ORIGINAL

Predictive factors associated with poor outcomes for older adult inpatients in the convalescent rehabilitation ward

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Abstract : This study aimed to determine predictive factors associated with poor outcomes among older adult inpatients in the convalescent rehabilitation ward. We also examined the validity of factors that were identified as predictive of poor outcomes. Study subjects were 104 older adult inpatients in the convalescent rehabilitation ward, divided into two groups based on outcome at discharge. Group I included the outcomes of death or transfer to an acute care hospital and Group II included all other outcomes. Data were retrospectively collected from older adults' medical records, including: activities of daily living, swallowing grade, nutritional index, and blood biochemistry data. Logistic regression analysis was used to extract predictive factors associated with poor outcomes. Next, we calculated the Stratum-specific likelihood ratio (SSLR) for each extracted factor. Two items were extracted as predictive factors with AUCs ≥ 0.7 : N-terminal pro-brain natriuretic peptide (NT-proBNP) and days from onset to hospitalization. The SSLRs showed the risk for a poor outcome increased when NT-proBNP was ≥ 2500 pg/ml, and when there were ≥ 35 days from onset to hospitalization. Our findings suggest these predictive factors provide a valid index to predict poor outcomes among older adults from the early stage of admission. J. Med. Invest. 67 : 304-310, August, 2020

Keywords **:** *convalescent rehabilitation ward, poor outcome, predictive factors, stratum-specific likelihood ratio*

INTRODUCTION

The convalescent rehabilitation ward system started in Japan in 2000 (1). The convalescent rehabilitation ward is a sub-acute-phase-particularized rehabilitation ward (2). The disabled patients on whom acute phase treatment has finished are, regardless of the patients' ages, eligible for admission to convalescent rehabilitation ward. The diseases concerned are legally limited to stroke, femoral neck fracture, disuse syndrome following prolonged bed rest, or others (3).

Convalescent rehabilitation wards provide intensive rehabilitation based on inter-professional collaboration, and promote re-integration of patients in a state of physical and mental recovery (4). However, an increasing number of patients admitted to the convalescent rehabilitation ward have severe conditions. This may be attributable to factors such as acceptance of critically ill patients based on the Nichijo-seikatsu-kino-hyokahyo and shortening of hospitalization days in acute care hospitals (5). Nichijo-seikatsu-kino-hyokahyo form evaluates 13 items of basic daily activities such as turning over in bed and communicating with others. 13 items are scored on a scale of 0-1 or 0-2 ; the total score (0-19 points) is lower if the patient is independent and higher if a higher level of care is required. A score of 10 or more is considered a severe case.

The rate of sudden change or death due to complications during hospitalization in the convalescent rehabilitation ward has been reported as 5.4%-10.7% (6-8). A number of patients with severe conditions cannot achieve convalescent rehabilitation ward goals because of recurrence or exacerbation of the cause disease, comorbidity, or past illness. Therefore, it is important to understand factors that may predict poor outcomes on admission to the ward. Understanding these predictive factors will help in determining appropriate risk management and rehabilitation policies. In the context of convalescent rehabilitation wards, many studies have used Activities of daily living (ADL) as a predictive factor, with return to home as the outcome (9,10). However, few studies have considered death or transfer to an acute care hospital as outcomes.

Previous reports have investigated patients with stroke who died or were transferred to hospital urgently (11), and explored the characteristics of patients who referred hospital because of complications or recurrence (8,12). In contrast, few studies have focused on outcome prediction for patients with severe conditions (7). In this study, we aimed to clarify predictive factors related to poor outcomes for older adult inpatients in a convalescent rehabilitation ward, and examined whether these factors were valid predictors of poor outcomes.

METHODS

Design

This study used a retrospective cohort design.

Subjects

Study subjects were 147 inpatients aged 65 years or older who were admitted to the inpatient convalescent rehabilitation ward of our hospital between October 2015 and August 2017. Exclusion criteria were patients in a hospital, a special nursing home, a nursing home, or a geriatric health services facility before admission to a convalescent rehabilitation wards (n = 40), patients discharged temporarily for gastrostomy (n = 2), and patients with missing data (n = 1). Total 104 subjects were included in the

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analysis (43 males, 61 females ; mean age 83.1 ± 7.5 years).

Subjects were divided into two groups based on their outcomes at discharge. Group I included those with death or transfer to an acute care hospital. Group II included all other outcomes (discharge to home, sanatorium medical facility, special nursing home, nursing home, or geriatric health services facility). In this study, Group I subjects were defined as those with poor outcomes who failed to complete convalescent rehabilitation.

Assessment items

The main assessment items were patients' basic information ; ADL, swallowing grade, nutritional indicators, and blood biochemical data. The 26 assessment items are shown in Table 1. "Days from onset to hospitalization" was defined as the period from the date of admission to an acute care hospital after onset or injury, or from the date of surgery in an acute care hospital until admission to a convalescent rehabilitation ward. Assessment items were investigated retrospectively from patients' medical records. We used admission data, as well as information regarding outcomes and hospitalization days. In addition, we examined the complications that caused poor outcomes.

Statistical analysis

We performed comparisons between the two groups for each assessment item. Multivariate analysis was used to extract predictive factors related to outcomes.

Next, Stratum-specific likelihood ratios (SSLR) were calculated to clarify the validity of identified predictive factors. The SSLR quantifies how test results in a given stratum will change the probability that a patient has the disease in question (13). Likelihood ratios > 10 or < 0.1 show large and often conclusive changes in probability from pretest to posttest. Likelihood ratios of 5-10 and 0.1-0.2 show moderate shifts in pretest to posttest probability. Likelihood ratios of 2-5 and 0.5-0.2 show small changes in probability. Finally, likelihood ratios of 1-2 and 0.5-1 show very small changes in probability (14).

Mann-Whitney U tests and chi-square tests were used for comparisons between the two groups. Extraction of predictive factors was performed by logistic regression analysis, with discharge outcome as the objective variable. Assessment items that showed a significant difference between the two groups were used as explanatory variables. We used variable forward selection (likelihood ratio) as the variable input method. The problem of multicollinearity was addressed using Spearman's rank correlation coefficient. When the correlation coefficient between each explanatory variable was ≥ 0.7, one side was excluded.

The Area under the curve (AUC) was determined by receiver operating characteristic curve analysis. The AUC is used as an index of diagnostic accuracy, with an AUC ≥ 0.7 representing high diagnostic accuracy (15). We used IBM SPSS Statistics version 25 for statistical analyses, with the significance level set at < 5%. The SSLR calculations were performed using Microsoft Excel.

Ethical considerations

This study was conducted with the approval of the Naruto Yamakami Hospital Ethics Committee (2018-01-1). Informed consent was obtained from all subjects. The analysis was conducted with consideration of protecting patients' personal information.

RESULTS

Seventeen cases (16%) were assigned to Group I, and 87 cases (84%) to Group II. The results of the comparison between the two groups are shown in Table 2. The outcomes for two groups are shown in Table 3. The most common complications that caused poor outcomes were chronic heart failure exacerbation (n = 5), fracture (n = 3), and pneumonia (n = 2). Exacerbation of chronic renal failure, abdominal aortic aneurysm development, recurrence of cerebral infarction, cholangitis, malignant tumor, acute abdomen, and deterioration of nutritional status were each observed in one case.

The explanatory variables for the logistic regression analysis selected was the total Functional independence measure (FIM) score because the total FIM score had a correlation coefficient of ≥ 0.7 for the Nichijo-seikatsu-kino-hyokahyo, along with motor and cognitive FIM scores. Similarly, the Geriatric nutritional risk index (GNRI) was selected because the correlation coefficient between GNRI and Alb was ≥ 0.7. Other explanatory variables were shown in Table 4. As a result, N-terminal pro-brain natriuretic peptide (NT-proBNP) and days from onset to hospitalization were extracted as predictive factors related to death and transfer to an acute care hospital (Table 4). The discrimination predictive value was 85.6%. Table 5 shows the AUCs for the two predictive factors (NT-proBNP and days from onset to hospitalization) were ≥ 0.7.

Table 1. Assessment items

Basic attributes	Age, Sex, Cause disease (Cerebrovascular disease, Locomotive, Disuse syndrome), History of heart failure, History of coronary artery disease, Days from onset to hospitalization, Hospitalization days, Outcomes (Death / Transfer to an acute care hospital, Discharge to home, Sanatorium medical facility, Special nursing home, Nursing home, Geriatric health services facility), Nichijo-seikatsu-kino-hyokahyo
ADL	Total FIM, Motor FIM, Cognitive FIM
Swallowing ability	Swallowing grade
Nutrition indicators	Body mass index, Geriatric nutritional risk index
Blood biochemical data	NT-proBNP (pg/ml), TP (g/dl), Alb (g/dl), A/G ratio, AST (U/L), ALT (U/L), BUN (mg/dl), CRE (mg/dl), WBC (g/dl), RBC (g/dL), Hb (g/dl)

FIM, Functional independence measure ; NT-proBNP, N-terminal pro-brain natriuretic peptide ; TP, Total protein ; Alb, Albumen ; A/G ratio, Albumin/Globulin ratio ; AST, Aspartate transaminase; ALT, Alanine transaminase; BUN, Blood urea nitrogen ; CRE, Creatinine ; WBC, White blood cell ; RBC, Red blood cell ; Hb, Hemoglobin.

Table 2. Subjects' basic attributes

Assessment items		Total n = 104	Group I n = 17 (16%)	Group II n = 87 (84%)	p-value
Age (years), mean ± SD		83.1 ± 7.5	84.4 ± 6.3	82.9 ± 7.7	0.650
Sex (n), male/female		43/61	10/7	33/54	0.110
Cause disease					
Cerebrovascular disease, n (%)		23 (22)	6 (35)	17 (20)	0.152
Locomotive, n (%)		55 (53)	5 (29)	50 (57)	0.034
Disuse syndrome, n (%)		26 (25)	6 (35)	20 (23)	0.284
History of heart failure, n (%)		17 (16)	6 (35)	11 (13)	0.032
History of coronary artery disease, n (%)		8 (8)	1 (6)	7 (8)	1.000
Days from onset to hospitalization (days)		28 (17-39)	39 (28-52)	24 (17-35)	0.002
Hospitalization days (days)		87 (56-89)	39 (26-59)	88 (84-89)	< 0.001
Nichijo-seikatsu-kino-hyokahyo (score)		5 (3-9)	8 (4-14)	5 (2-8)	0.027
Total FIM (score)		60 (34-81)	41 (22-73)	62 (38-83)	0.009
Motor FIM (score)		37 (19-55)	21 (13-50)	37 (22-56)	0.018
Cognitive FIM (score)		21 (13-38)	14 (8-22)	25 (14-33)	0.009
Swallowing grade		9 (8-10)	9 (6-10)	9 (8-10)	0.022
BMI		20.0 (17.4-22.0)	19.6 (15.4-21.8)	20.2 (17.6-22.4)	0.267
GNRI		89.2 (82.2-95.6)	82.9 (76.5-88.4)	90.4 (83.1-96.8)	0.002
Blood biochemical data					
NT-proBNP (pg/ml)		356 (164-874)	1530 (489-2436)	272 (150-663)	< 0.001
TP (g/dl)		6.2 (5.9-6.7)	6.2 (5.7-6.4)	6.4 (5.9-6.7)	0.228
Alb (g/dl)		3.4 (3.1-3.7)	3.1 (2.9-3.3)	3.5 (3.2-3.8)	0.001
A/G ratio		1.2 (1.0-1.4)	1.1 (0.9-1.3)	1.3 (1.1-1.4)	0.041
AST (U/L)		20 (17-27)	22 (20-25)	20 (16-28)	0.214
ALT (U/L)	M	14 (9-19)	12 (10-16)	14 (9-20)	0.412
	F	15 (11-25)	13 (8-31)	15 (11-24)	0.717
BUN (mg/dl)		17.3 (13.2-23.0)	19.8 (14.9-34.0)	16.9 (12.8-21.6)	0.085
CRE (mg/dl)	M	0.69 (0.53-0.90)	0.71 (0.58-0.93)	0.69 (0.52-0.86)	0.555
	F	0.69 (0.54-0.99)	0.81 (0.65-1.56)	0.68 (0.52-0.95)	0.085
WBC (g/dl)		58 (47-346)	72 (43-91)	56 (48-78)	0.455
RBC (g/dl)	M	382 (317-418)	318 (299-413)	385 (337-419)	0.226
	F	371 (338-409)	351 (298-392)	372 (339-411)	0.422
Hb (g/dL)	M	11.9 (10.4-13.1)	12.3 (11.1-13.2)	11.6 (10.2-13.1)	0.300
	F	11.4 (9.5-12.3)	12.2 (10.4-13.2)	11.3 (9.4-12.1)	0.147

Data shown as median (interquartile range), except for Age, Gender, Underlying disease and History of heart failure and coronary artery disease.
SD, Standard deviation; FIM, Functional independence measure; BMI, Body mass index; GNRI, Geriatric nutritional risk index; NT-proBNP, N-terminal pro-brain natriuretic peptide; TP, Total protein; Alb, Albumen; A/G ratio, Albumin/Globulin ratio; AST, Aspartate transaminase; ALT, Alanine transaminase; BUN, Blood urea nitrogen; CRE, Creatinine; WBC, White blood cell; RBC, Red blood cell; Hb, Hemoglobin.

Table 3. Outcomes

Group I	n = 17 (16%)
Death, n (%)	6 (6)
Transfer to an acute care hospital, n (%)	11 (11)
Group II	n = 87 (84%)
Discharge to home, n (%)	30 (29)
Sanatorium medical facility, n (%)	16 (15)
Special nursing home, n (%)	14 (13)
Nursing home, n (%)	11 (11)
Geriatric health services facility, n (%)	16 (15)

The SSLRs are shown in Table 6. When NT-proBNP was ≥ 2500 pg/ml, the SSLR was 20.5 and the posterior probability was 80%. When NT-proBNP was ≤ 400 pg/ml, the SSLR was 0.4 and the posterior probability was 7%. When there were 35-44 days from onset to hospitalization, the SSLR was 2.8 and the posterior probability was 36%. At ≥ 45 days from onset to hospitalization, the SSLR was 2.6 and the posterior probability was 33%. Further, when there were 0-14 days from onset to hospitalization, the SSLR was 0.2 and the posterior probability was 5%. At 15-24 days from onset to hospitalization, the SSLR was 0.4 and the posterior probability was 8%.

DISCUSSION

This study revealed that initial data for NT-proBNP and days from onset to hospitalization were predictive factors for death or transfer to an acute care hospital among older adult inpatients in the convalescent rehabilitation ward. Because the AUC was 0.789 for NT-proBNP and 0.741 for days from onset to hospitalization, these factors were confirmed to have diagnostic performance.

The poor outcome group (Group I) accounted for 16% of our sample. This was higher than the 5.4%-10.7% reported in previous studies (6-8). In Group I, 35% of subjects had a history of heart failure (Table 2). In addition, there were five cases (29%)

Table 4. Predictive factors associated with poor outcomes

	Regression coefficient	p-value	Odds ratio	95%CI
NT-proBNP (pg/ml)	-2.245	0.001	0.106	0.028-0.401
Days from onset to hospitalization	-0.042	0.023	0.958	0.924-0.994

CI, Confidence interval ; NT-proBNP, N-terminal pro-brain natriuretic peptide.
Objective variable : Group I (Death/Transfer to an acute care hospital) and Group II (Discharge to home, Sanatorium medical facility, Special nursing home, Nursing home, Geriatric health services facility).
Explanatory variables : Locomotive, History of heart failure, Days from onset to hospitalization, total Functional independence measure score, Swallowing grade, Geriatric nutritional risk index score, NT-proBNP, Albumin/Globulin ratio.

Table 5. Receiver operating characteristic curve analysis of NT-proBNP and days from onset to hospitalization

	AUC	95%CI	p-value
NT-proBNP (pg/ml)	0.789	0.671-0.907	< 0.001
Days from onset to hospitalization	0.741	0.615-0.867	0.002

AUC, Area under the curve ; CI, Confidence interval ; NT-proBNP, N-terminal pro-brain natriuretic peptide.

Table 6. Stratum-specific likelihood ratio of NT-proBNP and days from onset to hospitalization

NT-proBNP (pg/ml)	Group I	Group II	Sensitivity	Specificity	LR (95%CI)	Posterior probability (%)
< 400	4	52	0.24	0.4	0.4 (0.2-0.9)	7
400-899	2	22	0.12	0.75	0.5 (0.1-1.5)	8
900-1499	3	4	0.18	0.95	3.8 (1.0-14.1)	43
1500-1999	3	4	0.18	0.95	3.8 (1.0-14.1)	43
2000-2499	1	4	0.06	0.95	1.3 (0.2-7.6)	20
≥ 2500	4	1	0.24	0.99	20.5 (3.5-120.8)	80
Days from onset to hospitalization						
0-14	1	21	0.06	0.76	0.2 (0.1-1.2)	5
15-24	2	23	0.12	0.74	0.4 (0.1-1.5)	8
25-34	2	20	0.12	0.77	0.5 (0.2-1.7)	9
35-44	5	9	0.29	0.9	2.8 (1.1-7.1)	36
≥ 45	7	14	0.41	0.84	2.6 (1.2-5.2)	33

LR, Likelihood ratio ; NT-proBNP, N-terminal pro-brain natriuretic peptide.

of exacerbation of chronic heart failure as the cause of poor outcomes, and there were more cardiovascular diseases (e.g., heart failure) in our sample compared with previous studies (5,8,12). A reason for this may be that our subjects had an average age of 83.1 years and were older than subjects in previous studies (mean age 71.9-76.0 years) (6-8). It has been reported that heart failure increases rapidly among those in their 80s (16). NT-proBNP is a biomarker for heart failure, and its concentration in blood increases with severity. The median NT-proBNP level in Group I was 1530 pg/ml, which was significantly higher compared with Group II (272 pg/ml). BNP is an important predictor of in-hospital mortality in acute heart failure (17). It was reported that high initial NT-proBNP levels and increases in NT-proBNP levels were useful for screening for risk for death or emergency transfer (18), which was consistent with the finding obtained in this study. In this study, a history of heart failure was not a predictive factor. The reason for this was considered that a history of heart failure could not reflect the current clinical status of the subjects. However, there was a significant difference between the two groups, so a medical history should be checked before the admission.

The median days from onset to hospitalization in Group I was 39 days, which was significantly longer than in Group II (24 days). We observed that many Group I subjects experienced complications such as cardiac dysfunction. Tokunaga *et al*. reported that for patients with stroke, a later transfer from an acute hospital to a convalescent rehabilitation ward was associated with a lower initial FIM and higher rates of patient death or transfer to an acute care hospital (19). In addition, complications have been reported as the main cause of long-term hospitalization for patients with acute stroke (20). These findings suggest that days from onset to hospitalization could reflect patients' physical status in an acute care hospital.

Total FIM score, swallowing grade, GNRI, and A/G ratio were not significantly associated from the multivariate analysis in this study. Although each of these factors was considered to be related to returning to home (21-23), our results suggested that they did not predict poor outcomes. In the convalescent rehabilitation ward, ADL improvement has been reported to be affected by complications (24). Patients with high medical risk may have difficulty improving ADL. Therefore, progress in ADL improvement was considered more important than ADL on admission. Swallowing grade which was used to assess swallowing function in this survey is one of the scales to classify the severity of dysphagia. This tool is a 10-grade scale scored from grade 1 (swallowing difficult or not possible, not indicated for swallowing training) to grade 10 (normal swallowing function) (25). Dysphagia causes aspiration pneumonia and leads to death in severe cases (26). However, in this study, the median swallowing grade for Group I was 9, and few subjects had severe dysphagia. Therefore, there were no subjects with severe pneumonia leading to poor outcomes. Malnutrition is considered a poor prognostic factor (27), and patients who show no improvement in nutritional status may have serious complications. Conversely, patients who improve with nutritional support during hospitalization were reported to show improved ADL thereafter (28). Therefore, it is thought that nutritional condition at admission alone cannot predict the risk for poor outcomes.

In this study, SSLRs were calculated to clarify the validity and criteria for predictive factors. The interpretation of SSLR has excellent discrimination ability when the likelihood ratio is ≥ 10 or ≤ 0.1, and greatly changes the posterior probability. The SSLR for NT-proBNP indicated it was more likely to lead to a poor outcome at ≥ 2500 pg/ml, whereas ≤ 400 pg/ml was unlikely to lead to a poor outcome. In addition, although the likelihood ratio was not high when NT-proBNP was 900-1499 pg/ml and 1500-1999 pg/ml (3.8), the posterior probability increased to 43%. NT-proBNP levels above 900 pg/ml may indicate there is likely to be heart failure requiring treatment (29) ; our findings showed the same tendency.

In terms of days from onset to hospitalization, the posterior probability for 35-44 days was 36% and that for ≥ 45 days or more was 33%. This was about twice the previous probability of 16%. The 16% probability shown here reflects the probability of patients with poor outcomes as identified in this study. For this reason, when the days from onset to hospitalization was more than 1 month, the number of patients with high medical risk leading to a poor outcome increased. However, both likelihood ratios and posterior probabilities were lower when days from onset to hospitalization was 24 days or less (Table 6). Thus, when days from onset to hospitalization was 24 days or less, the risk of poor outcome was lowered.

The predictive factors in this study were quantitative variables, and the results were stratified using SSLRs. Therefore, it was possible to calculate the sensitivity, specificity, likelihood ratio, and posterior probability for each layer. In addition, the criteria for predictive factors became clear in predicting poor outcomes, as these two factors could predict patients' with poor outcomes by calculating the posterior probability at admission. The posterior probability for the two predictive factors can be shown by multiplying the likelihood ratio of the predictive factors.

Group I (39 days) had significantly shorter hospitalization days in the convalescent rehabilitation ward compared to Group II (88 days). Stabilization of a patient's general condition is a prerequisite for the implementation of rehabilitation. As seen in Group I, patients with high NT-proBNP levels at admission and long duration of treatment in acute care hospitals were likely to have difficulty achieving adequate rehabilitation. It may be necessary to consider continued care in acute care hospitals or admission control in general wards for such patients. Convalescent rehabilitation wards require careful risk management because of the increasing numbers of patients with severe conditions. It may be possible to use NT-proBNP and days from onset to hospitalization as an index for predicting poor outcomes to identify patients requiring risk management from the time of admission. In particular, BNP is an indicator of cardiac rehabilitation effects (30,31), and cardiac rehabilitation may reduce BNP and NT-proBNP (31). Therefore, it may also be necessary to consider cardiac rehabilitation for patients with high NT-proBNP levels at admission.

Given global population aging, it is expected that the increased number of patients with heart failure will result in a "heart failure pandemic" (32). Japan has an aging rate of 27.7% (33), and a rapid increase in patients with heart failure has been predicted (34). The age of patients being admitted to convalescent rehabilitation wards is also increasing each year, with admission of older adults aged over 75 years reported at 63.4% (6). In addition, it is predicted that an increasing number of older adults will have complications such as cardiac dysfunction. It is therefore important to understand medical risks from the early stage after admission.

This was a retrospective study involving 104 subjects from a single institution with an average age of 83.1 years. Therefore, we did not examine whether the identified predictive factors could be applied to younger age groups. In further studies, multiple institutions may need to work together to examine predictive factors across a range of age groups to predict outcomes with greater accuracy.

CONCLUSION

NT-proBNP and days from onset to hospitalization can be considered predictive factors associated with poor outcomes among older adults receiving inpatient convalescent rehabilitation. Our findings suggested NT-proBNP of ≥ 2500 pg/ml or ≥ 35 days from onset to hospitalization could be related to poor outcomes among older adult inpatients in the convalescent rehabilitation ward. We concluded that outcomes for older adult inpatients could be predicted with data for NT-proBNP and days from onset to hospitalization from the early stage of admission in the convalescent rehabilitation setting.

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DISCLOSURE STATEMENT

The authors declare no conflicts of interest.

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