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ORIGINAL ARTICLE

Impact of the Comorbidity Polypharmacy Score on Clinical Outcome in Patients with Hip Fracture undergoing surgery Using Real-World Data

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ABSTRACT

BACKGROUND

The Comorbidity Polypharmacy Score (CPS) is calculated by the number of drugs carried plus the number of comorbidities on admission and divided into three categories (minor, 0–7; moderate, 8–14; and severe, 15+). This study investigates whether CPS can predict the clinical outcomes in older patients with hip fractures undergoing surgery.

METHODS

This retrospective longitudinal study used a multicenter hospital-based database containing the Diagnosis Procedure Combination. Consecutive patients with hip fractures (ICD-10 codes S720 and S721) who were aged ≥65 years between April 2014 and August 2020 were included. We evaluated the predictive association between the CPS and Barthel Index (BI) efficiency. The primary outcome was defined as the BI efficiency, and the secondary outcome was the length of hospital stay.

RESULTS

We enrolled 11,564 patients, and 80.5% of them were female. The mean age was 83.9 ± 6.5 years. The BI efficiency was the lowest in the CPS severe group with a median [interquartile range] of 0.67 [0.10, 1.43]. The length of hospital stay was the highest in the CPS severe group, with a median of 35 [21, 58]. Additionally, multiple linear regression analysis revealed that the CPS was independently associated with the BI efficiency (β = −0.100, 95% CI: −0.040, −0.029; $P < 0.001$) and the length of hospital stay (β = 0.047, 95% CI: 0.199, 0.366; $P < 0.001$).

CONCLUSIONS

An increased CPS score is associated with low BI efficiency and longer length of hospital stay in patients with hip fractures.

KEY WORDS

Comorbidity Polypharmacy Score, hip fracture, rehabilitation, Barthel Index efficiency

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INTRODUCTION

In our aging society, older patients who need rehabilitation after hip fracture is growing. The research has also developed that can predict rehabilitation outcomes. In those studies, polypharmacy and comorbidity are said to be important for predicting rehabilitation outcomes, and the Comorbidity Polypharmacy Score (CPS), which takes these two factors into account, may have high predictive accuracy [1–6]. Polypharmacy describes the potential dangers associated with the simultaneous use of many medications [1–3]. In recent years, the definition of polypharmacy has changed. Numerical definitions of polypharmacy are variable and difficult [4]. Polypharmacy has been defined as the harmful use of many medications. However, it is more than just taking a large number of medications; it is a condition that leads to problems such as the increased risk of adverse drug events, medication errors, and decreased medication adherence [5]. Polypharmacy affects the rehabilitation outcome in patients with hip fractures. In our previous study conducted on patients with hip fractures, we found that the use of six or more drug types was associated with a lower Barthel Index (BI) efficiency and longer hospital stays [6].

A previous systematic review and meta-analysis reported an association between comorbidity burden and functional outcome in patients suffering from stroke or hip fracture [7]. Thus, to predict the functional prognosis of rehabilitation patients, evaluating the severity-weighted comorbidity is preferred. Furthermore, Nossaman et al. concluded that the Charlson Comorbidity Index and CPS might be useful for predicting hospital length of stay in geriatric trauma patients [8]. These reports indicate that both comorbidity and the CPS are important predictors of clinical outcomes in rehabilitation patients.

The CPS is expected to play a more important role than polypharmacy and comorbidity in the prediction of rehabilitation outcome. The CPS has been reported to be useful as a predictor of readmission and also a prognostic indicator [1–3]. The CPS was first reported in 2011 [1]. It assigns one point for each disease process or comorbidity and one point for each drug the patient is taking before admission; there is no maximum score [9–11]. The primary characteristic of CPS is that it encompasses all disease processes and evaluates their severity based on the number of medications. Blain Chaise Housley et al. reported that in trauma patients, the CPS is correlated with readmissions within 30 days [4]. The CPS was found to be a significantly stronger predictor of readmission than patient age [1]. A retrospective validation study concluded that in older trauma patients, the CPS is an independent predictor of all-cause morbidity and mortality [2]. In patients undergoing surgery for an osteoporotic hip fracture, CPS was reported to be a better predictor of mortality risk than the presence of polypharmacy existence in the first 2 years [6]. The early recognition of an elevated CPS may aid in discharge planning and guide interventions to reduce readmission rates in older patients.

However, the relationship between the CPS and rehabilitation outcome remains a controversial issue, and only a few studies have investigated the impact of the number of drug types on rehabilitation outcome patients with hip fractures [6, 12]. Therefore, in the present study, we aimed to investigate whether CPS can predict the BI efficiency and the length of hospital stay postoperatively using real-world data in patients with hip fractures undergoing surgery.

METHODS

STUDY DESIGN AND SOURCES

We conducted a retrospective cohort study using a hospital database constructed by the Japan Medical Data Center. The Japan Medical Data Center's medical institution data includes non-Diagnosis Procedure Combination (DPC) hospitals, the number of hospitals by bed size is close to the national average, making the data highly nationally representative. Data can be collected regardless of the insurance a patient has, providing abundant coverage of the elderly population over the age of 65. The database contains the DPC, which is a case-mix patient classification system launched in 2002 by the Ministry of Health, Labour and Welfare of Japan, and it is linked with a lump-sum per diem payment system. The details of the DPC database have been reported in previous studies [13, 14]. The DPC survey was conducted between April 2014 and August 2020 in patients with hip fractures and includes as many as 100 participating hospitals with 3 million patients across Japan. The database includes the following: patient age and gender, main diagnoses, preexisting comorbidities, and postadmission complications as coded by the *International Classification of Disease and Related Health Problems*, 10th revision (ICD-10). All data regarding the diagnosis and comorbidities in the present study were recorded by attending physicians.

ETHICAL CONSIDERATIONS

This study was conducted in accordance with the

principles of the Declaration of Helsinki. The requirement for informed consent was waived because all data in the JMDC Claims Database were anonymized and deidentified. All data were compliant with the a new ICH guideline on General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines. Therefore, ethical review is deemed unnecessary and the IRB's ethical review is not required.

STUDY POPULATION

The study population was identified using the following procedure. First, participants from the overall population who met the inclusion criteria were identified. Inclusion criteria were patients aged ≥65 years with ICD-10 code S720 and S721 and who underwent surgery. Second, participants who met the exclusion criteria were excluded from the study. Exclusion criteria were patients who did not bring any medication to the hospital; in addition, participants for whom BI data were missing were excluded from the study.

MEASUREMENTS

The rehabilitation outcome was considered as activities of daily living (ADL), which were evaluated using the BI. The BI score is calculated using the following categories: (1) feeding, (2) moving back and forth between a wheelchair and bed, (3) grooming, (4) using a toilet, (5) bathing, (6) walking on a level surface, (7) moving up and downstairs, (8) dressing, (9) bowel continence, and (10) bladder continence. We divided the evaluation of the 10 aforementioned categories into two to four levels, with scores ranging from 0 to 100. A higher score was considered to indicate a higher degree of personal ADL capacity [15]. We defined the number of drugs as follows, drugs were the types of drugs the patient was taking at the time of admission but does not include external medicine. The CPS was calculated as follows: the number of drugs carried at admission plus the number of comorbidities at admission. We then divided the patients into three groups based on a previous study: minor, CPS 0–7; moderate, CPS 8–14; and severe, CPS ≥15, respectively [2].

OUTCOMES

The primary outcome was defined as the ADL indicator as follows: BI efficiency (BI at discharge minus BI at admission)/length of hospital stay. This value shows functional gain per day. A negative value indicates worsened functional status during the rehabilitation unit stay; 0–0.49 show slow rehabilitation efficiency; 0.50–1 reflects moderate rehabilitation efficiency; and >1 indicates high efficiency [16, 17]. The secondary outcome was the length of hospital stay. We selected the other predictors based on a previous study that investigated the relationship between the number of medications taken and ADL [12]. We compared the outcomes among patients with hip fractures who were aged ≥65 years or older and divided them into four groups based on CPS: minor, CPS 0–7; moderate, CPS 8–14; and severe, CPS ≥15 [2].

STATISTICAL ANALYSIS

For the statistical analyses, we used the IBM Statistical Package for the Social Sciences software version 27 (IBM, Armonk, NY, USA). Normally distributed data were expressed as mean ± standard deviations, and non-normally distributed data were expressed as medians and interquartile ranges. We used the chi-squared test to compare the proportions of categorical data. Analysis of variance was employed to compare independent samples of normally distributed contentious variables and the Kruskal–Willis test to compare non-normally distributed variables. To determine whether the CPS was independently associated with BI efficiency and length of hospital stay, we conducted a multiple linear regression analysis. To assess the categorical variables in this analysis, we made dummy variables for the fracture type (femoral neck fracture and pertrochanteric fracture), surgery type (hemiarthroplasty, osteosynthesis, and other surgeries), bed capacity, and hospitalization duration, depending on the number of categorical variables. The independent variables were age, gender, body mass index, type of fracture, type of surgery, admission with the ambulance, BI at admission, number of beds, rehabilitation per week, and year of hospitalization.

RESULTS

A total of 73,856 inpatients with hip fractures at admission were identified in the DPC database during the study period. We excluded 4,940 patients who were younger than 65 years, 4,128 patients with an ICD-10 code other than S720 and S721, 43,824 patients with zero medicines brought to the hospital at the time of admission, 5,314 patients with missing values for BI efficiency, and 4,086 patients who did not undergo surgery. Thus, we eventually included 11,564 patients in this study (**Fig. 1**).

A total of 4,433 patients were categorized as minor (CPS 0–7; 38.3%), 5,831 patients as moderate (CPS 8–14;

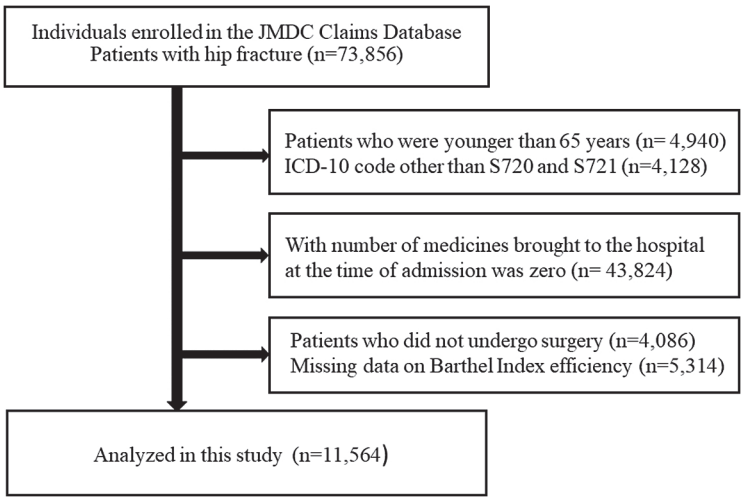

Fig. 1 **Study flow of the data extraction from the database**

50.4%), and 1,300 as severe (CPS ≥15; 11.2%).

Of the patients, 9,310 (80.5%) were female, and the mean age was 83.9 ± 6.5 years. In addition, 5,656 (48.9%) had a femoral neck fracture, and 5,908 (51.1%) had a pertrochanteric fracture. The median [interquartile range] BI scores at admission and discharge were 5 [0.0, 15] and 45 [15, 80], respectively (**Table 1**).

The comparison of the outcome of BI efficiency (BI gain per day) and the length of hospital stay (day) (**Table 1**) showed that BI efficiency was the lowest with CPS severe (median [interquartile range] 0.67 [0.10, 1.43]), followed by CPS moderate (median [interquartile range] 0.71 [0.00, 1.50]) and CPS minor (median [interquartile range] 0.87 [0.10, 1.89]; $P < 0.001$). The length of hospital stay was the highest with CPS severe (median [interquartile range] 35 [21, 58]), followed by CPS moderate (median [interquartile range] 31 [20, 52]) and CPS minor (median [interquartile range] 30 [19, 50]; $P < 0.001$).

Table 2 lists the association between of Barthel Index efficiency and Length of hospital stay with Comorbidity-Polypharmacy Score. In terms of BI efficiency, CPS without adjustment (β = −0.092, 95% confidence interval [CI]: −0.038, −0.026; $P < 0.001$), and CPS with adjustment for other predictors, (β = −0.100, 95% CI: −0.040, −0.029; $P < 0.001$) were independently associated with ADL.

Furthermore, for the length of hospital stay, CPS with the unadjusted model (β = 0.060, 95% CI: 0.246, 0.461; $P < 0.001$) and CPS with the adjusted model (β = 0.047, 95% CI: 0.199, 0.366; $P < 0.001$) were associated with a longer hospital stay.

DISCUSSION

We investigated whether CPS can predict the clinical outcome in patients with hip fractures undergoing surgery. The findings of the present study indicate that the CPS has an effect on the rehabilitation outcomes of both BI efficiency and length of hospital stay. From this result, it can be said that calculating the CPS post-operative is important for predicting patients' clinical outcomes in acute care hospitals. The number of medications and comorbidities are strongly correlated and necessary factors in the calculation of the CPS. Therefore, we thought that the CPS that takes both parameters into account would be a better predictor of the ADL than any other single parameter.

In the present study, the BI efficiency was significantly lower in elderly patients with high CPS than in those with CPS minor to moderate. This might be due to adverse drug events associated with polypharmacy and comorbidities. In addition, our previous study demonstrated that patients taking six or more types of drugs had a lower BI efficiency [12]. Therefore, the use of CPS, which is available during admission to predict postoperative ADL in patients undergoing surgery for hip fracture, may be useful with clinical judgement. It may also be able to lead to subsequent rehabilitation pharmacotherapy interventions. Moreover, we would like to conduct

Table 1 Comparison of clinical outcomes and patient characteristics

		Total, n = 11,564	CPS minor (0–7) n = 4,433	CPS moderate (8–14) n = 5,831	CPS severe (≥15) n = 1,300	*p*-value
Barthel index efficiency, median (25–75%)		0.76 (0.07–1.67)	0.87 (0.10–1.89)	0.71 (0.00–1.50)	0.67 (0.10–1.43)	<0.001[b]
Length of hospital stay, median (25–75%)		31 (20–52)	30 (19–50)	31 (20–52)	35 (21–58)	<0.001[b]
Data at the time of admission						
Age, mean ± SD		83.9 ± 6.5	83.6 ± 6.8	84.2 ± 6.3	83.3 ± 6.5	<0.001[a]
Gender (%)	Female	9,310 (80.5)	3,648 (82.3)	4,674 (80.2)	988 (76.0)	<0.001[c]
BMI, mean ± SD		20.8 ± 3.6	20.7 ± 3.6	20.8 ± 3.6	21.2 ± 3.7	<0.001[a]
Type of fracture (%)	Femoral neck fracture	5,656 (48.9)	2,180 (49.2)	2,834 (48.6)	642 (49.4)	0.793[c]
	Pertrochanteric fracture	5,908 (51.1)	2,253 (50.8)	2,997 (51.4)	658 (50.6)	
Type of surgery (%)	Osteosynthesis	7,274 (62.9)	2,806 (63.3)	3,680 (63.1)	788 (60.6)	0.007[c]
	Hemiarthroplasty	3,991 (34.5)	1,524 (34.4)	2,008 (34.4)	459 (35.3)	
	Other surgeries	299 (2.6)	103 (2.3)	143 (2.5)	53 (4.1)	
Admission with ambulance (%)		6,451 (55.8)	2,536 (21.9)	3,202 (27.7)	713 (6.2)	0.055[c]
BI at admission, median (25%–75%)		5.0 (0.0–15)	5.0 (0.0–20)	5.0 (0.0–15)	5.0 (0.0–15)	0.610[b]
Facility data						
Number of beds (%)	20–99	578 (5.0)	194 (4.4)	272 (4.7)	112 (8.6)	<0.001[c]
	100–199	2,514 (21.7)	989 (22.3)	1,262 (21.6)	263 (20.2)	
	200–299	2,238 (19.4)	836 (18.9)	1,139 (19.5)	263 (20.2)	
	300–499	4,116 (35.6)	1,601 (36.1)	2,082 (35.7)	433 (33.3)	
	500+	2,118 (18.3)	813 (18.3)	1,076 (18.5)	229 (17.6)	
Data at the time of discharge						
Total number of rehabilitation times, median (25%–75%)		25 (13–48)	24 (12–48)	25 (13–48)	27 (14–51)	<0.001[b]
Rehabilitation times/week, median (25%–75%)		3.6 (1.9–6.9)	3.4 (1.7–6.9)	3.6 (1.9–6.9)	3.9 (2.0–7.3)	<0.001[b]
BI at discharge, median (25%–75%)		45 (15–80)	50 (20–85)	45 (15–75)	45 (15–75)	<0.001[b]

a: ANOVA test, b:Kruskal-Willis test, c: chi-square test
Abbreviation: CPS, Comorbidity-Polypharmacy Score, BMI, Body Mass Index, BI, Barthel Index

further study to determine the effectiveness of a high-risk approach based on the CPS in predicting ADL or clinical trials with high-risk group using CPS to improve ADL.

In this study, a higher CPS was associated with a longer length of hospital stay. A previous study demonstrated that in patients with proximal fractures, factors associated with a longer length of hospital stay were a period from hospitalization to surgery of more than 3 days, a period from surgery to the beginning of the rehabilitation of more than 1 day, admission to a private hospital, and the presence of infectious complications [18]. Thombs et al. reported a relationship between higher CPS and longer ICU and hospital lengths of stay in patients with acute burn injury [19]. Therefore, CPS might be a useful indicator for predicting the length of hospital stay. In this finding, we aimed to evaluate not

Table 2 Association between of Barthel Index efficiency and Length of hospital stay with Comorbidity-Polypharmacy Score (n = 11,564)

	β	95% CI		*p*-value	Adjusted R^2
Unadjusted model					
Barthel Index efficiency (BI gain per day)	−0.092	−0.038	−0.026	<0.001	0.008
Length of hospital stay (day)	0.060	0.246	0.461	<0.001	0.003
Adjusted model[1)]					
Barthel Index efficiency (BI gain per day)	−0.100	−0.04	−0.029	<0.001	0.220
Length of hospital stay (day)	0.047	0.199	0.366	<0.001	0.458

Abbreviation: β; Beta-coefficient, CI; Confidencial Interval
[1)] Multiple regression analysis was conducted using analysis of covariance adjusting for age, gender, body mass index, type of fracture, type of surgery, admission with ambulance, barthel index at admission, number of beds, rehabilitation per week, year of hospitalization.

only the number of medications and comorbidities but also the CPS, both of which were considered appropriate in patients with hip fractures undergoing surgery.

Notably, CPS is a predictive indicator and useful in identifying high-risk groups; therefore, it can contribute to a high-risk treatment approach in patients with hip fracture .undergoing surgery. Rehabilitation pharmacotherapy conducted during the treatment should consider the contents of training in rehabilitation [20, 21]. Appropriate use of medications is also required for old patients. A previous study in patients with hip fractures showed that a multidisciplinary approach is appropriate and is associated with reductions in the length of hospital stay, mortality, and postoperative complications [22]. Thus, combination therapy (both rehabilitation and pharmacotherapy) is useful for improving clinical outcomes in rehabilitation patients.

This study has a few limitations. First, more than half of all patients were excluded from the analysis due to missing BI efficiency values, zero medicines brought to the hospital at the time of admission, ICD-10 codes other than S720 and S721, age less than 65 years, and no surgery. Regarding the exclusion of patients without medication upon admission, excluding those who were really taking medication but failed to bring it with them would make the study unrealistic and limit the population to which the results could be applied. Conversely, including people who were not actually taking medication may lead to underestimation of adverse drug events and make the interpretation of the results more difficult. Second, the DPC database was insufficient in terms of the details or information in some areas, such as the degree of fracture, rehabilitation content, cognitive impairment, sarcopenia, frailty, cachexia, American Society of Anesthesiologists physical status, and details of the BI measurement were not evaluated in this study. Considering the lack of absolute cutoff for the CPS, we conducted multiple linear regression analysis. Sensitivity analysis may be necessary to identify clinically useful outcomes. Further studies are required to evaluate the association between CPS and clinical outcomes in rehabilitation patients.

CONCLUSIONS

The patients with hip fracture undergoing surgery with high CPS was associated with lower BI efficiency and longer hospital stays. The CPS is easy to calculate at admission and can be a useful indicator for predicting rehabilitation outcomes in patients with hip fracture undergoing surgery.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

REFERENCES

1. Evans DC, Gerlach AT, Christy JM, Jarvis AM, Lindsey DE, Whitmill ML, et al. Pre-injury polypharmacy as a predictor of outcomes in trauma patients. *Int J Crit Illn Inj Sci* 2011;1:104–9.
2. Holmes M, Garver M, Albrecht L, Arbabi S, Pham TN. Comparison of two comorbidity scoring systems for older adults with traumatic injuries. *J Am Coll Surg* 2014;219:631–7.
3. Evans DC, Cook CH, Christy JM, Murphy CV, Gerlach AT, Eiferman D, et al. Comorbidity-polypharmacy scoring facilitates outcome prediction in older trauma patients. *J Am Geriatr Soc* 2012;60:1465–70.
4. Housley BC, Stawicki SPA, Evans DC, Jones C. Comorbidity-polypharmacy score predicts readmission in older trauma

patients. *J Surg Res* 2015;199:237–43.
5. Mubang RN, Stoltzfus JC, Cohen MS, Hoey BA, Stehly CD, Evans DC, et al. Comorbidity-polypharmacy score as predictor of outcomes in older trauma patients: A retrospective validation study. *World J Surg* 2015;39:2068–75.
6. Camur S, Celik H. Prediction of the mortality with comorbidity—Polypharmacy score in the osteoporotic hip fractures. *Acta Chir Orthop Traumatol Cech* 2019;86:320–3.
7. Kabboord AD, van Eijk M, Fiocco M, van Balen R, Achterberg WP. Assessment of comorbidity burden and its association with functional rehabilitation outcome after stroke or hip fracture: A systematic review and meta-analysis. *J Am Med Dir Assoc* 2016;1;17:1066.e13–1066.e21.
8. Nossaman VE, Larsen BE, DiGiacomo JC, Manuelyan Z, Afram R, Shukry S, et al. Mortality is predicted by comorbidity Polypharmacy score but not Charlson comorbidity Index in geriatric trauma patients. *Am J Surg* 2018;216:42–5.
9. Stawicki SP, Kalra S, Jones C, Justiniano CF, Papadimos TJ, Galwankar SC, et al. Comorbidity polypharmacy score and its clinical utility: A pragmatic practitioner's perspective. *J Emerg Trauma Shock* 2015;8:224–31.
10. Chua MT, Bhandari K, Ong VY, Kuan WS. Road crashes in older persons and the use of comorbidity polypharmacy score in an Asian population. *Ann Acad Med Singap* 2017;46:185–94.
11. Justiniano CF, Evans DC, Cook CH, Eiferman DS, Gerlach AT, Beery PR, et al. Comorbidity-polypharmacy score: A novel adjunct in post-emergency department trauma triage. *J Surg Res* 2013;181:16–9.
12. Maki H, Wakabayashi H, Nakamichi M, Momosaki R. Impact of number of drug types on clinical outcome in patients with acute hip fracture. *J Nutr Health Aging* 2019;23:937–42.
13. Momosaki R, Yasunaga H, Matsui H, Fushimi K, Abo M. Proton pump inhibitors versus histamine-2 receptor antagonists and risk of pneumonia in patients with acute stroke. *J Stroke Cerebrovasc Dis* 2016;25:1035–40.
14. Yasunaga H, Hashimoto H, Horiguchi H, Miyata H, Matsuda S. Variation in cancer surgical outcomes associated with physician and nurse staffing: A retrospective observational study using the Japanese Diagnosis Procedure Combination Database. *BMC Health Serv Res* 2012;28;12:129.
15. Mahoney FI, Barthel DW. Functional evaluation: The Barthel index. *Md State Med J* 1965;14:61–5.
16. Sánchez-Rodríguez D, Miralles R, Muniesa JM, Mojal S, Abadía-Escartín A, Vázquez-Ibar O. Three measures of physical rehabilitation effectiveness in elderly patients: A prospective, longitudinal, comparative analysis. *BMC Geriatr* 2015;29;15:142.
17. Rinkaewkan P, Kuptniratsaikul V. The effectiveness of inpatients rehabilitation for spinal cord patients in Siriraj Hospital. *Spinal Cord* 2015;53:591–7.
18. Takahashi C, Fushimi K, Matsuda S. Factors associated with a protracted hospital stay after hip fracture surgery in Japan. *Geriatr Gerontol Int* 2011;11:474–81.
19. Thombs BD, Singh VA, Halonen J, Diallo A, Milner SM. The effects of preexisting medical comorbidities on mortality and length of hospital stay in acute burn injury: Evidence from a national sample of 31,338 adult patients. *Ann Surg* 2007;245:629–34.
20. Wakabayashi H. Rehabilitation pharmacotherapy: A combination of rehabilitation and pharmacotherapy. *J Gen Fam Med* 2018;5;19:43–4.
21. Kose E, Wakabayashi H. Rehabilitation pharmacotherapy: A scoping review. *Geriatr Gerontol Int* 2020;20:655–63.
22. Reguant F, Arnau A, Lorente JV, Maestro L, Bosch J. Efficacy of a multidisciplinary approach on postoperative morbidity and mortality of elderly patients with hip fracture. *J Clin Anesth* 2019;53:11–9.