

*Original Article***Association of polypharmacy at hospital discharge with nutritional intake, muscle strength, and activities of daily living among older patients undergoing convalescent rehabilitation after stroke**

Ayaka Matsumoto, RPh,¹ Yoshihiro Yoshimura, MD, PhD,² Sayuri Shimazu, RD,³
 Fumihiko Nagano, RPT,⁴ Takahiro Bise, RPT,⁴ Yoshifumi Kido, OTR,⁴ Ai Shiraishi, DH,⁵
 Takako Sunahara, Ns⁶

¹Department of Pharmacy, Kumamoto Rehabilitation Hospital, Kumamoto, Japan

²Center for Sarcopenia and Malnutrition Research, Kumamoto Rehabilitation Hospital, Kumamoto, Japan

³Department of Nutritional Management, Kumamoto Rehabilitation Hospital, Kumamoto, Japan

⁴Department of Rehabilitation, Kumamoto Rehabilitation Hospital, Kumamoto, Japan

⁵Department of Dental Office, Kumamoto Rehabilitation Hospital, Kumamoto, Japan

⁶Department of Nursing, Kumamoto Rehabilitation Hospital, Kumamoto, Japan

ABSTRACT

Matsumoto A, Yoshimura Y, Shimazu S, Nagano F, Bise T, Kido Y, Shiraishi A, Sunahara T. Association of polypharmacy at hospital discharge with nutritional intake, muscle strength, and activities of daily living among older patients undergoing convalescent rehabilitation after stroke. *Jpn J Compr Rehabil Sci* 2022; 13: 41–48.

Objective: To investigate the association between polypharmacy at discharge and nutritional intake, muscle strength, and activities of daily living (ADL) among older patients undergoing convalescent rehabilitation after stroke.

Methods: This cross-sectional study involved hospitalized patients aged 65 or older who underwent convalescent rehabilitation after stroke. Polypharmacy was defined as the use of six or more medications. Study outcomes included energy intake, protein intake, handgrip strength (HG), and motor subscore of Functional Independence Measure (FIM-motor) at hospital discharge. Multiple linear regression analysis was used to examine the association between polypharmacy at discharge and outcomes.

Results: Of 361 eligible patients (mean [±SD] age, 78.3±7.7 years; 49.3% male), 62.9% had polypharmacy. Multiple regression analysis revealed that polypharmacy

at discharge was negatively associated with energy intake ($\beta = -0.122, p = 0.003$), protein intake ($\beta = -0.133, p = 0.013$), HG ($\beta = -0.070, p = 0.022$), and FIM-motor score ($\beta = -0.069, p = 0.031$) at discharge.

Conclusion: The impact of polypharmacy should be considered when designing nutritional management strategies for rehabilitation patients to maximize rehabilitation outcomes.

Key words: polypharmacy, rehabilitation pharmacotherapy, stroke, nutritional management

Introduction

Nutritional management is important for older adults. Malnutrition commonly occurs in older adults [1], and is associated with adverse outcomes including decline in activities of daily living (ADL), dysphagia, and death [2, 3]. Malnutrition, weight loss, sarcopenia, and decreased nutritional intake are independent factors that negatively affect functional recovery in hospitalized older patients [4–6]. Malnutrition is commonly observed in older patients undergoing rehabilitation [7], and is negatively associated with rehabilitation outcomes and physical function [8]. Energy consumption increases with the amount of physical activity among older individuals undergoing rehabilitation. Therefore, it is clinically important to improve malnutrition in this patient population through aggressive nutritional management to maximize favorable outcomes.

Polypharmacy is a major cause of frailty [9]. The number of prescribed drugs is often high among older individuals due to multimorbidity [10]. Polypharmacy is not only a problem of a high number of medications, but also contributes to an increased risk for adverse

Correspondence: Yoshihiro Yoshimura, MD, PhD
 Center for Sarcopenia and Malnutrition Research,
 Kumamoto Rehabilitation Hospital, 760 Magate, Kikuyomachi,
 Kikuchi-gun, Kumamoto 869–1106, Japan.
 E-mail: hanley.belfus@gmail.com

Accepted: June 27, 2022.

Conflicts of Interest: We declare no conflict of interest.

drug events leading to poor outcomes, such as decline in physical and cognitive function [11]. As such, polypharmacy may be associated with the development of malnutrition [12], which may also contribute to the risk for adverse drug events owing to altered pharmacokinetics.

However, there is a lack of evidence regarding the impact of polypharmacy on rehabilitation. Polypharmacy is prevalent, especially among hospitalized patients undergoing rehabilitation [13]. Therefore, clarifying the relationship between polypharmacy and nutritional intake, muscle strength, and ADL may facilitate the mitigation of the negative effects of polypharmacy to improve nutritional status and maximize outcomes among older patients undergoing rehabilitation.

Accordingly, we investigated the association between polypharmacy at hospital discharge and nutritional intake, muscle strength, and ADL among older patients undergoing rehabilitation after stroke.

Subjects and methods

1. Subjects

This cross-sectional study included 849 post-stroke patients admitted to a post-acute care hospital with convalescent rehabilitation wards containing 135 beds between January 2015 and December 2020. Patients with missing data, altered consciousness (indicated by a Japan Coma Scale score of 3 [14]), pacemaker implantation that could interfere with bioelectrical impedance analysis (BIA), those transferred to other hospitals or wards during rehabilitation, and those under 65 years of age were excluded.

2. Methods

Basic information, including age, sex, stroke type, stroke history, length of stay (LOS) in convalescent rehabilitation wards, and nutritional risk assessed according to the Geriatric Nutritional Risk Index (GNRI) [15] was collected by reviewing medical records. Premorbid ADL according to the modified Rankin Scale (mRS) [16] and assessment of comorbidity severity according to the Charlson Comorbidity Index (CCI) [17] were evaluated by medical doctors. Swallowing status was evaluated using the Food Intake Level Scale (FILS) [18] by a nurse. Within 72 h of admission, BIA using a bioimpedance device (S10, InBody, Tokyo, Japan) for skeletal muscle mass, handgrip strength (HG), and Functional Independence Measure (FIM) scores [19] for physical (FIM-motor) and cognitive functions (FIM-cognitive) were measured by a physical therapist or occupational therapist. The HG of the non-dominant hand (or, in the case of hemiparesis, the non-paralyzed hand) was measured using a Smedley hand dynamometer (TTM, Tokyo, Japan), with the greatest of three measurements recorded. Sarcopenia was diagnosed when both skeletal muscle mass index

(SMI) and HG fell below cut-off values specific to older Asian adults based on the Asian Working Group for Sarcopenia 2019 (AWGS 2019) criteria [2]. Energy and protein intake were estimated by nurses and dietitians, who visually determined the ratio of actual intake to the amount provided to the patients. Within 72 h after hospitalization and before discharge, the intake of three meals each for breakfast, lunch, and dinner (nine meals in total) were recorded, and the average of each value divided by three was defined as daily intake [20]. Nutritional intake was calculated by dividing each intake value by actual body weight at admission and discharge. The total rehabilitation therapy units received during hospitalization (units per day, 1 unit = 20 min of therapy) were calculated by reviewing patient medical records.

3. Drug information

Medication information was collected through medical chart review. Information regarding medications on admission was routinely provided by a pharmacist. Information at discharge was obtained for those prescribed continuously from two weeks before discharge until the day of discharge. Among all prescriptions, only regularly prescribed oral medications were included in the study. More specifically, medications for transient acute illnesses (e.g., antibiotics for infections, such as urinary tract infections and/or pneumonia), patch medications, eye drops, nasal drops, drugs for use as needed, and over-the-counter medications were excluded from the analysis. In the present study, polypharmacy was defined as the use of six or more medications based on the increased risk for adverse drug events reported among hospitalized older adults treated with six or more medications [21]. Potentially inappropriate medications (PIMs) were defined based on the 2019 Beers criteria of the American Geriatric Society [22] as potentially inappropriate in most older adults. Medications at admission tended to be influenced by treatment for the primary disease and complications in acute care hospitals, and medications at discharge tended to be influenced by convalescent rehabilitation. In this study, the association between polypharmacy (defined as medications taken at discharge) and outcomes was investigated to determine the impact of pharmacotherapy during convalescent rehabilitation.

4. Outcomes

The primary outcome was energy intake at the time of discharge. Secondary outcomes included nutritional assessment according to protein intake, GNRI, and HG at discharge, and ADL assessed according to the FIM-motor score at discharge.

5. Statistical analysis

For parametric data, results are expressed as mean (standard deviation [SD]), while median and 25th to

75th percentiles (interquartile range [IQR]) describe nonparametric data, and number and percentage (%) were used to describe categorical data. Differences with $p < 0.05$ were considered to be statistically significant. All analyses were performed using SPSS version 21 (IBM Corporation, Armonk, NY, USA).

Patients were classified into polypharmacy and non-polypharmacy groups based on the number of medications at discharge, and univariate analysis was performed between the two groups for all items of basic patient information at admission. Outcomes at admission and discharge were compared for each group, and univariate analysis of discharge outcomes was performed between the two groups. Comparisons between groups were performed using the t -test, Mann-Whitney U test, chi-squared test, and Wilcoxon signed-rank sum test, depending on the type and correspondence of variables.

Multiple linear regression analysis was performed to determine whether polypharmacy at discharge was independently associated with energy intake, protein intake, GNRI, HG, and FIM-motor scores at discharge. Covariates selected to adjust for bias included age range, sex (male), stroke type, LOS, CCI, total rehabilitation therapy (units/day), and FIM-motor and FIM-cognitive, FILS, GNRI, HG, SMI, and energy intake on admission. Multicollinearity was assessed using the variance inflation factor, with values ranging from 1 to 10 indicating the absence of multicollinearity.

6. Ethics

This study was conducted in accordance with the Declaration of Helsinki and Ethical Guidelines for Medical and Health Research Involving Human Subjects. This study was approved by the institutional review board of the hospital (approval number: 175-2109152). Participants were able to withdraw from the

study at any time through an opt-out procedure. Due to constraints imposed by the retrospective study design, informed written consent could not be obtained from all participants.

Results

A total of 849 stroke patients were admitted during the study period. Of these patients, those with altered consciousness ($n = 35$), a pacemaker ($n = 5$), those transferred to other hospitals or wards during rehabilitation ($n = 16$), those under 65 years of age ($n = 138$), and those with missing data ($n = 294$) were excluded. After applying the exclusion criteria, 361 patients were ultimately included in the analysis (Figure 1).

The baseline characteristics of the enrolled participants are summarized in Table 1. The included patients had a mean (SD) age of 78.3 (7.7) years, and 49.3% were male.

The median GNRI score was 95 (IQR 88–103), suggesting that many patients were at a nutritional risk. The median energy and protein intake were 27.7 kcal/kg/day (IQR 23.3–33.2 kcal/kg/day) and 1.04 g/kg/day (IQR 0.89–1.21 g/kg/day), respectively. The median HG was 16.8 (IQR 9.2–23.5) kg, and the median FIM-motor score was 42 (IQR 18–64), suggesting that a large number of patients exhibited low muscle strength and were physically dependent at baseline. The median number of medications taken at admission and discharge was 5 (IQR 3–7) and 7 (IQR 4–9), respectively; the number of prescribed drugs increased during hospitalization in convalescent rehabilitation wards. When the patients were divided into two groups (i.e., polypharmacy and non-polypharmacy), 227 (62.9%) had polypharmacy according to the total number of medications at

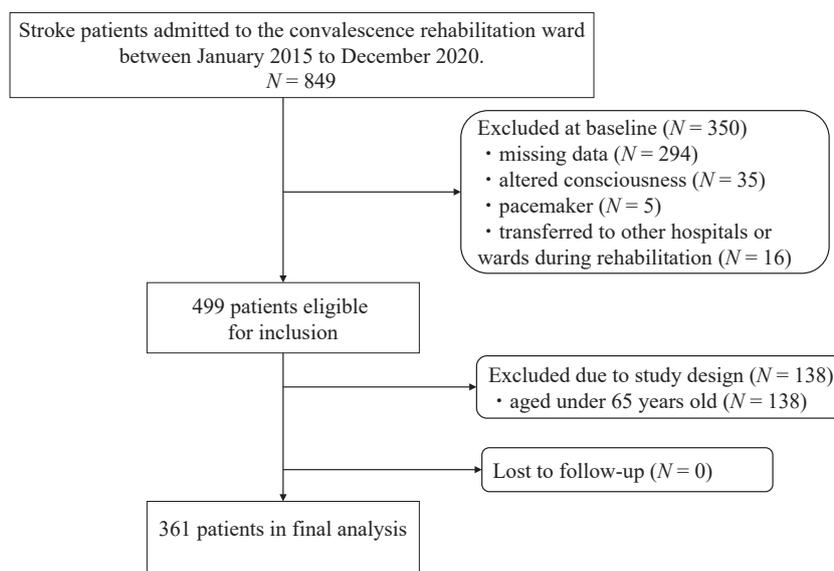


Figure 1. Flowchart of participant screening, inclusion criteria, and follow-up.

Table 1. Baseline characteristics of participants and between-group comparison of patients with or without polypharmacy.

	Total (N = 361)	Polypharmacy (+) (N = 227)	Polypharmacy (-) (N = 134)	p-Value
Age, y, mean (SD)	78.3 (7.7)	78.5 (7.5)	78.0 (8.1)	0.486 ¹⁾
Sex, male, n (%)	178 (49.3)	114 (50.2)	64 (47.8)	0.652 ³⁾
Stroke type, n (%)				
Cerebral infarction	254 (70.3)	169 (74.4)	85 (63.4)	0.027 ³⁾
Cerebral hemorrhage	89 (24.6)	49 (21.6)	40 (29.9)	0.078 ³⁾
Subarachnoid hemorrhage	18 (4.9)	9 (4.0)	9 (6.7)	0.246 ³⁾
Stroke history, n (%)	98 (27.1)	70 (30.8)	28 (20.9)	0.040 ³⁾
Premorbid mRS, median [IQR]	0 [0-2]	1 [0-2]	0 [0-1]	0.010 ²⁾
FIM, score, median [IQR]				
Total	63 [33-89]	58 [31-85]	79 [36-93]	0.007 ²⁾
Motor	42 [18-64]	39 [18-60]	54 [19-69]	0.020 ²⁾
Cognitive	20 [13-27]	18 [12-26]	23 [14-28]	0.003 ²⁾
FILS, median [IQR]	7 [7-10]	7 [7-10]	8 [7-10]	0.222 ²⁾
CCI, median [IQR]	3 [1-4]	3 [2-4]	3 [1-3]	0.010 ²⁾
Nutritional status				
GNRI, median [IQR]	95 [88-103]	94 [87-103]	96 [88-104]	0.326 ²⁾
BMI, kg/m ² , median [IQR]	21.9 [19.8-24.4]	21.9 [20.0-24.6]	21.9 [19.4-24.0]	0.256 ²⁾
Energy intake, kcal/kg/day, median [IQR]	27.7 [23.3-33.2]	26.9 [23.2-32.3]	29.4 [23.6-36.0]	0.043 ²⁾
Protein intake, g/kg/day, median [IQR]	1.04 [0.89-1.21]	1.03 [0.89-1.19]	1.07 [0.90-1.29]	0.173 ²⁾
Muscle-related variables				
HG, kg, median [IQR]	16.8 [9.2-23.5]	16.7 [9.2-23]	17.2 [10.0-24.8]	0.527 ²⁾
SMI, kg/m ² , median [IQR]	6.06 [5.03-7]	6.15 [5.06-6.99]	5.99 [4.92-7.07]	0.512 ²⁾
Sarcopenia, n (%)	196 (54.3)	127 (55.9)	69 (51.5)	0.412 ³⁾
Length of stay, days, median [IQR]	91 [56-139]	98 [59-142]	87 [51-134]	0.070 ²⁾
Rehabilitation ^a , units/day, median [IQR]	8.2 [7.6-8.6]	8.2 [7.4-8.5]	8.3 [7.8-8.6]	0.015 ²⁾
Number of total medications on admission, median [IQR]	5 [3-7]	6 [5-8]	3 [2-5]	<0.001 ²⁾
Number of total medications at discharge, median [IQR]	7 [4-9]	8 [7-9]	4 [3-5]	—
Number of any PIMs on admission, median [IQR]	1 [0-1]	1 [1-1]	0 [0-1]	<0.001 ²⁾
Number of any PIMs at discharge, median [IQR]	1 [0-2]	1 [1-2]	0 [0-1]	<0.001 ²⁾

¹⁾t-test; ²⁾Mann-Whitney U test; ³⁾chi-square test.

^a Rehabilitation therapy (including physical, occupational, and speech and swallowing therapy) performed during hospitalization (1 unit = 20 min).

BMI, body mass index; CCI, Charlson's Comorbidity Index; FILS, Food Intake Level Scale; FIM, Functional Independence Measure; GNRI, Geriatric Nutritional Risk Index; HG, handgrip strength; mRS, modified Rankin Scale; PIMs, potentially inappropriate medications; SMI, skeletal muscle mass index.

Table 2. Univariate analysis of outcomes at admission and discharge for patients with and without polypharmacy, and univariate analysis of discharge outcomes for patients with or without polypharmacy.

	Polypharmacy (+) (N = 227)			Polypharmacy (-) (N = 134)			Comparison of outcomes at discharge between the two groups	
	At admission	At discharge	p-Value	At admission	At discharge	p-Value	p-Value	
Energy intake, kcal/kg/day	26.9 [23.2-32.3]	28.3 [25.1-32.6]	<0.001 ¹⁾	29.4 [23.6-36.0]	30.5 [26.2-35.6]	<0.001 ¹⁾	0.005 ²⁾	
Protein intake, g/kg/day	1.03 [0.89-1.19]	1.10 [0.94-1.28]	<0.001 ¹⁾	1.07 [0.90-1.29]	1.18 [0.99-1.36]	<0.001 ¹⁾	0.068 ²⁾	
GNRI	94 [87-103]	97 [90-104]	<0.001 ¹⁾	96 [88-104]	98 [91-104]	0.003 ¹⁾	0.728 ²⁾	
HG, kg	16.7 [8.9-23.3]	18.5 [11.6-25.5]	<0.001 ¹⁾	17.2 [10.0-24.8]	20 [13.8-28.5]	<0.001 ¹⁾	0.103 ²⁾	
FIM-motor, score	39 [18-60]	74 [42-86]	<0.001 ¹⁾	54 [19-69]	82 [66-88]	<0.001 ¹⁾	<0.001 ²⁾	

¹⁾Wilcoxon signed-rank sum test, ²⁾Mann-Whitney U test. FIM, Functional Independence Measure; HG, handgrip strength; GNRI, Geriatric Nutritional Risk Index. Data are expressed in median [IQR].

discharge. A between-group comparison revealed that cerebral infarction, stroke history, mRS, and CCI were significantly higher, whereas FIM-total, FIM-motor, FIM-cognitive, energy intake, and rehabilitation units were significantly lower in patients with polypharmacy than in those without at baseline, respectively. The number of PIMs was also significantly higher in patients with polypharmacy.

Results of the univariate analysis of the outcomes in the polypharmacy and non-polypharmacy groups at discharge are summarized in Table 2. Energy intake, protein intake, GNRI, HG, and FIM-motor scores increased significantly from admission to discharge in both groups. Univariate analysis of outcomes at discharge revealed that patients with polypharmacy exhibited significantly lower energy intake (28.3 [IQR 25.1-32.6] vs. 30.5 [IQR 26.2-35.6]; $p = 0.005$) and FIM-motor scores (74 [IQR 42-86] vs. 82 [IQR 66-88]; $p < 0.001$) than those without polypharmacy. Protein intake, GNRI, and HG were not significantly different between the two groups.

The results of multivariate analyses of patient outcomes associated with polypharmacy are summarized in Table 3. Polypharmacy at discharge was independently associated with energy intake ($\beta = -0.122, p = 0.003$), protein intake ($\beta = -0.133, p = 0.013$), HG ($\beta = -0.070, p = 0.022$), and FIM-motor score ($\beta = -0.069, p = 0.031$), but not GNRI ($\beta = 0.011, p = 0.746$).

Discussion

This study examined the association between polypharmacy and nutritional intake, muscle strength, and ADL in older patients undergoing convalescent rehabilitation after stroke. As a result, we report two new findings: polypharmacy at discharge was negatively associated with nutritional intake; and polypharmacy at discharge was negatively associated with muscle strength and ADL.

Polypharmacy at discharge was negatively associated with nutritional intake. It was not associated with GNRI but was independently associated with both energy and protein intake. The observed association between polypharmacy and nutritional intake may be influenced by the direct effects of drugs, such as gastrointestinal symptoms and anorexia, owing to the increased risk for adverse drug events with polypharmacy, as well as the patient background that may cause polypharmacy. Factors that may contribute to polypharmacy include multimorbidity and conditions that increase the number of medications required during hospitalization for treatment. In the multivariate analysis, CCI was used as an adjustment factor, and the results demonstrated that polypharmacy at discharge was negatively associated with nutritional intake, independent of CCI. It is likely that this effect was not only due to comorbidities but also, at least in part, to polypharmacy itself. Previous studies

Table 3. Multivariate analyses for patient outcomes of polypharmacy.

	Energy intake at discharge		Protein intake at discharge		GNRI at discharge		HG at discharge		FIM-motor at discharge	
	β	p-Value	β	p-Value	β	p-Value	β	p-Value	β	p-Value
Age	-0.004	0.929	-0.094	0.145	-0.077	0.046	-0.070	0.045	-0.033	0.362
Sex (male)	0.063	0.242	0.068	0.337	-0.152	0.001	0.092	0.022	-0.083	0.047
Stroke type										
Cerebral infarction	0.106	0.236	0.073	0.510	-0.098	0.169	0.032	0.623	0.077	0.267
Cerebral hemorrhage	0.147	0.095	0.085	0.441	-0.089	0.208	0.066	0.314	0.096	0.161
Subarachnoid hemorrhage	(reference)	—	(reference)	—	(reference)	—	(reference)	—	(reference)	—
LOS	0.119	0.029	0.143	0.048	0.075	0.088	0.079	0.050	0.154	<0.001
FIM-motor on admission	0.105	0.185	0.158	0.124	0.027	0.675	-0.076	0.197	0.535	<0.001
FIM-cognitive on admission	-0.035	0.569	-0.100	0.224	-0.011	0.828	0.127	0.006	0.181	<0.001
CCI	-0.076	0.087	0.013	0.817	0.020	0.580	0.024	0.461	-0.042	0.225
Daily units for PT, OT, ST	0.008	0.848	0.050	0.394	-0.008	0.824	0.015	0.637	0.026	0.428
FILS on admission	0.176	0.003	0.171	0.043	0.033	0.492	-0.035	0.420	0.084	0.067
GNRI on admission	-0.513	<0.001	-0.431	<0.001	0.701	<0.001	0.079	0.048	0.033	0.425
HG on admission	0.131	0.057	0.028	0.740	0.013	0.815	0.632	<0.001	0.163	0.002
SMI on admission	-0.375	<0.001	-0.290	<0.001	0.183	<0.001	0.141	0.002	0.049	0.296
Energy intake on admission	0.082	0.057	—	—	-0.028	0.431	-0.010	0.758	-0.021	0.518
Protein intake on admission	—	—	0.312	<0.001	—	—	—	—	—	—
Polypharmacy	-0.122	0.003	-0.133	0.013	0.011	0.746	-0.070	0.022	-0.069	0.031

CCI, Charlson's Comorbidity Index; FILS, Food Intake Level Scale; FIM, Functional Independence Measure; GNRI, Geriatric Nutritional Risk Index; HG, handgrip strength; LOS, length of stay; OT, occupational therapy; PT, physical therapy; SMI, skeletal muscle mass index; ST, swallowing therapy.

have reported that an increased number of PIMs [23] and anticholinergic load [24] are associated with nutritional status among older patients undergoing convalescent rehabilitation. In the present study, the number of PIMs was significantly higher in the polypharmacy group than that in the non-polypharmacy group. We speculate that the probability of using PIMs and anticholinergic drugs is higher in those receiving polypharmacy. No association was found with GNRI. Nutritional risk may have improved due to rehabilitation and comprehensive nutritional management by a multidisciplinary team. The GNRI is calculated from serum albumin level, actual weight, and ideal weight; however, many post-stroke patients experience chronic inflammation, which affects serum albumin levels. It is possible that the results of this study may have been affected by the current situation. Therefore, in the future, it will be necessary to examine the relationship between polypharmacy and nutritional status using an assessment tool that can evaluate nutritional status more accurately. Malnutrition and sarcopenia are commonly found among older patients undergoing convalescent rehabilitation. Due to the increased energy expenditure from rehabilitation and exercise therapy, aggressive nutritional management is needed. Moreover, improving nutritional status requires multifaceted interventions, such as nutritional management and training, during which the impact of polypharmacy should also be considered.

Polypharmacy at discharge was negatively associated with muscle strength and ADL. A previous study reported that polypharmacy at admission was negatively associated with physical function improvement in older patients undergoing rehabilitation after a stroke [9]. However, the assessment of polypharmacy according to prescriptions on admission to rehabilitation hospitals is strongly affected by the acute care hospital attending physicians' prescriptions for treatment and post-onset complications in the acute care hospital, and the possibility that prescriptions may change during convalescent rehabilitation has not been considered. The present study examined the impact of the number of medications taken at discharge on patient outcomes. The findings suggest that polypharmacy, as assessed by the number of drugs, including changes in prescription during convalescent rehabilitation, affects outcomes. Therefore, to maximize favorable rehabilitation outcomes, it is necessary to consider the impact of polypharmacy.

Medication management or pharmacotherapy is important in older patients undergoing rehabilitation. The LOS in the recovery phase was longer than that in the acute phase, ranging from 1 to 6 months, making it easier to observe changes after drug adjustments and providing an opportunity to review prescriptions. One factor that may contribute to polypharmacy in convalescent rehabilitation wards is that medications prescribed for acute treatment continue to be prescribed thereafter [25, 26]. Therefore, a review of prescriptions when patients

transition from acute care to rehabilitation is required. Post-stroke patients experience various complications, such as spasticity, pain, dysuria, cognitive dysfunction, insomnia, and depression after stroke onset. In the process of functional recovery, it is also necessary to examine whether symptomatic prescriptions for complications are administered without reconsideration [27]. While rehabilitation focuses on training for functional recovery, pharmacotherapy tends to focus on disease treatment [28]. Without considering rehabilitation and pharmacotherapy together, the negative impact of drugs on outcomes can be overlooked. The results of this study suggest that the number of medications increases during convalescent rehabilitation and that polypharmacy at discharge is associated with nutrition-related outcomes. Therefore, measures addressing the negative effects of polypharmacy in convalescent rehabilitation wards may promote the effectiveness of nutritional management in maximizing rehabilitation outcomes.

The present study had some limitations, the first of which was its cross-sectional, single-center design, which may limit its generalizability to other geographical regions. Second, the effects of individual medications were not considered. Owing to the nature of the study design, we were unable to examine medications that lead to polypharmacy or specific medications that are more likely to be introduced in patients undergoing rehabilitation. Some drugs have side effects associated with undernutrition, whereas others increase motivation and appetite. These drugs may be combined in terms of the total number of drugs used. Therefore, further research is needed to determine how specific drugs affect rehabilitation outcomes.

Conclusion

The study suggests that polypharmacy is negatively associated with nutritional intake, muscle strength, and ADL in older patients undergoing convalescent rehabilitation after stroke. To maximize favorable rehabilitation outcomes, it is necessary to consider the impact of polypharmacy along with nutritional management.

Acknowledgments

We would like to express our deepest gratitude to the Nutrition Support Team of Kumamoto Rehabilitation Hospital for their support of this study.

References

1. Yoshimura Y, Wakabayashi H, Bise T, Tanoue M. Prevalence of sarcopenia and its association with activities of daily living and dysphagia in convalescent rehabilitation ward inpatients. *Clin Nutr* 2018; 37(6 Pt A): 2022–8.
2. Chen LK, Woo J, Assantachai P, Auyeung TW, Chou MY, Iijima K, et al. Asian Working Group for Sarcopenia:

- 2019 Consensus Update on Sarcopenia Diagnosis and Treatment. *J Am Med Dir Assoc* 2020; 21(3): 300–7.e2.
3. Yoshimura Y, Wakabayashi H, Bise T, Nagano F, Shimazu S, Shiraishi A, et al. Sarcopenia is associated with worse recovery of physical function and dysphagia and a lower rate of home discharge in Japanese hospitalized adults undergoing convalescent rehabilitation. *Nutrition* 2019; 61: 111–8.
 4. Volkert D, Beck AM, Cederholm T, Cruz-Jentoft A, Goisser S, Hooper L, et al. ESPEN guideline on clinical nutrition and hydration in geriatrics. *Clin Nutr* 2019; 38(1): 10–47.
 5. Wojziszke J, van Wijngaarden J, van den Berg C, Cetinyurek-Yavuz A, Diekmann R, Luiking Y, et al. Nutritional status and functionality in geriatric rehabilitation patients: a systematic review and meta-analysis. *Eur Geriatr Med* 2020; 11(2): 195–207.
 6. Yoshimura Y, Wakabayashi H, Nagano F, Bise T, Shimazu S, Kudo M, et al. Sarcopenic obesity is associated with activities of daily living and home discharge in post-acute rehabilitation. *J Am Med Dir Assoc* 2020; 21(10): 1475–80.
 7. Yoshimura Y. Rehabilitation nutrition care in convalescent rehabilitation. *J Jpn Soc Parenteral Enteral Nutr* 2016; 31(4): 959–66.
 8. Marshall S, Bauer J, Isenring E. The consequences of malnutrition following discharge from rehabilitation to the community: a systematic review of current evidence in older adults. *J Hum Nutr Diet* 2014; 27(2): 133–41.
 9. Kose E, Toyoshima M, Okazoe S, Oka R, Shiratsuchi Y, Hayashi H. The relationship between polypharmacy and recovery of activities of daily living among convalescent stroke patients: a propensity score-matched analysis. *Eur Geriatr Med* 2017; 8(3): 250–5.
 10. Calderón-Larrañaga A, Poblador-Plou B, González-Rubio F, Gimeno-Feliu LA, Abad-Díez JM, Prados-Torres A. Multimorbidity, polypharmacy, referrals, and adverse drug events: are we doing things well? *Br J Gen Pract* 2012; 62(605): e821–6.
 11. Fried TR, O’Leary J, Towle V, Goldstein MK, Trentalange M, Martin DK. Health outcomes associated with polypharmacy in community-dwelling older adults: a systematic review. *J Am Geriatr Soc* 2014; 62(12): 2261–72.
 12. Jyrkkä J, Enlund H, Lavikainen P, Sulkava R, Hartikainen S. Association of polypharmacy with nutritional status, functional ability and cognitive capacity over a three-year period in an elderly population. *Pharmacoepidemiol Drug Saf* 2011; 20(5): 514–22.
 13. Nakamura J, Kitagaki K, Ueda Y, Nishio E, Shibatsuji T, Uchihashi Y, et al. Impact of polypharmacy on oral health status in elderly patients admitted to the recovery and rehabilitation ward. *Geriatr Gerontol Int* 2021; 21(1): 66–70.
 14. Shigematsu K, Nakano H, Watanabe Y. The eye response test alone is sufficient to predict stroke outcome—reintroduction of Japan Coma Scale: a cohort study. *BMJ Open* 2013; 3(4): e002736.
 15. Bouillanne O, Morineau G, Dupont C, Coulombel I, Vincent JP, Nicolis I, et al. Geriatric Nutritional Risk Index: a new index for evaluating at-risk elderly medical patients. *Am J Clin Nutr* 2005; 82(4): 777–83.
 16. Banks JL, Marotta CA. Outcomes validity and reliability of the modified Rankin scale: implications for stroke clinical trials: a literature review and synthesis. *Stroke* 2007; 38(3): 1091–6.
 17. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987; 40(5): 373–83.
 18. Kunieda K, Ohno T, Fujishima I, Hojo K, Morita T. Reliability and validity of a tool to measure the severity of dysphagia: the Food Intake LEVEL Scale. *J Pain Symptom Manage* 2013; 46(2): 201–6.
 19. Ottenbacher KJ, Hsu Y, Granger CV, Fiedler RC. The reliability of the functional independence measure: a quantitative review. *Arch Phys Med Rehabil* 1996; 77(12): 1226–32.
 20. Sawaya AL, Tucker K, Tsay R, Willett W, Saltzman E, Dallal GE, et al. Evaluation of four methods for determining energy intake in young and older women: comparison with doubly labeled water measurements of total energy expenditure. *Am J Clin Nutr* 1996; 63(4): 491–9.
 21. Kojima T, Akishita M, Kameyama Y, Yamaguchi K, Yamamoto H, Eto M, et al. High risk of adverse drug reactions in elderly patients taking six or more drugs: analysis of inpatient database. *Geriatr Gerontol Int* 2012; 12(4): 761–2.
 22. The 2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. *J Am Geriatr Soc* 2019; 67(4): 674–94.
 23. Kose E, Hirai T, Seki T. Change in number of potentially inappropriate medications impacts on the nutritional status in a convalescent rehabilitation setting. *Geriatr Gerontol Int* 2019; 19(1): 44–50.
 24. Kose E, Hirai T, Seki T, Yasuno N. Anticholinergic load and nutritional status in older individuals. *J Nutr Health Aging* 2020; 24(1): 20–7.
 25. Gamble JM, Hall JJ, Marrie TJ, Sadowski CA, Majumdar SR, Eurich DT. Medication transitions and polypharmacy in older adults following acute care. *Ther Clin Risk Manag* 2014; 10: 189–96.
 26. Mixon AS, Neal E, Bell S, Powers JS, Kripalani S. Care transitions: a leverage point for safe and effective medication use in older adults—a mini-review. *Gerontology* 2015; 61(1): 32–40.
 27. Clarke CL, Witham MD. The effects of medication on activity and rehabilitation of older people – opportunities and risks. *Rehabil Process Outcome* 2017; 6: 1179572717711433.
 28. Yoshimura Y, Matsumoto A, Momosaki R. Pharmacotherapy and the role of pharmacists in rehabilitation medicine. *Prog Rehabil Med* 7; 20220025.