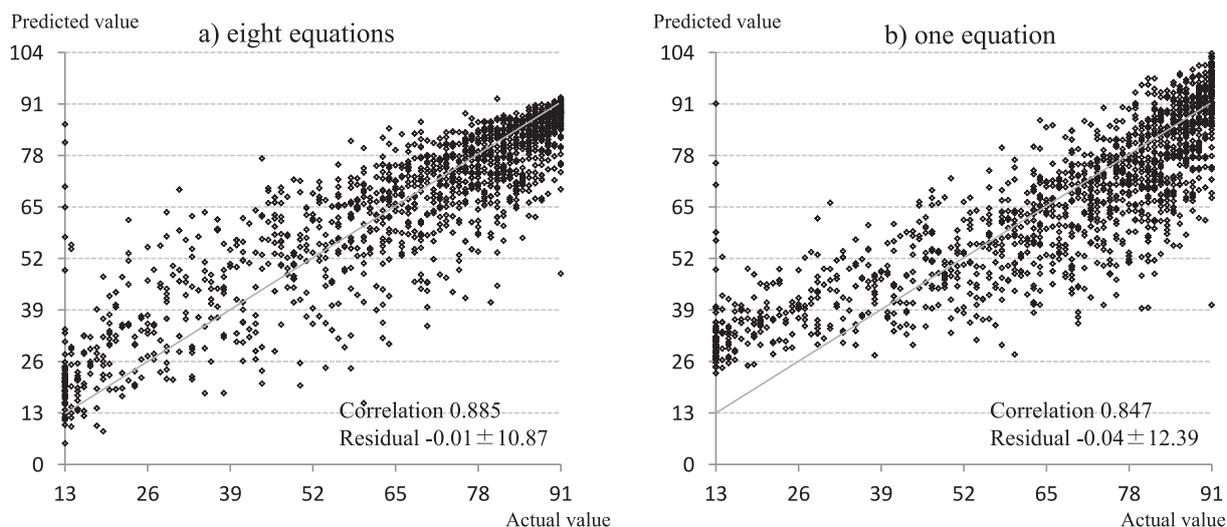
## Discussion

In comparison to a single predictive formula, the use of eight predictive formulas resulted in a greater correlation between actual values and predicted values, as well as smaller residual; these results are identical to those of a previous study in which age and FIM score at admission were used to create six predictive formulas [12]. The present study is the fifth to have investigated the correlation between actual

**Table 1.** Multiple regression analysis to predict motor FIM score at discharge (eight predictive formulas).

Group	A	B	C	D	E	F
Age	Under 69					
cFIM at admission	cFIM 5-9					
mFIM at admission	mFIM 13-30					
Number of patients	39	6	0	91	308	209
mFIM at admission	1.576 ( 0.417, ①), $p < 0.01$			0.680 ( 0.202), $p = 0.06$	0.460 ( 0.428, ①), $p < 0.001$	0.382 ( 0.334, ①), $p < 0.001$
cFIM at admission	0.537 ( 0.041), $p = 0.73$			0.049 ( 0.017), $p = 0.86$	0.209 ( 0.118, ③), $p < 0.05$	0.034 ( 0.028), $p = 0.66$
Age	-0.269 (-0.145), $p = 0.20$			-0.573 (-0.287, ②), $p < 0.01$	-0.178 (-0.157, ②), $p < 0.001$	-0.064 (-0.092), $p = 0.15$
NSKH at admission	-2.255 (-0.348, ②), $p < 0.05$			-1.430 (-0.304, ①), $p < 0.01$	-0.358 (-0.104), $p = 0.07$	-0.228 (-0.054), $p = 0.43$
Post-onset duration of hospitalization	-0.452 (-0.322, ③), $p < 0.01$			-0.195 (-0.143), $p = 0.13$	-0.059 (-0.069), $p = 0.14$	-0.081 (-0.150, ②), $p < 0.05$
Pre-onset mRS	0.565 ( 0.042), $p = 0.70$			-1.806 (-0.148), $p = 0.13$	-0.136 (-0.014), $p = 0.76$	-0.380 (-0.048), $p = 0.46$
Constant	67.327			99.259	61.148	61.871
Significance level	$p < 0.001$			$p < 0.001$	$p < 0.001$	$p < 0.001$
Adjusted coefficient of determination $R^{*2}$	0.56			0.21	0.34	0.15
Group	Over 70					
Age	cFIM 5-9					
cFIM at admission	mFIM 13-30					
Number of patients	102	9	2	186	396	117
mFIM at admission	1.413 ( 0.390, ①), $p < 0.001$			0.984 ( 0.269, ①), $p < 0.001$	0.574 ( 0.429, ①), $p < 0.001$	0.356 ( 0.461, ①), $p < 0.001$
cFIM at admission	1.186 ( 0.749), $p = 0.11$			0.573 ( 0.184, ③), $p < 0.01$	0.170 ( 0.074), $p = 0.09$	0.121 ( 0.161, ②), $p < 0.05$
Age	-0.384 (-0.148), $p = 0.054$			-0.772 (-0.249, ②), $p < 0.001$	-0.281 (-0.111, ④), $p < 0.01$	-0.111 (-0.142), $p = 0.06$
NSKH at admission	-1.334 (-0.255, ②), $p < 0.05$			-0.890 (-0.172, ④), $p < 0.05$	-0.637 (-0.151, ②), $p < 0.01$	-0.143 (-0.064), $p = 0.45$
Post-onset duration of hospitalization	-0.100 (-0.091), $p = 0.22$			-0.173 (-0.121, ⑤), $p < 0.05$	-0.143 (-0.130, ③), $p < 0.01$	-0.020 (-0.058), $p = 0.45$
Pre-onset mRS	-2.036 (-0.221, ③), $p < 0.01$			-1.475 (-0.113), $p = 0.06$	-0.639 (-0.056), $p = 0.16$	-0.278 (-0.061), $p = 0.43$
Constant	52.523			90.36	67.969	63.647
Significance level	$p < 0.001$			$p < 0.001$	$p < 0.001$	$p < 0.001$
Adjusted coefficient of determination $R^{*2}$	0.47			0.33	0.38	0.34

FIM, Functional Independence Measure; mFIM, motor FIM; cFIM, cognitive FIM; NSKH, *Nichijo-seikatsu-kino-hyokahyo*; mRS, modified Rankin Scale. Numerical value of independent variables, regression coefficient; circled number, numbers were given in the order of higher standard partial regression coefficient.



**Figure 2.** Relationship between actual values and predicted values.

◇, each patient; Actual value, actual value of FIM at discharge; Predicted value, predicted value of FIM at discharge.

**Table 2.** Multiple regression analysis to predict motor FIM score at discharge (one predictive formula).

Number of patients		1,448
Explanatory variables	mFIM at admission	0.408 ( 0.405, ①), $p < 0.001$
	cFIM at admission	0.422 ( 0.159, ③), $p < 0.001$
	Age	- 0.223 ( - 0.124, ④), $p < 0.001$
	NSKH at admission	- 1.229 ( - 0.281, ②), $p < 0.001$
	Post-onset duration of hospitalization	- 0.109 ( - 0.063, ⑤), $p < 0.001$
	Pre-onset mRS	- 0.939 ( - 0.052, ⑥), $p < 0.001$
Constant		65.340
Significance level		$p < 0.001$
Adjusted coefficient of determination $R^2$		0.72

The explanation of this table is the same as in Table 1.

and predicted values [1, 2, 9, 12], but yielded the third-highest correlation among these studies (Table 3). Similarly, the present study is the fourth to have investigated the residual of actual value minus predicted value [2, 6, 12], but yielded the second-smallest mean residual, trailing only that reported by Tokunaga et al. [12]; as well as the second-smallest standard deviation in residual, behind only that reported by Sonoda et al. [2].

In the present study, we also investigated which factors among age, pre-onset mRS, post-onset duration of hospitalization, motor FIM score at admission, cognitive FIM score at admission, and NSKH at admission significantly affected motor FIM score at discharge in which of eight groups of patients divided by age, cognitive FIM score at admission, and motor FIM score at admission.

When we created only a single predictive formula, all six independent variables were significant. However, in multiple regression analysis with patients divided

into eight groups based on age, cognitive FIM score at admission, and motor FIM score at admission, only two to five of the six independent variables were significant in any given group. Of the six independent variables (factors), the factor most frequently found to be significant was motor FIM score at admission (in seven of eight groups), followed by NSKH at admission (five groups), age (four groups), post-onset duration of hospitalization (four groups), and cognitive FIM score at admission (three groups). Pre-onset mRS was significant in only one group (Group G). These results are consistent with a report by Sonoda et al. [17], who stated that “inhibitory factors in rehabilitation do not necessarily demonstrate uniform effects in all patient groups”.

In the report by Sonoda et al. [17], age affected patients with a motor FIM score at admission of 13–30. In contrast, we found that age was also a significant independent variable in Groups D, E, J, and K; therefore, age was also a significant independent

**Table 3.** Reports which used multiple regression analysis to predict FIM score at discharge in stroke patients who were hospitalized in *Kaifukuki* rehabilitation wards.

Reports (Reference numbers)	1	2	3	4	5	6	7	8	9	10	11	12	This study
Stratification										Five groups by age	Three groups by FIM at admission	Six groups by age and FIM at admission	Eight groups by age, mFIM and cFIM at admission
mFIM at admission	○	○	○	○	○	○	○	○	○	○	○	○	○
cFIM at admission	○	○		○		○	○	○				○	○
Age	○	○		○	○	○	○	○	○	○	○	○	○
NSKH at admission				○	○							○	○
Post-onset duration of hospitalization	○	○	○			○			○	○		○	○
Pre-onset mRS	○					○		○				○	○
Comorbidities	○		○							○			
SIAS							○		○				
Type of stroke								○		○			
GCS at admission	○												
Deviation in tape bisection			○										
Neglect								○					
Sex										○			
Orientation									○				
HDS-R											○		
Adjusted coefficient of determination $R^{*2}$	0.66		0.798	0.719	0.708	0.649	0.64			0.57-0.76	0.5-0.64	0.14-0.55	0.15-0.56
Correlation between the measured value and the predicted value	0.84	0.88							0.93			0.893	0.885
Residual		8.06 ± 6.29				-0.28 ± 12.88						0 ± 13.63	-0.01 ± 10.87

HDS-R, Hasegawa dementia scale-revised; GCS, Glasgow Coma Scale; SIAS, Stroke Impairment Assessment Set; Reports, numbers are the reference numbers. Residual, obtained by subtracting the predicted value from the measured value; Other explanations are the same as Table 1.

variable for patients whose motor FIM score at admission was 31–69. Moreover, among patients with a motor FIM score at admission of 13–30, age was not a significant independent variable in patients with a cognitive FIM score at admission of  $\leq 9$  (Groups A and G). These results can be summarized as follows: age exerts a significant effect in patients with a cognitive FIM score at admission of  $\geq 10$  and a motor FIM score at admission of 13–69.

Sonoda et al. [17] reported that motor FIM score at admission is useful for predicting motor FIM score at discharge in patients with a motor FIM score at admission of 31–69. In contrast, in the present study, motor FIM score at admission was a significant independent variable in Group E (age  $\leq 69$  years, cFIM 10–35, mFIM 31–69), Group J (age  $\geq 70$  years, cFIM 10–35, mFIM 13–30), and group L (age  $\geq 70$  years, cFIM 10–35, mFIM 70–91). Sonoda et al. [17] presented a group of patients with motor FIM scores of 31–69, a group which we further stratified in the present study into four groups (Groups B, E, H, and K) based on age and cognitive FIM score at admission. Both Sonoda et al. [17] and the present study found that patients corresponding to our Group E (age  $\leq 69$  years, cFIM 10–35, mFIM 31–69) were affected by cognitive function. However, among patients with motor FIM scores at admission of 31–69, Groups B and G had few patients, while Group K demonstrated a regression coefficient for motor FIM score at admission

that, despite being positive, was not significant ( $p = 0.09$ ). In Groups J and L in the present study, motor FIM score at admission was a significant positive independent variable; this result can be interpreted to mean that, in individuals aged  $\geq 70$  years, cognitive function affects motor FIM score at discharge in patients with a wide range of motor FIM scores at admission.

Pre-onset mRS was a significant independent variable only in Group G, thus permitting the conclusion that pre-onset mRS significantly affects severe patients aged  $\geq 70$  years with a cognitive FIM score at admission of  $\leq 9$  and a motor FIM score at admission of  $\leq 30$ . Severe patients with low motor FIM and cognitive FIM scores at admission included large numbers of patients who were already severe (in terms of pre-onset mRS); thus, pre-onset mRS likely exerted a major effect. In fact, while Group G comprised only 7.0% (102/1,465) of all patients in the present study, the group included eight patients with a pre-onset mRS of grade 5, thus accounting for 36.4% (8/22) of all patients with a pre-onset mRS of grade 5.

The NSKH, which implies the level of need for nursing care, significantly affected severe patients with a cognitive FIM score at admission of  $\leq 9$  and a motor FIM score at admission of  $\leq 30$  (Groups A and G). Among patients aged  $\leq 69$  years, a cognitive FIM score at admission  $\geq 10$  significantly affected patients with motor FIM scores at admission of  $\leq 30$  (Group

D); whereas among patients aged  $\geq 70$  years, the same range of cognitive FIM scores significantly affected not only patients with motor FIM scores at admission of  $\leq 30$  (Group J), but also patients with motor FIM scores at admission of 31–69 (Group K). Thus, for elderly patients with a high level of need for nursing care (i.e. elderly patients with low cognitive FIM and motor FIM scores at admission), NSKH score was considered to be a significant independent variable.

Listed below are some of the limitations of the present study. First, multiple regression analysis results vary based on the types of patients examined and the independent variables used. Although past studies (Table 3) often used the six items used in the present study, some studies also included other independent variables such as complications and Stroke Impairment Assessment Set. The “Guidelines for Clinical Research and Studies on Stroke” state that basic patient information should include the following: sex, age, independence or non-independence in activities of daily living prior to onset, stroke type, lesion of stroke, post-onset duration of hospitalization, presence/absence of hemispatial neglect, and presence/absence of aphasia [20]. It would be desirable to conduct an investigation similar to the present study but which incorporates all factors which could affect motor FIM score at discharge.

Second, four groups (B, C, H, and I) had few patients, thus prohibiting multiple regression analysis. This was due to the fact that motor FIM score at admission and cognitive FIM score at admission are correlated; a cognitive FIM score at admission of  $\leq 9$  combined with a motor FIM score at admission of 31–69 or 70–91 is seldom observed.

Third, results vary according to the cutoff point used for the strength of the effect of age or cognitive function on outcomes. For example, the conclusion of Sonoda et al. that “age affected patients with motor FIM scores at admission of 13–30” and the conclusion of the present study that “age significantly affected patients with a cognitive FIM score at admission of  $\geq 10$  and a motor FIM score of admission of 13–69” may seem to differ from each other. However, considering that the effect of age was greater in “patients with a cognitive FIM score at admission of  $\geq 10$  and a motor FIM score at admission of 13–30” than in “patients with a cognitive FIM score at admission of  $\geq 10$  and a motor FIM score at admission of 31–69” and that analysis of “patients with a motor FIM score at admission of 13–30” included patients with cognitive FIM scores at admission of both  $\leq 9$  and  $\geq 10$ , the conclusion of the present study is in fact identical to the conclusion reached by Sonoda et al. [17].

Fourth, we presumed to divide patients into groups based on continuous variables; therefore, different group divisions may yield different conclusions. We cannot say whether the use of a different group division

method, such as quartiles, would yield the same conclusions as those of the present study; this matter should be investigated in a future study.

Fifth, the clinical usefulness of the results of the present study is unclear. For example, although there is a conceivable scenario in which multiple regression analysis for predicting motor FIM scores at discharge could be used to identify patients for whom cognitive FIM score at admission is a significant independent variable and thus focus their rehabilitation on cognitive function, further investigation is necessary to determine whether such applications would be useful.

Based on the absence of a linear relationship between factors and motor FIM improvement, as well as on the fact that factors do not demonstrate uniform effects in all patient groups, the present study stratified patients based on age, motor FIM score at admission, and cognitive FIM score at admission to create eight predictive formulas; we then used these formulas to determine which of six independent variables (factors) were significant in which patient groups. This method is considered useful in determining the types of patient groups in whom these factors significantly affect motor FIM scores at discharge.

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