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Original Article

Association Between the Number of Medications and Degree of Ambulatory Independence in Older Patients with Post-Hip Fracture Surgery: A Single-Center Retrospective Cohort Study

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ABSTRACT

Background/Purpose: Polypharmacy, defined as the use of five or more oral medications, has been reported to be associated with rehabilitation outcomes. However, the association between polypharmacy and postoperative rehabilitation outcomes has not been thoroughly investigated. Here, we aimed to determine whether polypharmacy or the number of medications on admission was associated with the degree of ambulatory independence at the time of discharge in patients who underwent hip fracture (HF) surgery.

Methods: This single-center retrospective observational study included patients admitted to an acute care hospital following surgery for HF. The outcome measure was the degree of ambulatory independence at discharge, as assessed using the Functional Ambulation Category (FAC). The outcome in this study was defined as achieving a FAC score of ≥ 3, corresponding to ambulatory independence at the supervision level or higher. Logistic regression analysis was conducted to investigate the association between achieving FAC ≥ 3 and medication status.

Results: We evaluated 273 patients (215 women; median age = 87 years). The median number of medications was eight; 70.0% of patients met the criteria for polypharmacy. Using logistic regression analysis, the number of medications (odds ratio [OR] = 0.912; $p < 0.01$) was a significant predictor of FAC ≥ 3. The cutoff value for the number of medications was 7.5.

Conclusion: The number of medications used, rather than the presence of polypharmacy, was associated with degree of ambulatory independence at discharge in aged patients with HF. Monitoring medication counts can aid in predicting rehabilitation outcomes.

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1. INTRODUCTION

Polypharmacy, defined as the use of five or more oral medications,[1–3] increases with age.[4] It has garnered attention from healthcare professionals since Kojima et al. reported its association with a higher frequency of adverse drug events and increased risk of falls.[5,6] Subsequent research has established an association between polypharmacy and various health issues. Regarding musculoskeletal disorders, multivariate analyses have revealed an increased risk of fall-related fractures in older adults;[7] meta-analyses have strongly suggested an association with sarcopenia.[8] Similarly, in internal medicine, polypharmacy has been identified as an independent predictor of survival in patients with cirrhosis,[9] cardiac pacemaker implantation,[10] and non-dialysis renal failure.[11] Recently, Togashi et al. have elucidated the association between dysphagia and polypharmacy in hospitalized older patients using multivariate analysis and highlighted the need for appropriate medication prescriptions.[12] In Japan, the prevalence of polypharmacy has decreased since 2014,[13] and reduction policies were implemented in 2016.[14] Despite these measures, approximately half of the population aged 85 years and older still experience polypharmacy.[2]

Recently, the association between polypharmacy and rehabilitation outcomes has been reported. Polypharmacy has been associated with continence control,[15] activities of daily living (ADL), energy intake, and swallowing function in stroke patients.[16–18] Additionally, it is associated with a high risk of hip fracture (HF), a common traumatic disease in rehabilitation medicine, and high readmission rates.[19,20] However, the association between polypharmacy and postoperative rehabilitation outcomes has not yet been thoroughly investigated. Maki et al. reported an association between the number of medications administered during hospitalization and the Barthel Index efficiency at discharge.[21] Nevertheless, its specific impact on ADL, particularly its association with degree of ambulatory independence, remains unclear.

Hence, this study aimed to investigate the association between medication status at admission and degree of ambulatory independence at the time of discharge in patients with HF after surgery.

2. METHODS

2.1. Study Design and Participants

This was a single-center retrospective cohort study including patients admitted to an acute care hospital with 320 beds. This study included 332 patients with HF who underwent surgery between April 2017 and August 2023. The exclusion criteria were the inability to ambulate before the injury, age < 65 years, comorbidities of other acute illnesses (e.g., head trauma), development of other acute illnesses (e.g., respiratory infections) during hospitalization, complications of other fractures, injuries sustained during hospitalization, discharge due to death, choice of conservative treatment, and exacerbation of comorbidities during hospitalization. The goal of postoperative physical therapy was to initiate gait training on the second postoperative day for osteosynthesis and on the fourth postoperative day for bipolar hip arthroplasty (BHA). Other treatment programs included general joint range-of-motion exercises, muscle strengthening exercises, and cardiopulmonary endurance exercises, which were implemented according to pain in the patients and physical recovery status.

2.2. Data Collection

The baseline characteristics of the participants at admission and degree of ambulatory independence at discharge were retrospectively collected from electronic medical records. The following general information was collected before injury: age, sex, height, body weight, and body mass index (BMI). Additionally, serum albumin levels and estimated glomerular filtration rate (eGFR) were obtained from biochemical test results at admission. The Geriatric Nutritional Risk Index (GNRI) was calculated as previously described.[22] Furthermore, although we investigated whether the participants used walking aids (e.g., canes), we were unable to identify the specific type of walking aid or the presence of a caregiver.

Additionally, information on fracture types, surgical methods, number of days from admission to surgery (time to surgery, TTS), comorbidities, and number of medications administered at admission was collected. Fractures were classified into femoral neck and femoral trochanteric fractures without investigating the clinical severity of each type. Surgical methods were categorized as osteosynthesis or BHA. Data on the operative time, blood loss, anesthesia time, and types of implants used were not investigated. Comorbidities included type 2 diabetes mellitus (T2DM), hypertension (HT), chronic heart failure (CHF), chronic kidney disease (CKD), and dialysis. These baseline characteristics were selected based on multiple previous studies that examined rehabilitation-related outcomes in patients with hip fractures.[23–26]

Medications were counted based on the number of drugs brought at admission. Polypharmacy was defined as taking six or more drugs. Eye drops, nasal drops, inhalers, topical drugs, and injection drugs were not included in the count. Medications administered irregularly to temporarily improve symptoms, such as antipyretic and analgesic drugs,

were excluded. Finally, degree of ambulatory independence at discharge was assessed using the Functional Ambulation Category (FAC), which is a widely used clinical evaluation index of ambulatory independence in hip fracture studies.[27–29] The FAC rates ambulatory independence on a 6-level scale from 0–5, with higher numbers indicating greater independence. Previous studies including stroke patients aged 60–70 years defined independent ambulation as FAC ≥ 4.[30–32] However, over 70% of patients with HF in Japan are older than 80 years.[33] Furthermore, the participants in this study were postoperative patients scheduled for transfer to other facilities for continued rehabilitation. Considering their advanced age and expected short hospital stay, achieving independent ambulation (FAC ≥ 4) during acute hospitalization was challenging. Therefore, the outcome in this study was defined as achieving a FAC score of ≥ 3, corresponding to ambulatory independence at the supervision level or higher.

2.3. Statistical Analyses

First, the participants were divided into two groups for analysis: those with FACs ≥ 3 at discharge (FAC ≥ 3 group) and those with FACs ≤ 2 (FAC ≤ 2 group). Subsequently, the baseline characteristics were compared between these groups. Chi-squared tests of independence were performed for categorical variables. If multiple cells had expected values of < 5, Fisher's exact test was performed. Considering numerical variables, Shapiro–Wilk tests were first conducted to determine if the variables were normally distributed. If variables were not normally distributed, the Wilcoxon rank-sum test was used. If the variables were normally distributed, Levene's test was performed to check for homoscedasticity. If Levene's test indicated unequal variances, Welch's two-sample *t*-test with an unequal variance correction was used. Otherwise, the standard two-sample t-test was used. If the variances were not equally distributed and data were not normally distributed, the Mann–Whitney U test was used.

Next, multiple logistic regression analysis was performed using the Akaike Information Criterion stepwise method, with FAC ≥ 3 as the dependent variable and baseline characteristics as the independent variables, to determine the influence of each variable. Given the potential multicollinearity between the number of medications and polypharmacy, two analytical models were created: one including only the number of medications (Model 1) and the other including only polypharmacy (Model 2). The results were determined using a likelihood ratio test, and the OR and 95% confidence intervals (95% CI) for each selected variable were calculated. Multicollinearity between the dependent variable and each selected variable was evaluated using the variance inflation factor (VIF), with a VIF ≥ 5 indicating multicollinearity. The goodness of fit for the models was assessed using the Hosmer–Lemeshow test.

Finally, Receiver Operating Characteristic (ROC) curve analysis was performed for continuous variables identified by multiple logistic regression analysis. The area under the curve (AUC) was calculated, and the cut-off value was determined using the Youden Index. Sensitivity, specificity, percentage of correct classifications, positive predictive value (PPV), and negative predictive value (NPV) were calculated to evaluate goodness of fit. All analyses were performed using R (version 4.2.1; CRAN, freeware) and R Commander 2.7-1. The Hosmer–Lemeshow test was conducted using the Resource Selection package. The level of significance for all tests was set at $p = 0.05$.

2.4. Ethical Considerations

This study was approved by the Ethical review Board of Omuta City Hospital (approval number: No. 2324. Data were anonymized in accordance with the Declaration of Helsinki to protect personal information. Written informed consent was not obtained due to the retrospective nature of the study. Therefore, an opt-out system was adopted that allowed participants to decline participation.

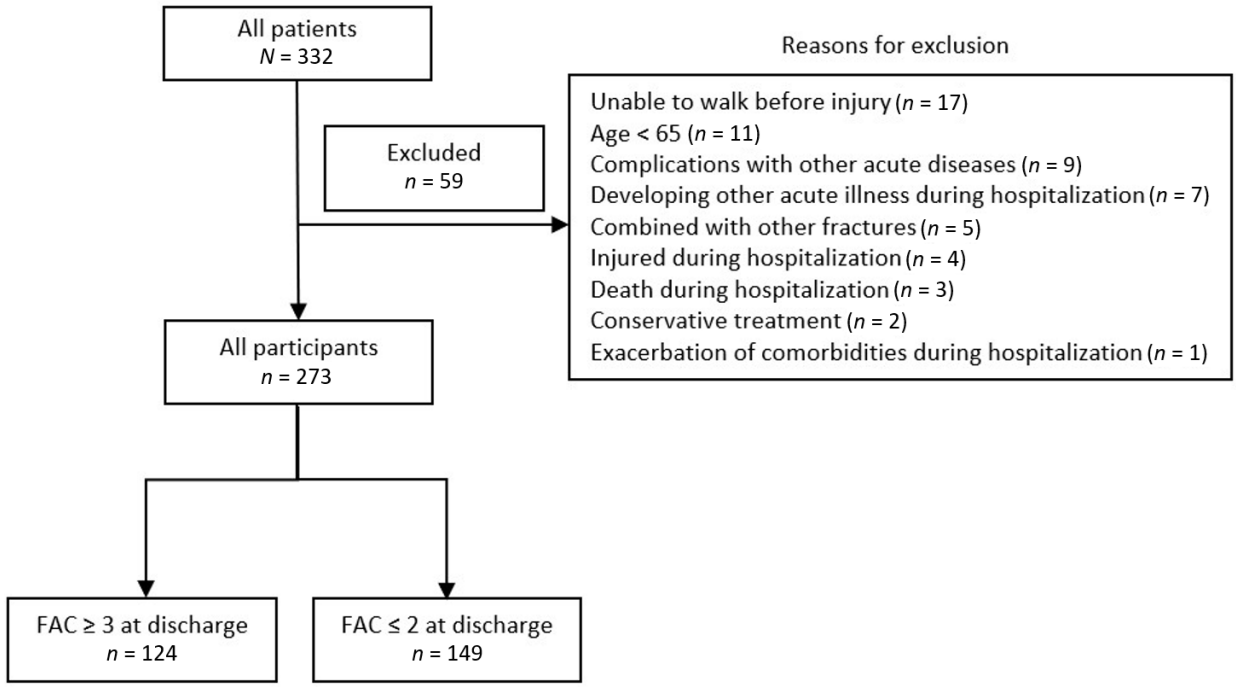
3. RESULTS

Figure 1 shows the study flow chart. Overall, 59 patients met the exclusion criteria, leaving 273 patients for evaluation. Among them, 124 patients were in the FAC ≥ 3 group, and 149 were in the FAC ≤ 2 group. Table 1 presents a comparison of the baseline characteristics of the two groups. The overall median age was 87 years (interquartile range [IQR] = 80–91), with 78.8% of the participants being women. The median BMI was 19.4 kg/m² (IQR = 17.5–21.7), the mean GNRI was 90.0 ± 10.8; the median eGFR was 58.3 mL/min/1.73 m² (IQR = 41.8–72.1). In addition, 61.5% of the participants used walking aids. Age was significantly lower in the FAC ≥ 3 groups than in the FAC ≤ 2 group (85 *vs.* 88 years, $p < 0.001$). The use of walking aids was also significantly lower in the FAC ≥ 3 group (54.8% *vs.* 67.1%, $p < 0.05$). The overall rate of femoral neck fractures was 56.8%; 38.1% of the participants underwent BHA. The overall median TTS was 5 days (IQR = 3–7) and was significantly shorter in the FAC ≥ 3 group (4 *vs.* 6 days, $p < 0.01$). Comorbidities included T2DM in 21.6%, HT in 60.4%, CHF in 20.1%, and CKD in 14.3% of patients. The proportion of patients undergoing dialysis was 0.7%. The median number of medications was 8 (IQR = 5–10), with 70.0% of the participants experiencing polypharmacy. Both the number of medications and prevalence of polypharmacy were significantly lower in the FAC ≥ 3 groups (7 *vs.* 8

medications, $p < 0.05$ and 64.5% *vs.* 74.5%, $p < 0.05$, respectively). No significant differences were found in the other variables between the two groups.

Table 2 lists the results of multiple logistic regression analysis. In Model 1, age (OR = 0.921; 95% CI = 0.888–0.953; $p < 0.001$) and the number of

Figure 1. Study flow chart



Abbreviation: FAC, Functional Ambulation Category.

Table 1. Comparison of baseline characteristics of the participants

		Total (n = 273)	FAC ≥ 3 (n = 124)	FAC ≤ 2 (n = 149)	p value
Demographic characteristics					
Age (year)		87 (80–91)	85 (77–90)	88 (84–92)	< 0.001[a]***
Sex (women, %)		215 (78.8)	95 (76.6)	120 (80.5)	0.310[b]
BMI (kg/m^2)		19.4 (17.5–21.7)	19.4 (17.5–21.7)	19.5 (17.5–22.2)	0.688[a]
GNRI		90.0 ± 10.8	91.3 ± 11.3	88.9 ± 10.6	0.083[c]
eGFR (mL/min/1.73m^2)		58.3 (41.8–72.1)	57.9 (45.1–72.1)	58.6 (38.7–72.1)	0.366[a]
Use of walking aids before injury (%)		168 (61.5)	68 (54.8)	100 (67.1)	0.026[b]*
Factors of fracture and surgery					
Type of fracture (Femoral neck, %)		155 (56.8)	78 (62.9)	77 (51.7)	0.085[b]
Type of surgery (BHA, %)		104 (38.1)	49 (39.5)	55 (36.9)	0.730[b]
TTS (day)		5 (3–7)	4 (3–7)	6 (4–8)	0.004[a]**
Comorbidities and medication status					
Comorbidity (%)	T2DM	59 (21.6)	31 (25.0)	28 (18.8)	0.240[b]
	HT	165 (60.4)	70 (56.5)	95 (63.8)	0.170[b]
	CHF	55(20.1)	21 (16.9)	34 (22.8)	0.210[b]
	CKD	39 (14.3)	14 (11.3)	25 (16.8)	0.180[b]
	Dialysis	2 (0.7)	2 (1.6)	0 (0)	0.120[d]
Number of medications		8 (5–10)	7 (4–10)	8 (6–10)	0.033[a]*
Polypharmacy (%)		191 (70.0)	80 (64.5)	111 (74.5)	0.048[b]*

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.
Notes: Characteristics of the participants are shown as mean ± deviation or median (interquartile range 25%–75%) for parametric and non-parametric data, respectively. Statistical tests were conducted using [a], Mann–Whitney U test; [b], chi-square independence test; [c], two-sample t-test; and [d], Fisher's exact test.
Abbreviations: BHA, bipolar hip arthroplasty; BMI, body mass index; CHF, chronic heart failure; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; FAC, functional ambulation category; GNRI, geriatric nutritional risk index; HT, hypertension; TTS, time to surgery; T2DM, type 2 diabetes mellitus.

medications (OR = 0.912; 95% CI = 0.853–0.972; $p < 0.01$) were identified as significant variables. In Model 2, only age (OR = 0.924; 95% CI = 0.891–0.956; $p < 0.001$) was a significant variable. The VIF for all variables was < 5, indicating no multicollinearity with an FAC of ≥ 3 at discharge. The likelihood ratio test results were significant ($p < 0.01$) for both models and the Hosmer–Lemeshow test showed good goodness of fit with $p = 0.83$ for Model 1 and $p = 0.22$ for Model 2. Figure 2 shows the ROC curves for the number of medications administered and age. The AUC was 0.575, with a cutoff value of 7.5 medications. The goodness-of-fit metrics showed a sensitivity of 54.4%, specificity of 56.1%, overall correct classification rate of 55.3%, PPV of 51.1%, and NPV of 59.3%. In regard to age, the AUC was 0.649, with a cutoff value of 86.5. The goodness-of-fit metrics revealed a sensitivity of 57.6%, specificity of 67.6%, overall correct classification rate of 63.0%, PPV of 60.0%, and NPV of 65.4%.

4. DISCUSSION

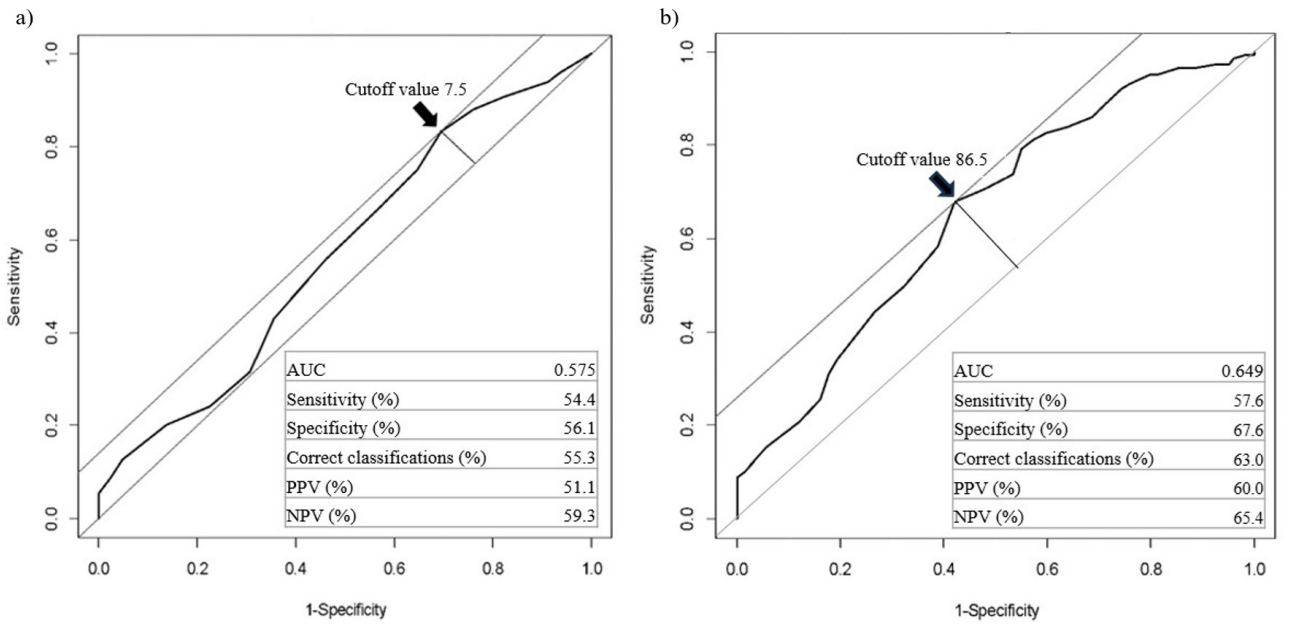
This study aimed to evaluate the association between the medication status at admission and degree of ambulatory independence at discharge in older patients with HF following surgery. Previous studies have indicated that ADL recovery efficiency,[21] length of stay,[34] and readmission rates[20] in patients with HF are associated with polypharmacy or the number

Table 2. Factors related to FAC ≥ 3 at discharge: Results of logistic regression analysis

	Estimate	*SE*	*p* value	OR	95% CI		VIF
					Lower	Upper	
Model 1							
(Intercept)	7.935	1.638	< 0.001		123.845	77792.611	
Age	-0.083	0.018	< 0.001	0.921	0.888	0.953	1.042
Number of medications	-0.093	0.033	0.005	0.912	0.853	0.972	1.016
TTS	-0.052	0.029	0.075	0.949	0.894	1.003	1.031
Model 2							
(Intercept)	7.240	1.584	< 0.001		68.216	34586.880	
Age	-0.079	0.018	< 0.001	0.924	0.891	0.956	1.031
Polypharmacy	-0.509	0.280	0.069	0.601	0.346	1.039	1.003
TTS	-0.046	0.028	0.109	0.956	0.901	1.008	1.033

Notes: In Model 1, all variables except 'polypharmacy' were used as independent variables, while in Model 2, all variables except 'number of medications' were used as independent variables. The results in Chi-square test were $p < 0.01$ (Model 1 and 2), while the Hosmer–Lemeshow goodness-of-fit test showed $p = 0.83$ (Model 1) and $p = 0.22$ (Model 2).
Abbreviations: CI, confidence interval; OR, odd ratio; *SE*, standard error; TTS, time to surgery; VIF, variance inflation factor.

Figure 2. ROC curves for a) the number of medications administered and b) age



Abbreviations: AUC, area under the curve; NPV, negative predictive value; PPV, positive predictive value; ROC, receiver operating characteristic.

of medications. However, its specific association with degree of ambulatory independence after surgery remains unclear. In this study, we analyzed demographic information, degree of ambulatory independence before injury, and medical information, such as nutritional status, renal function, surgery-related factors, comorbidities, and number of medications to assess their association with degree of ambulatory independence at discharge from an acute care hospital. Consequently, the number of medications prescribed before injury, rather than the presence of polypharmacy, was associated with achieving ambulatory independence at the supervision level or higher at discharge in patients with HF. The median age of the study participants was 87 years, indicating a notably older population, which likely contributed to the high number of prescribed medications. More than 70% of the participants are classified into the polypharmacy category. Therefore, the number of medications may be a significant factor affecting degree of ambulatory independence, rather than the mere presence of polypharmacy.

Two mechanisms have been proposed to explain the delayed recovery of ambulatory ability after surgery for HF in patients who receive multiple medications. The first mechanism suggests that patients who receive multiple medications may have a relative deficiency in the nutrients necessary for tissue repair. Polypharmacy has been associated with a potential pro-inflammatory state because of the presence of multiple diseases.[35] The added stress of fractures and surgical intervention may exacerbate this state, leading to further depletion of nutrients, and consequently, delayed functional recovery. The second mechanism is sarcopenia. Patients with sarcopenia have a significantly increased risk for polypharmacy.[36] Thus, sarcopenia is likely to be more prevalent in patients taking multiple medications, potentially affecting degree of ambulatory independence at discharge. Kanaya et al. observed that postoperative patients with HF with sarcopenia had lower ADL levels and cognitive function at discharge than did those without sarcopenia.[37] However, the specific association between sarcopenia and ambulatory ability remains unclear, necessitating further research with a quantitative evaluation of sarcopenia.

This study has few limitations. The first limitation concerns the study design; 59 cases (17.8% of the total) were excluded, resulting in a difference in the number of samples between the two groups. Furthermore, because this was a single-center retrospective observational study, causality could not be inferred. The second aspect pertains to data collection. The degree of ambulatory independence of the participants before injury was not evaluated using the FAC. Instead, the assessment relied on interviews with the patients and their families. Consequently, an accurate classification using the FAC was not possible, and degree of ambulatory independence before the injury was classified solely based on the use or absence of walking aids. This limitation hindered a thorough examination of the association between pre-injury ambulatory ability and degree of ambulatory independence at discharge. In addition, the effect of dementia was not investigated. Dementia increases the incidence of postoperative complications in patients with HF.[38] Furthermore, it affects degree of ambulatory independence at discharge in this study. Although the volume of physical therapy administered may have impacted the results of rehabilitation, this study was unable to explore this relationship due to limitations of data collection.

The third limitation is the inability to correctly classify the calculated cutoff value for the number of medications. This may be due to the high prevalence of polypharmacy among study participants. Future studies targeting patients across a wider age range are needed to evaluate the impact of the number of medications more accurately.

5. CONCLUSION

In conclusion, achieving ambulatory independence at the supervision level or higher at discharge from an acute care hospital in older patients after HF surgery was associated with the number of prescribed medications, rather than the presence of polypharmacy. The cutoff value for FAC ≤ 2 was 7.5 medications, which may serve as a useful tool for predicting acute rehabilitation outcomes. Monitoring the number of medications taken by patients is clinically important; however, the inability to classify correctly remains an issue that needs to be addressed. Thus, future studies targeting a broader age range of older population are necessary for evaluating the impact of medication count on rehabilitation outcomes more accurately.

CONFLICTS OF INTEREST

The researchers claim no conflicts of interest.

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