

Investigate Targeted Factors to Achieve Prediction Goal in Stroke Convalescence in Terms of Causal Relationships of Prediction Error

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Abstract

Background and Purpose: To investigate target functional independence measure (FIM) items to achieve the prediction goal in terms of the causal relationships between prognostic prediction error and FIM among stroke patients in the convalescent phase using the structural equation modeling (SEM) analysis. Methods: A total of 2992 stroke patients registered in the Japanese Rehabilitation Database were analyzed retrospectively. The prediction error was calculated based on a prognostic prediction formula proposed in a previous study. An exploratory factor analysis (EFA) then the factor was determined using confirmatory factorial analysis (CFA). Finally, multivariate analyses were performed using SEM analysis. Results: The fitted indices of the hypothesized model estimated based on EFA were confirmed by CFA. The factors estimated by EFA were applied, and interpreted as follows: "Transferring (T-factor)," "Dressing (D-factor)," and "Cognitive function (C-factor)." The fit of the structural model based on the three factors and prediction errors was supported by the SEM analysis. The effects of the D- and C-factors yielded similar causal relationships on prediction error. Meanwhile, the effects between the prediction error and the T-factor were low. Observed FIM items were related to their domains in the structural model, except for the dressing of the upper body and memory (p < 0.01). Conclusions: Transfer, which was not heavily considered in the previous prediction formula, was found in causal relationships with prediction error. It is suggested to intervene to transfer together with positive factors to recovery for achieving the prediction goal.

Keywords

Prediction Error, Functional Independence Measure, Stroke, Convalescent Phase, Structural Equation Modeling

1. Introduction

In stroke rehabilitation, intervention strategies depend on each phase (acute, convalescent, and maintenance) because of various issues (e.g., functional impairment, disturbances in activities of daily living (ADL), and participation restriction, respectively) that need to be resolved [1] [2]. Clearly, a realistic goal is to allow stroke patients to maintain their motivations and achieve effective rehabilitation outcomes within limited periods. Prognostic prediction necessary for discharge has been based on numerous factors, such as age, length of hospitalization from initial admission, admission functional independence measure (FIM), and Rankin Scale score (RS) [3]-[8]. ADL and gait are important for the post-stroke period as they pertain to the completion of various functions related to the patients' return to their homes after hospital discharge. In view of these, in previous stroke studies, the predictions of ADL and gait had been reported, based on the model, which used the associations between self-care, motor-FIM (m-FIM) and cognitive FIM (c-FIM) [9] [10] [11] [12]. In addition, after hospitalization, most stroke patients experienced various events, which are recurrent owing to stroke, and lead to training abeyance owing to the treatments they undergo for the complications or additional illness they cause. Moreover, they also have various symptoms excepting physical motor side caused by stroke. These factors have considerable impact on stroke recovery. For these reasons, it has been considered that the recovery levels after stroke constitute a variable even if same motor functional level at the admission depends on individual characteristics which depend on the event they have after hospitalization [5]. Therefore, it has been reported that the accuracy of prognostic prediction based on FIM was not high [13] [14]. Hence, various factors have been added or deleted to calculate a model or crated multiple prediction formula for an improved accuracy [15]. However, these formulas mostly estimate correlations, and causal relationships are thus unclear. Moreover, the rehabilitation approaches the factors that were mainly reported positive for prediction outcome from previous studies. Alternatively, there are only a few studies about an influence of factors, which make prediction error cause or excepted factors from prediction formula. There is a prior report example that involved two factors, which are admission FIM score and prolonged hospital stay, associated with inaccurate prediction of walking that influenced discharge outcomes [5]. Therefore, it is possible to achieve predicted score by prediction formula if it considers the positive factors responsible for FIM improvements but also the negative factors, and leads to an effective rehabilitation intervention to aid discharge. The study aims to clarify the targeted FIM items for achieving of prediction based on the causal relationships between the prediction error, which is different from the prediction formula to the real score, and FIM gain in the convalescent phase using structural equation modeling (SEM) analysis.

2. Materials and Method

2.1. Subjects

The medical data in this study used anonymized observational data from the Japanese Rehabilitation Database (JRD) pertaining to patients in the stroke/recovery rehabilitation phase wards (January 2016 version, Japan Association of Rehabilitation Database, Tokyo, Japan). Initially, data collection was not subject to ethical review because the data consisted solely of observation data obtained during normal medical treatment activities at medical institutions and did not contain personal information. However, they applied the use of secondary data for ethics review again, requesting that the ethical committee issue a letter of approval confirming that there were no ethical issues, which was then had approved by the Ethics Committee of the Japanese Association of Rehabilitation Medicine (November 14, 2014). The study complied with the principles of the Declaration of Helsinki as well. Therefore, the need for informed consent was waived owing to the a) retrospective and observational design of the study and b) the use of secondary data. A flowchart of the subject in this study is shown in Figure 1. The inclusion criteria were as follows: age < 100 years, days from onset to admission < 77 days, and length of ward stay (LOS) < 250 days. Similarly, the FIM and RS scores at admission and discharge, and baseline characteristics (e.g., data on sex, recurrence, complications, etc.) were collected. Prediction error was defined as a difference (observed-estimated values) using the prediction formula. However, the maximum limit of the estimated value was set to 126 points, and was the same as the maximum limit of FIM. Individual FIM scores were modified to estimate the FIM gain (at discharge-at admission). Moreover, the exclusion criteria included death, changing hospitals owing to sudden and worsened outcomes, and outliers that were set by the interquartile range. Finally, the data of 2922 cases were analyzed.

2.2. Statical Analysis

The formula used for prognostic predictions allowed calculations based on multiple regression factorial analysis (forced entry) according to JRD referencing. The data were classified based on estimated total FIM (t-FIM) score, following which, patients with scores > estimated t-FIM score were classified as the achieved group and the remaining as the non-achieved group. The data were randomly divided for modeling development and verification to allow the validation of the model using cross-validation (CV, stratified five-fold cross-validation). The correlation analysis was performed to extract factors based on subscales in the cases of total FIM items. This was followed by an exploratory factorial analysis (EFA)



Figure 1. Data sampling flowchart with reason for exclusion. JRD, Japanese Rehabilitation Database.

to select the appropriate number of factors from the data. EFA techniques were defined to explain patterns of covariances among observed variables using latent constructs [15] [16]. FIM was extensively used as a tool to evaluate the status of patients throughout the recovery process, and consisted of 18 items, wherein m-FIM comprised 13 items and c-FIM comprised 5 items. The maximum score was 126 points, and an indicator level was used which was classified from level 1 (total assistance) to 7 (independence). EFA (maximum likelihood method) was applied with a minimum eigenvalue for the retention set for values >1.0. The data were screened for factorability using the described criteria of the Kaiser-Myer-Olkin (KMO) measure of sample adequacy, and Bartlett's test of sphericity [17]. The factorial analysis was rotated by promax rotation based on the assumption that there were correlations among factors. The number of factors needed to be retained was based on the Kaiser rule and a scree plot. The quality or stability of the solution was assessed by several indicators, including the minimum number of loading variables per major factor, magnitudes of the loadings, and residual and reproduced correlations [18]. Items with factor loadings <0.40 (as the exclusion condition on any of the factors) were deleted. The validity of the selected factors by EFA was determined using confirmatory factorial analysis (CFA). CFA was used to investigate the validity of each item and identify common factors, thus verifying the contrast statistic of the hypothesis, as well as the analysis of covariance instead of correlation. For the CFA, the Chi-square test was used to assess the fit of the model. Moreover, the adequacy of the model fit to the data was assessed based on a comparative fit index (CFI) (range 0 - 1, recommended values \geq 0.95), goodness-of-fit index (range 0 - 1, recommended values \geq 0.90), root-mean-square error of approximation (RMSEA) (range 0 - 1, recommended values \leq 0.06), and the standardized RMS residual (SRMR) (range 0 - 1, recommended values \leq 0.08) [15] [16] [17] [19] [20]. Finally, a model including t-FIM-dif was conducted by multivariate analyses, which were performed using SEM analysis. SEM analysis is a multivariate statistical analysis technique used to analyze structural relationships. All nonsignificant associations (p \geq 0.05) were eliminated. Relevant nonsignificant coefficients were retained and are displayed using dashed arrows.

3. Results

In total, the data from 6875 stroke patients were registered on JRD. Of these, the 3953 patients who failed to meet the inclusion criteria were excluded, and the 2992 patients who met the criteria were ultimately included in this study. Among all of participants in this study, 1211 (41.4%) were female, and the mean age was 70 years. The achieved rate of the prognostic prediction score was 37.3%. The RS score before admission, and the m-FIM and c-FIM scores at admission were 0.62, 46.36, and 22.22, respectively. The baseline characteristics of subjects in each group are listed in Table 1. Table 2 lists the multiple regression analysis outcomes of the main parameters for t-FIM prognostic prediction with an average CV value of 0.69.

Table 1. Descriptive characteristics of subjects.

	Overall $(n = 2922)$	Achieved group (n = 1089)	Non-achieved group (n = 1833)
Age	70.03 ± 12.02	71.35 ± 11.3	69.25 ± 12.37†
Female, %, (n)	41.44 (1221)	43.75 (476)	40.10 (735)
Days from onset to admission	34.8 ± 14.72	35.17 ± 15.22	34.59 ± 14.42
Length of ward stay	101.9 ± 44.27	108.87 ± 41.16	97.76 ± 45.53†
RS before admission	0.62 ± 1.2	0.54 ± 1.1	$0.66 \pm 1.26^{*}$
Average number of units/day	5.35 ± 2.03	5.36 ± 2.08	5.34 ± 2.0
m-FIM on admission	46.36 ± 22.44	42.16 ± 17.7	$48.86 \pm 24.5 \dagger$
c-FIM on admission	22.22 ± 8.69	21.21 ± 7.67	$22.82\pm9.19\dagger$
m-FIM on discharge	67.46 ± 21.23	75.96 ± 11.45	62.41 ± 23.92†
c-FIM on discharge	26.19 ± 7.78	28.25 ± 5.77	$24.96 \pm 8.53 \dagger$
Stroke recurrence positive, %, (n)	0.94 (n = 28)	0.73 (n = 8)	1.09 (n = 20)
Hypertension positive, %, (n)	66.51 (n = 1990)	70.02 (n = 765)	66.83 (n = 1225)
Complications positive, %, (n)	13.28 (n = 388)	13.32 (n = 145)	13.26 (n = 243)

Achieved group: observed total FIM > estimated total FIM; RS: Rankin scale; m-FIM: motor Functional Independence Measure; c-FIM: cognitive Functional Independence Measure; Units: duration of rehabilitation of 20 minutes is considered as 1 unit. *p < 0.05; $\dagger p < 0.01$; Mann-Whitney U test.

	Standardized coefficient			
	В	SE	β	
Age	-0.34	0.03	-0.15 †	
Days from onset to admission	-0.15	0.03	-0.08 †	
m-FIM on admission	0.59	0.02	0.48†	
c-FIM on admission	1.123	0.05	0.36 †	
RS before admission	-0.92	0.41	-0.03 *	

Table 2. Multiple regression analysis for t-FIM prognosis prediction (forced entry).

The Average of stratified 5-fold cross-validation was 0.69. B: unstandardized coefficient; SE: standard deviation of the error; t-FIM: total Functional Independence Measure; m-FIM: motor Functional Independence Measure; c-FIM: cognitive Functional Independence Measure; RS: Rankin Scale. *p < 0.05; †p < 0.01.

Nine observed items were used for analysis. Model fit indices, Kaiser's rule, and the scree plot suggested a three-factor solution in the CFA, which accounted for 59.7% of the variance. Correlations between inter-factors after using the eigenvalue-one criterion and promax factor rotation are presented in **Table 3**. The fitted of indices of the hypothesized model were CFI = 0.996, TLI = 0.993, SRMR = 0.016, and RMSEA = 0.035. All these outcomes are indicative of a good model fit.

Factor 1 contented three items, and two items related to transfer were shown. Factor 2 has dressing activities, and Factor 3 has five items related to cognitive function. Thus, the factors by CFA were applied according to the following naming convention: "Transfer (T-factor)," "Dressing (D-factor)," and "Cognitive (C-factor)." SEM was employed to quantify the relationship between three factors and prediction error. The proposed model was CFI = 0.994, TLI = 0.984, SRMR = 0.018, and RMSEA = 0.051, and the model fit created in this study was good. Findings based on the path coefficients are shown three factors had positive influences on prediction errors in **Figure 2**. The T-factor was low (coefficient = 0.12) and affected lower to prediction errors compared another factor. The impacts of both the C- and D-factors are similar level to the prediction error. The coefficient between the T- and C-factors was 0.59, and was higher relation compared with the other outcomes. All coefficients were significant at p < 0.001 except dressing of the upper body (Dressing U/B) and memory gain.

4. Discussion

The present study investigated the causal relationships between prediction error and FIM based on a prediction prognostic formula according with multifacility data (JRD) using factor analysis and SEM. The main findings explained a structural model of prediction error with FIM and the three-factor (toileting, dressing, cognitive) influenced prediction error. In three factors related to prediction error, and problem solving and dressing lower body (Dressing L/B) had the mainly influence.

	Factor 1	Factor 2	Factor 3	Uniqueness
Transfer-B/C gain	0.90	0.60	0.44	0.18
Transfer-T gain	0.94	0.61	0.43	0.09
Toileting gain	0.78	0.73	0.43	0.33
Bladder gain	0.62	0.52	0.45	0.60
Bowel gain	0.62	0.47	0.45	0.61
Dressing U/B gain	0.64	0.93	0.40	0.16
Dressing L/B gain	0.63	0.95	0.37	0.05
Bathing gain	0.40	0.55	0.31	0.70
Memory gain	0.40	0.36	0.79	0.37
Solving gain	0.40	0.37	0.73	0.47
Comprehension gain	0.38	0.30	0.71	0.49
Social gain	0.37	0.31	0.66	0.57
Expression gain	0.36	0.31	0.65	0.57

Table 3. Confirmatory factor analysis with promax rotation.

Transfer-B/C: Transfer Bed/Chair Wheelchair; Transfer-T: Transfer Toilet; Bladder: Bladder Management; Bowel; Bowel Management; Dressing U/B: Dressing Upper Body; Dressing L/B: Dressing Lower Body; Social: Social Interaction; Solving: Problem Solving; gain: at discharge-at admission; gain: at discharge-at admission. Values in bold indicate a difference of >0.6.



Figure 2. The structural equation model of prognostic prediction error (standardized path coefficients). Values of factor loading and error variables are shown. The inter-relationships of residual variables are not shown. Chi-square test (191.99, p < 0.001), CFI = 0.990, TLI = 0.984, SRMR = 0.018, RMSEA = 0.051. †p < 0.01; boxes: observed variables; circles: latent variables; Transfer-T: Transfer Toilet; Transfer-B/C: Transfer Bed/Chair Wheelchair; Dressing U/B: Dressing Upper Body; Dressing L/B: Dressing Lower Body; Social: Social Interaction; Solving: Problem Solving; gain: at discharge-at admission.

Estimated t-FIM score was calculated based on a formula that has been reported in a previous study using JRD. The predictor that is considered for motor prognostic prediction in post-stroke has shown the initial grade of paresis, which is important [3] [18]. In addition, age, and period from the onset of hospitalization impact on the FIM recovery [21] [22]. The estimation formula in this study was reflected by these factors. A relevant formula has been proposed using admission RS in a recent publication [18]. The coefficient of determination was compared with the use of RS before hospitalization or upon admission, and both results were quite similar. Accordingly, the use of RS before admission would not be inferior. Moreover, the CV was reasonable, and a permissible range supported the generalizability of the prediction model in this study.

Patients have to deal with dual tasks (DTs) when they perform behavioral and cognitive tasks during their daily life activities. Moreover, performing DTs is related with a complex sensorimotor action that is based on appropriate attention distribution/division of executive function like those related to gait and postural control in daily living [23]. However, these functions are vulnerable to the effects of stroke. For this reason, it has been reported that people with cognitive dysfunction have not exhibited considerable progress regarding the reduction rate of falls and fall-related injuries [24]. Furthermore, cognitive function constitutes an independent prognostic factor of mobility recovery [23]. Such a highly complex exercise depends on working memory (WM), and the processes of switching and allocation of paying attention and WM are interlinked. Prefrontal cortex (PFC) and WM are highly related with these processes. Furthermore, symptoms have been reported. These do not only include physical disability but also uncontrolled emotion and cognition dysfunction that lower motivation in post-stroke cases. These disorders are related with inappropriate decision-making, behaviors, and execution dysfunction [25].

It is important to consider that the decision-making processes and behaviors that impact rehabilitation constitute factors influencing prognostic prediction. It has been reported that decisions were influenced by the trade-off between reward and punishment, and has defined an optimal behavior in new situations, which have not been clearly comprehended. PFC has been involved in decision making is more active when these patients have to pay attention or conduct functions consciously. However, PFC in post-stroke cases does not work much compared with healthy individual cases in the same age range owing to cognitive dysfunction [26]. Post-stroke cases have been associated with many rehabilitation failures, and patients have been unable to solve these failures by themselves owing to cognitive impairment. Patient experiences cause them to fall into a vicious cycle of negative thoughts. In these states, the decision-making process is influenced by punishments (such as negative feelings of self-defeat) rather than by rewards [27]. Therefore, it was considered that the recovery process was influenced by the C-factor.

Moreover, PFC has associations with the mirror neural system (MNS). The MNS is defined as a simulating system for deeply learning others' activities, un-

derstanding the purpose of activities rooted on imitation behaviors, action understanding, and automatic mimicry [25], and contributing to the reconstruction of activities after stroke. Visual and auditory stimulations influence the MNS and contribute toward activation of motor areas of the brain. In addition, a deeper understanding is needed for the reconstruction of activities to fit patients' needs for activity training. For the reason, it was assumed that the extracted C-factor in this study was essential for MNS simulation, and the dysfunctions in C-factor likely influenced the recovery process.

Cognitive control in PFC is the defined ability of executing complicated activities or updating information, and switching attention. Automatic or habitual responses can help deal with everyday situations, but for tasks that are more novel, uncertain, or complex, cognitive control is more important. To reconstruct ADL requires a lot of load in cognitive control in post-stroke patients to control movements accompanied by involuntary movements [28]. Thus, task execution in such patients involves higher levels of concentration.

In addition, self-care in post-stroke periods exhibits a gap between capacity and performance ability, and patients feel a difference between reality and their imaginations. In these situations, it may be difficult for post-stroke patients to control their emotions and maintain their concentration, leading to PFC dysfunction.

Inappropriate emotion regulation is considered a self-regulation failure that assigns priority to short-term mood repair over achieving long-term goals. That causes PFC to be unable to execute appropriate control on performed tasks. Therefore, stroke patients have to deal constantly with cognitive, motivational, and emotional information, resulting in PFC overload, and thereby, inappropriate behaviors, such as not participating in rehabilitation. It means they leave an opportunity to improve their function and ADL. Therefore, it was assumed that the prediction errors occurred because of the C-factor, which has a relevant with the PFC.

From the motor functional perspective, two items, that is transferring, and Dressing L/B, were included in three factor extracted in this study. It has been reported that Dressing L/B in the D-factor was included in the prognostic prediction formula and had a positive influence in previous studies. However, these items have reported it is moderate difficulty activities for recovery progressing in post-stroke.

Therefore, it was considered that Dressing L/B have both sides, positive and negative for achieving to progress prediction. On other hands, there are only a few papers on transferring which report on the relationship with the FIM. Transferring is a basic skill that is essential for getting out of bed, and wheelchair is used when the patients cannot walk or experience problems walking; thus, transferring expands their activities. Bedside rehabilitation is effective for improving FIM. However, bedside is limited in conducting more dynamic activities like gait [29]. It makes discharge destination depend on impact based on the pe-

riod between transferring from the bed/wheelchair to the initiation of an activity [30]. Moreover, transferring has been assigned prediction for ADL dependence, and the FIM score was impacted [10]. Transferring is comprised of several activities like sitting, standing, and turning around, and is influenced by trunk and lower limb functions. The difficulty level of transferring is moderate in ADL performance like Dressing L/B [31] [32]. Thus, it was assumed that transfer function impacted to prediction error like Dressing L/B as well.

This study had some limitations. First, participants' lesions could not be reflected enough because not all participants in this study had prefrontal dysfunction. Second, the influences of factors related to a characteristic of hierarchy with t-FIM (e.g., ceiling or floor effect) were not reflected in factorial analysis; therefore, the impact was not considered for modeling SEM. Future research should investigate the SEM between FIM gain and prediction error after hierarchy with t-FIM upon admission or according to stroke type and lesion.

5. Conclusion

In conclusion, this study investigated an SEM model in two groups that were divided based on prediction error. Three factors, namely, transfer, dressing, and cognitive, had causal relationships with prediction errors determined according to the JRD. The study's findings suggest transfer, not was considered in the previous predication formula much, was found in causal relationships with prediction error, and is more effective to intervene together with two FIM items, (solving problems in cognition, and Dressing L/B) to achieve the prediction goal. Moreover, it was shown to need being considered to approach moderate difficult activities. Future research should be conducted in hierarchy based on t-FIM score upon admission or stroke type and lesion, and should test and discuss the influences.

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Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

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