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Original article

Regular medications prescribed to elderly neurosurgical inpatients and the impact of hospitalization on potentially inappropriate medications

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Abstract

Objective: This study aimed to evaluate the regular medications prescribed to elderly neurosurgical inpatients in community hospitals in Japan.

Materials and Methods: Elderly patients (aged ≥ 65 years) who had been admitted to neurosurgery departments from April 2015 to March 2017 were enrolled in this study. We collected data on regular medications at the time of admission and discharge. Furthermore, we retrospectively analyzed factors associated with potentially inappropriate medications (PIMs). PIMs were defined as polypharmacy (≥ 6 medications used concurrently) or taking any of the unfavorable medications on the "list of drugs to be prescribed with special caution" in the "Guidelines for Medical Treatment and Its Safety in the Elderly 2015".

Results: We gathered data on over 1900 medications (mean number, 5.04) prescribed to 197 patients (mean age, 76.9 years). PIMs were observed in 51.3% of patients on admission. The most common prescriptions resulting in PIMs were benzodiazepine agents, followed by loop diuretics and H2 receptor antagonists. The multivariate analysis revealed that age (odds ratio, 1.08; $p < 0.01$) and the number of prescribers (odds ratio, 6.16; $p < 0.01$) were significantly related to PIMs on admission. PIM exposure at the time of discharge accounted for 39.1%, a 12.2% decrease.

Conclusion: More than half of the elderly patients were prescribed PIMs on admission; however, this exposure decreased by 12.2% at the time of discharge. Hospitalization is an optimal opportunity for reconsidering the necessity of medications and for changing the prescriptions according to patients' conditions.

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Introduction

Japan is a rapidly aging country. The number of elderly patients examined in hospitals is increasing. The department of neurosurgery is no exception, particularly in community hospitals in rural or suburban areas, many elderly patients are treated and admitted on a regular basis. Since most elderly patients have comorbidities and need medications, every doctor, including surgeons, is required to perform a minimal level of pharmaceutical management along with surgical treatments.

When prescribing medication to elderly patients, doctors must take special care in determining drug types and dosages because of the age-related changes in pharmacokinetics (e.g., drug absorption, distribution, metabolism, and excretion) and pharmacodynamics (physiologic effects of the drug)[1]. Elderly patients are liable to receive an increased number of medications because of increased comorbidities, and this can lead to the use of potentially inappropriate medications (PIMs). PIMs have been defined as medications that carry more risks than benefits, with clinically significant drug-drug or drug-disease interactions[2]. Several screening tools for PIMs are currently available: the Beers Criteria[3], Screening Tool of Older Person's Prescriptions (STOPP) and Screening Tool to Alert doctors to Right Treatment (START)[4], and Drug Burden Index[5]. These tools were developed in the USA and Europe, although they have been updated and used in many previous PIM studies, their direct application in Japan may still require extra attention because of differences in available medications, medical prac-

tices, and insurance systems. Recently, the Japan Geriatrics Society announced the "Guidelines for Medical Treatment and Its Safety in the Elderly 2015" (hereafter termed as "the safety guideline, 2015") specifically intended for Japanese elderly people[6, 7]. Thus far, only few articles based on the use of this guideline have been published. Furthermore, to the best of our knowledge, there is no report concerning PIMs prescribed to neurosurgical inpatients in community hospitals in Japan based on the use of this guideline.

Therefore, this study aimed to determine the regular medications prescribed to elderly neurosurgical inpatients in community hospitals in Japan and to analyze the factors associated with and problems related to PIMs.

Materials and Methods

Patients and hospitals

Elderly patients (aged ≥ 65 years) who were admitted to the neurosurgery department of two community hospitals from April 2015 to March 2017 were enrolled in this study. Because of relocation of the lead author, the first half of the study period was conducted in Ibaraki Seinan Medical Center Hospital (Sakai, Ibaraki, Japan) and the latter half in Kobari General Hospital (Noda, Chiba, Japan). Both hospitals were located in rural or suburban areas at the border between the Ibaraki, Chiba, and Saitama Prefectures, which both play important roles in providing secondary emergency medical services to surrounding medical districts. Because of the retrospective study design, we limited the patients to those whose primary doctor was the lead author to ensure accuracy of data collection. Patients who died during the hospital stay, who needed re-hospitalization during the study period or short-term hospitalizations (within a week) for scheduled examinations or treatments, and those for whom enough information was not available were excluded.

Study design

We collected data on regular medications (oral, inhalation, and hypodermic injectable medications) on admission and at the time of discharge. We categorized medicines according to the Anatomical Therapeutic Chemical (ATC) classification system and defined good outcome as returning home or transferring to a rehabilitation hospital at the time of discharge. In this study, several factors were evaluated for each patient, namely, age, sex, comorbidities, Fried' s frailty criteria[8] score (patients with the score of ≥ 2 were considered frail), living situation (did patients live with family members aged ≤ 64 years?), whether medication was prescribed by general practitioners, the number of prescribers, modified Rankin scale (mRS) score on admission, procedures performed in the hospital (whether patients received tubal feeding or underwent any surgery), length of hospitalization, and patients' outcome at the time of discharge.

PIM criteria

We defined PIMs as the state of polypharmacy (≥ 6 medications used concurrently) or taking any of the unfavorable medications on the "list of drugs to be prescribed with special caution" in "the safety guideline, 2015"[6, 7].

ATC classification system

The ATC classification system, recommended by the World Health Organization, is the most widely recognized classification system for medications[9], which divides medications into different groups across five levels according to the organ or system on which they act, and their therapeutic and chemical characteristics. In the present study, we used the first level of the ATC classification system with a slight modification, dividing medications into 14 main groups (Figure 1A).

Statistical analyses

All information was handled anonymously. To assess the associations between patients' baseline characteristics and each factor evaluated, we used Mann-Whitney U test for continuous variables and Fisher's exact test for categorical variables. Multivariate analysis with logistic regression analysis was conducted to determine the risk factors associated with PIMs on admission and good outcomes. The analysis of good outcomes was adjusted with modified Charlson comorbidity index.[10] All statistical analyses were performed using EZR version 1.36 (R version 3.4.1, R commander version 2.4-0), a graphical user interface for R (The R Foundation for Statistical Computing)[11]. A probability value of <0.05 was considered statistically significant.

Results

Patients

A total of 248 elderly patients were hospitalized during the study period. We excluded 51 ineligible patients (because of the following reasons: death during the hospital stay, 26; paucity of information, 7; re-hospitalization, 14; scheduled hospitalization, 3; others, 1); eventually, 197 patients were included in this study. Details of patient characteristics are presented in Table 1. The mean age was 76.9 years, and 55.3% of patients were male. The most common causes for patients' hospital admission were stroke (60.9%) and neurotrauma (25.4%). Frailty was observed in 15.2% of patients, and approximately 40% lived with family members aged ≤ 64 years. Two or more doctors prescribed medication to 48 (24.4%) patients, and on average, patients had 1.14 prescrib-

(A)

code	Contents and examples
A	Alimentary tract and metabolism (acid inhibitor, laxatives, hypoglycemic agent, insulin)
B	Blood and blood forming organs (anti-thrombotic agent, iron pill)
C	Cardiovascular system (antihypertensive drug, anti-arrhythmic, statin)
D	Dermatologicals
G	Genito-urinary system and sex hormones
H	Systemic hormonal preparations, excluding sex hormones and insulins (steroids, thyroid hormone)
J	Anti-infectives for systemic use (antibiotic drug, antifungal agent, vaccine)
L	Anti-neoplastic and immunomodulating agents
M	Musculo-skeletal system (NSAIDs, DMARDs, bisphosphonates)
N	Nervous system (hypnotic agent, antiepileptic drug, psychotropic agent)
P	Anti-parasitic products, insecticides and repellents
R	Respiratory system (antihistamine drug, bronchodilator, expectorant drug)
S	Sensory organs (ophthalmologic drug, drugs for dizziness or vertigo)
V	Various (contrast media, herbal medicine, others)

(B)

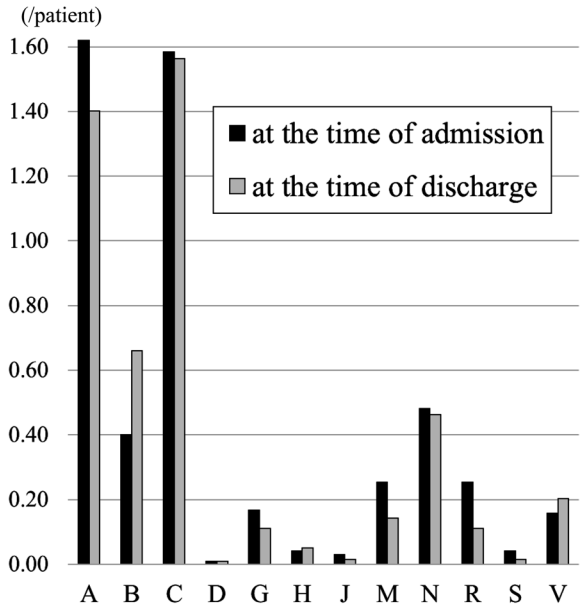

Figure 1 Regular medications according to the ATC classification system. In the first level of the ATC classification system, drugs are divided into 14 different groups (codes) according to the affected organ or system and their therapeutic and chemical characteristics. Contents and examples of each code are presented (A). The number of medications by ATC classification system code are shown (the vertical axis indicates the number of medications per person). Medications belonging to codes "A" and "C" are common at the time of admission, and the number of drugs in most categories was reduced at the time of discharge. No drugs were categorized under codes "L" or "P" in the present study (B). ATC: Anatomical Therapeutic Chemical, NSAIDs: non-steroidal anti-inflammatory drugs, DMARDs: disease-modifying anti-rheumatic drugs.

ers. General practitioners prescribed medications to half of the patients. Comorbidities related to the Charlson comorbidity index are also listed in Table 1. Dementia was the most prevalent disease (12.2%).

Regular medications prescribed at the time of admission and discharge

A total of 993 medications were prescribed to 197 patients on admission. The mean number of prescribed medications was 5.04 (range, 0–18) with polypharmacy observed in 40.1% of patients (Table 1). At the time of discharge, 935 medications were prescribed to the patients. Thirty-two (15.7%) patients were free of medications on admission, and almost all of them (31 out of 32) began to receive any medications during hospitalization; however, the number of medications at the time of discharge declined in 67 patients (34.0%). Based on the ATC classification system, medications categorized as codes "A" and "C" were most commonly administered on admission, followed by code "N" (Figure 1B). The number of medications of most codes prescribed to patients decreased at the time of discharge; however, prescription of code "B" medications increased by 51 medications (0.26/patient).

PIMs

At the time of admission, 51.3% of patients had been prescribed PIMs (Table 1). When limited to patients aged ≥ 75 years, PIMs were observed in ≥65% of patients. The most common prescriptions resulting in PIMs included benzodiazepine agents, followed by loop diuretics and H2 receptor antagonists (H2RA) (Figure 2). At the time of discharge, the percentage of patients prescribed PIMs had decreased by 12.2% (Table 1). The prescriptions of non-steroidal anti-inflammatory drugs (NSAIDs), H2RA, benzodiazepines, and loop diuretics all decreased to a large extent (> 10 prescriptions). We performed univariate and multivariate analyses to evaluate the factors associated with PIMs on admission (Table 2). The multivariate analysis revealed that, on admission, age (odds ratio [OR], 1.08; 95% confidence interval [CI], 1.03–1.13; $p < 0.01$) and number of prescribers (OR, 6.16; 95% CI, 3.09–12.30; $p < 0.01$) were significantly related to PIMs.

Table 1 Patient demographics and medications

Mean age (range)	76.9 (65–102)	Comorbidities	
young-old (65–74)	87 (44.2%)	congestive heart failure	9 (4.6%)
old-old (75–84)	70 (35.5%)	dementia	24 (12.2%)
oldest-old (>85)	40 (20.3%)	chron. pulmonary disease	13 (6.6%)
Male	109 (55.3%)	mild liver disease	7 (3.6%)
		severe liver disease	0 (0.0%)
Admission for stroke	120 (60.9%)	DM with complications	4 (2.0%)
Neurotrauma	50 (25.4%)	hemiplegia or paraplegia	8 (4.1%)
		renal disease	10 (5.1%)
Frailty	30 (15.2%)	AIDS/HIV	0 (0.0%)
Liv. w. family mem.	85 (43.1%)	rheumatologic disease	0 (0.0%)
General practitioner	99 (50.3%)	any malignancy	5 (2.5%)
Number of prescribers	1.14	metastatic solid tumor	3 (1.5%)
mRS on ad. average	3.51		
0	1 (0.5%)	Tubal feeding	20 (10.2%)
1	7 (3.6%)	Any surgery	41 (20.8%)
2	17 (8.6%)		
3	48 (24.4%)	Hospital stay [days]	26.4 (1–164)
4	114 (57.9%)		
5	10 (5.1%)	Good outcome	148 (75.1%)

	At the time of admission	At the time of discharge
Number of medications	5.04	4.75
Polypharmacy	79 (40.1%)	62 (31.5%)
Number of unfavorable drugs	0.82	0.56
PIMs	101 (51.3%)	77 (39.1%)

A good outcome is defined as returning home or transfer to a rehabilitation hospital at the time of discharge. Liv. w. family mem.: living with family members aged < 64 years; mRS: modified Rankin Scale; chron.: chronic; DM: diabetes mellitus; AIDS/HIV: acquired immunodeficiency syndrome/human immunodeficiency virus; PIMs: potentially inappropriate medications.

Factors associated with good outcomes

We analyzed the factors of good outcomes (Table 3) and found the significance of PIM exposure only in the univariate analysis; there was no significant association between PIMs at the time of admission and good outcomes (OR 0.85, 95% CI, 0.34–2.08; p = 0.716). Good outcomes were negatively associated with patients' age, frailty, requirement for tubal feeding, and mRS score on admission. Patients who lived with family members aged ≤ 64 years tended to have good outcomes evaluated in univariate analysis and unadjusted multivariate analysis; however, the results of multivariate analysis adjusted with modified Charlson comorbidity index were insignificant.

Discussion

We collected information on over 1900 medications prescribed to 197 patients at the time of admission and discharge. More than half of the elderly patients were exposed to PIMs on admission. Older age and multiple prescribing doctors were independently associated with PIMs on admission. The critical finding of this study was that the number of elderly patients with PIMs decreased by 12.2% at the time of discharge. Since pharmaceutical management is usually exercised by the doctor in charge during a hospital stay, even if patients have visited ≥2 departments before admission, hospitalizations lead to providing a greater opportunity to reconsider the necessity of each patient's medications. Moreover, from the patients' viewpoint, medications prescribed over an extended time period are difficult to change; however, patients with significant health issues resulting in hospital admission might more constructively consider accepting changes in their regular medications. At the same time, doctors may take this opportunity to adjust the patient's medication because it is much easier to detect and treat any deterioration in the patient's condition after changing medication. Consequently, hospitalization of patients resulted in reducing the use of PIMs in this study. Fur-

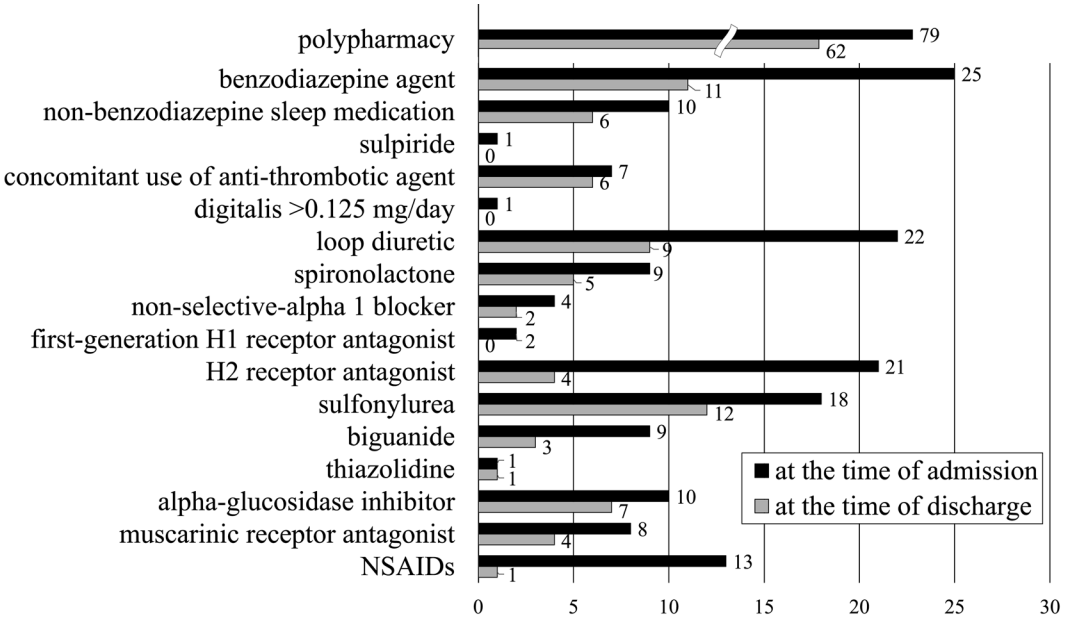

Figure 2 List of potentially inappropriate medications evaluated in this study. The horizontal axis indicates the number of persons prescribed potentially inappropriate medications. The number of polypharmacy and most of the unfavorable medications decreased at the time of discharge. NSAIDs: non-steroidal anti-inflammatory drugs.

Table 2 Factors associated with potentially inappropriate medications on admission

	Univariate analyses			Multivariate analysis		
	PIMs (+)	PIMs (−)				
Number (%)	101 (51.3%)	96 (48.7%)	p. value	OR	95% CI	p. value
Age	79.42	74.29	< 0.01**	1.08	1.03–1.13	< 0.01**
Male	53 (52.5%)	56 (58.3%)	0.474	1.20	0.58–2.49	0.624
Frailty	22 (21.8%)	8 (8.3%)	0.010*	2.24	0.78–6.40	0.133
Liv. w. family mem.	42 (41.6%)	43 (44.8%)	0.668	0.88	0.44–1.74	0.706
General practitioner	63 (62.4%)	36 (37.5%)	< 0.01**	1.44	0.72–2.89	0.300
Num. of prescribers	1.49 (0–4)	0.78 (0–3)	< 0.01**	6.16	3.09–12.3	< 0.01**
mRS on ad. Ave.	3.57	3.44	0.703	1.07	0.73–1.56	0.745
0	0 (0.0%)	1 (1.0%)				
1	4 (4.0%)	3 (3.1%)				
2	7 (6.9%)	10 (10.4%)				
3	22 (21.8%)	26 (27.1%)				
4	63 (62.4%)	51 (53.1%)				
5	5 (5%)	5 (5.2%)				

*p < 0.05, **p < 0.01. PIM: potentially inappropriate medication; OR: odds ratio; CI: confidence interval; Liv. w. family mem.: living with family members aged < 64 years; Num.: number; mRS on ad. Ave.: modified Rankin Scale score on admission; ave.: average.

thermore, Japan's public health insurance system recently began rewarding hospitals with the payment of a medical adjustment fee (Yakuzai-Sougou-Hyouka-Chousei-Kasan for inpatients and Yakuzai-Sougou-Hyouka-Chousei-Kanriryou for outpatients) when reducing ≥ 2 medications in patients prescribed ≥ 6 medications. In the present study, 40 patients (20.3%) became eligible for this adjustment fee; when limited to patients with polypharmacy on admission, as many as 50.6% (40 out of 79) of patients met the criteria. Therefore, hospitalization is an optimal opportunity for reconsidering the necessity of prescription medicines.

In previous studies in Japan, the mean age of patients

Table 3 Factors associated with good outcomes

	Univariate analyses			Multivariate analyses					
Outcome	Good	Poor		Unadjusted			Adjusted		
Number (%)	148 (75.1%)	49 (24.9%)	p. value	OR	95% CI	p. value	OR	95% CI	p. value
Age	74.99	82.73	< 0.01**	0.91	0.86–0.96	< 0.01**	0.92	0.87–0.98	< 0.01**
Male	91 (61.5%)	18 (36.7%)	< 0.01**	1.44	0.61–3.41	0.402	1.65	0.67–4.04	0.274
Frailty	8 (5.4%)	22 (44.9%)	< 0.01**	0.15	0.05–0.41	< 0.01**	0.16	0.06–0.47	< 0.01**
Liv. w. family mem.	70 (47.3%)	15 (30.6%)	0.047*	2.52	1.04–6.10	0.041*	2.34	0.95–5.76	0.066
PIMs	67 (45.3%)	34 (69.4%)	< 0.01**	0.74	0.31–1.77	0.499	0.85	0.34–2.08	0.716
Tubal feeding	9 (6.1%)	11 (22.4%)	< 0.01**	0.30	0.10–0.95	0.040*	0.30	0.09–0.99	0.048*
Any surgery	35 (23.6%)	6 (12.2%)	0.106	2.76	0.84–9.01	0.093	2.76	0.84–9.10	0.096
mRS on ad. average	3.37	3.92	< 0.01**	0.48	0.25–0.92	0.028*	0.40	0.20–0.80	< 0.01**
0	1 (0.7%)	0 (0.0%)							
1	7 (4.7%)	0 (0.0%)							
2	17 (11.5%)	0 (0.0%)							
3	42 (28.4%)	6 (12.2%)							
4	73 (49.3%)	41 (83.7%)							
5	8 (5.4%)	2 (4.1%)							

A good outcome is defined as returning home or transfer to a rehabilitation hospital at the time of discharge. The multivariate analysis was adjusted with modified Charlson comorbidity index. PIM exposure at the time of admission showed significance in the univariate analysis, but not in the multivariate analyses. Good outcomes were negatively associated with the patients' age, frailty, requirement of tubal feeding, and mRS score on admission. * $p < 0.05$, **$p < 0.01$. OR: odds ratio; CI: confidence interval; Liv. w. family mem.: living with family members aged < 64 years; PIMs: potentially inappropriate medications; mRS on ad.: modified Rankin Scale score on admission.

was 76.9–84.9 years, and the mean number of medications used per patient was 4.7–6.4[12–16]; this finding was similar to the conditions in the present study (mean age, 76.9 years; mean number of medications on admission, 5.04). Based on the ATC classification system, medications categorized as codes "A" and "C" were most commonly found at the time of admission (Figure 1B), which was not surprising because approximately 60% of patients in this study were hospitalized for acute stroke, and stroke patients often have comorbidities such as hypertension or diabetes mellitus. One cannot argue the importance of treating these conditions; however, the appropriateness of medication should be considered before prescribing prophylactic medications, such as antihypertensive agents or statins, to elderly patients. These medications require several years to realize their benefit[17]. Conversely, underprescribing appropriate medications is also a concern. Some studies suggested that the underutilization of medications was equal to, or even more prevalent than, overprescribing inappropriate medications[18, 19]. This study did not evaluate underutilization of medications. However, the fact that the number of code "B" medications increased at the time of discharge suggests that the required medications (e.g., antithrombotic agents for patients who suffered a stroke) were prescribed if necessary.

Previous surveys reviewing PIMs prescribed to Japanese patients aged ≥ 65 years revealed that they were prescribed to 37.5–56.1%[12, 13, 16] of patients based on the Beers Criteria and 40.4%[15] of patients based on STOPP. A report assessing PIMs according to "the safety guideline, 2015" found that the prevalence of PIM prescription was 69.9%[14], which was higher than that reported in the present study (51.3%). We attributed this result to the difference in the mean age (80.4 vs 76.9 years) and prescription history (only outpatients using medications vs including patients not using medication). This study evaluated PIMs based on the quality (ie, drugs to be prescribed with special caution) and quantity (i.e., polypharmacy) of medications. Originally, polypharmacy was defined as the use of multiple medications by a patient. However, multiple medications are often required to manage clinically-complex older adults; therefore, polypharmacy itself is not necessarily inappropriate. There is a concept of "appropriate polypharmacy", in which patients can benefit from the prescription of multiple medications provided the prescription is evidence-based, reflects patients' clinical conditions, and considers potential drug interactions[20]. We included polypharmacy into our PIM criteria because some reports indicated that it has been associated with increased risk of adverse drug events[21], drug-drug interactions[22], emergency department visits or admissions[23], fall and hip fractures[24], malnutrition[25], and prolonged lengths of hospital stay with increased economic burden and mortality[26]. The exact minimum number of medications used to define polypharmacy is not officially determined. However, previous studies in Japan as well as the Ministry of Health,

Labour and Welfare of Japan have defined polypharmacy as ≥ 6 concurrent used medications. Therefore, we adopted the same threshold.

Our study further supports the existing data that multiple prescribers were independently associated with PIM exposure on admission[27]. General practitioners tend to prescribe numerous medications leading to polypharmacy[28]; however, contrary to our expectations, medications prescribed by general practitioners were not a significant factor of PIMs in the present study. We did not find significant association between PIM exposure on admission and good outcomes through multivariate analysis. Most reports on the association between PIMs and outcomes or mortality revealed that they were not significantly associated. A systematic review of 18 retrospective cohort studies found that PIM, defined by the Beers Criteria, was associated with increased hospitalization rates but not mortality in patients aged ≥ 65 years in the community setting[29]. Only few studies identified correlations between PIMs and mortality or good outcomes assessed based on the Drug Burden Index[30, 31]. Further studies are needed to explain this issue.

Among PIMs, the number of H2RA and NSAIDs drastically declined during the hospital stay, which was attributed to the cessation of potentially unnecessary medications, switching of prescriptions to per-request usage, or existence of safer alternative medications. The most prevalent PIMs in this study were benzodiazepine agents, which accounted for 21.5% of PIMs when calculated with non-benzodiazepine hypnotics. Some patients were on ≥ 2 concomitant benzodiazepine class medications. The number of prescribed benzodiazepines in Japan is much higher than that in the USA. This difference is partly because of various benzodiazepines available in Japan, and the national insurance and medical reimbursement systems allow continued prescription renewal with minimal charge to patients[16]. Patients who have been taking benzodiazepine agents for a long period are sometimes addicted to the medication; however, new classes of hypnotics (e.g., melatonin receptor agonists and dual orexin receptor antagonists) have been launched in Japan. We hope that these medications will help patients to be free of benzodiazepines.

Although many studies and reports have been conducted on PIMs, most were assessed using the Beers Criteria or STOPP and are, in part, not applicable to the medical environment in Japan. To the best of our knowledge, this is the first study to evaluate PIMs in elderly neurosurgical inpatients assessed by "the safety guideline, 2015". This study illustrates the importance of pharmaceutical management during the patients' hospital stay by comparing regular medications prescribed to elderly Japanese patients before and after hospitalization. We believe that the present study provides valuable information to healthcare problems in elderly Japanese patients.

This study has several limitations. This was conducted in two institutions only, was limited to neurosurgical patients, and is not representative of the general population in Japan. The retrospective design may also introduce information bias. Furthermore, patients were not followed up after discharge; therefore, long-term outcomes and medication use were unclear. Finally, medication changes and drug preferences during the patients' hospitalization were at the discretion of the primary doctor; therefore, better options for medications could have been possible.

Conclusion

We evaluated PIMs in elderly neurosurgical inpatients and revealed that more than half of them were exposed to PIMs on admission. The prevalence of PIMs decreased by 12.2% at the time of discharge. Hospitalization is an optimal opportunity for reconsidering the necessity of medications and for changing the prescriptions according to the patients' conditions. Every doctor, including surgeons, must take an interest in pharmaceutical management of patients and strive to avoid PIMs.

Conflict of Interest: The authors declare to have no conflicts of interest.

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References

1. Cho S, Lau SW, Tandon V, *et al*. Geriatric drug evaluation: where are we now and where should we be in the future? Arch Intern Med 2011; 171: 937–940. [Medline] [CrossRef]
2. Spinewine A, Schmader KE, Barber N, *et al*. Appropriate prescribing in elderly people: how well can it be measured and optimised? Lancet 2007; 370: 173–184. [Medline] [CrossRef]
3. Beers MH, Ouslander JG, Rollingher I, *et al*. UCLA Division of Geriatric Medicine. Explicit criteria for determining inappropriate medication use in nursing home residents. Arch Intern Med 1991; 151: 1825–1832. [Medline] [CrossRef]
4. Gallagher P, Ryan C, Byrne S, *et al*. STOPP (Screening Tool of Older Persons Prescriptions) and START (Screening Tool to

Alert doctors to Right Treatment). Consensus validation. Int J Clin Pharmacol Ther 2008; 46: 72–83. [Medline] [CrossRef]
5. Hilmer SN, Mager DE, Simonsick EM, *et al*. A drug burden index to define the functional burden of medications in older people. Arch Intern Med 2007; 167: 781–787. [Medline] [CrossRef]
6. Kojima T, Mizukami K, Tomita N, *et al*. Working Group on Guidelines for Medical Treatment and its Safety in the Elderly. Screening tool for older persons appropriate prescriptions for Japanese: Report of the Japan Geriatrics Society Working Group on Guidelines for medical treatment and its safety in the elderly. Geriatr Gerontol Int 2016; 16: 983–1001. [Medline] [CrossRef]
7. The Japan Geriatrics Society Working Group on "Guidelines for Medical Treatment and its Safety in the Elderly." Guidelines for medical treatment and its safety in the elderly. 1st ed. Tokyo: Medicalview-sya2015.
8. Fried LP, Tangen CM, Walston J, *et al*. Cardiovascular Health Study Collaborative Research Group. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci 2001; 56: M146–M156. [Medline] [CrossRef]
9. The selection and use of essential medicines. Report of the WHO expert committee, 2005 (including the 14th model list of essential medicines). World Health Organ Tech Rep Ser 2006; 1–119. [Medline]
10. Quan H, Li B, Couris CM, *et al*. Updating and validating the Charlson comorbidity index and score for risk adjustment in hospital discharge abstracts using data from 6 countries. Am J Epidemiol 2011; 173: 676–682. [Medline] [CrossRef]
11. Kanda Y. Investigation of the freely available easy-to-use software EZR for medical statistics. Bone Marrow Transplant 2013; 48: 452–458. [Medline] [CrossRef]
12. Ishii S, Kojima T, Ezawa K, *et al*. The association of change in medication regimen and use of inappropriate medication based on beers criteria with adverse outcomes in Japanese long-term care facilities. Geriatr Gerontol Int 2017; 17: 591–597. [Medline] [CrossRef]
13. Sakuma M, Morimoto T, Matsui K, *et al*. Epidemiology of potentially inappropriate medication use in elderly patients in Japanese acute care hospitals. Pharmacoepidemiol Drug Saf 2011; 20: 386–392. [Medline] [CrossRef]
14. Komiya H, Umegaki H, Asai A, *et al*. Factors associated with polypharmacy in elderly home-care patients. Geriatr Gerontol Int 2018; 18: 33–41. [Medline]
15. Hamano J, Tokuda Y. Inappropriate prescribing among elderly home care patients in Japan: prevalence and risk factors. J Prim Care Community Health 2014; 5: 90–96. [Medline] [CrossRef]
16. Onda M, Imai H, Takada Y, *et al*. Identification and prevalence of adverse drug events caused by potentially inappropriate medication in homebound elderly patients: a retrospective study using a nationwide survey in Japan. BMJ Open 2015; 5: e007581. [Medline] [CrossRef]
17. Holmes HM, Hayley DC, Alexander GC, *et al*. Reconsidering medication appropriateness for patients late in life. Arch Intern Med 2006; 166: 605–609. [Medline] [CrossRef]
18. Higashi T, Shekelle PG, Solomon DH, *et al*. The quality of pharmacologic care for vulnerable older patients. Ann Intern Med 2004; 140: 714–720. [Medline] [CrossRef]
19. Steinman MA, Landefeld CS, Rosenthal GE, *et al*. Polypharmacy and prescribing quality in older people. J Am Geriatr Soc 2006; 54: 1516–1523. [Medline] [CrossRef]
20. Cadogan CA, Ryan C, Hughes CM. Appropriate Polypharmacy and Medicine Safety: When Many is not Too Many. Drug Saf 2016; 39: 109–116. [Medline] [CrossRef]
21. Nguyen JK, Fouts MM, Kotabe SE, *et al*. Polypharmacy as a risk factor for adverse drug reactions in geriatric nursing home residents. Am J Geriatr Pharmacother 2006; 4: 36–41. [Medline] [CrossRef]
22. Weng MC, Tsai CF, Sheu KL, *et al*. The impact of number of drugs prescribed on the risk of potentially inappropriate medication among outpatient older adults with chronic diseases. QJM 2013; 106: 1009–1015. [Medline] [CrossRef]
23. Lu WH, Wen YW, Chen LK, *et al*. Effect of polypharmacy, potentially inappropriate medications and anticholinergic burden on clinical outcomes: a retrospective cohort study. CMAJ 2015; 187: E130–E137. [Medline] [CrossRef]
24. Kojima T, Akishita M, Kameyama Y, *et al*. Factors associated with prolonged hospital stay in a geriatric ward of a university hospital in Japan. J Am Geriatr Soc 2012; 60: 1190–1191. [Medline] [CrossRef]
25. Ramgoolie P, Nichols S. Polypharmacy and the Risk of Malnutrition among Independently-living Elderly Persons in Trinidad. West Indian Med J 2015; 65: 323–327. [Medline]
26. Wang R, Chen L, Fan L, *et al*. Incidence and Effects of Polypharmacy on Clinical Outcome among Patients Aged 80+: A Five-Year Follow-Up Study. PLoS ONE 2015; 10: e0142123. [Medline] [CrossRef]
27. Green JL, Hawley JN, Rask KJ. Is the number of prescribing physicians an independent risk factor for adverse drug events in an elderly outpatient population? Am J Geriatr Pharmacother 2007; 5: 31–39. [Medline] [CrossRef]
28. Walckiers D, Van der Heyden J, Tafforeau J. Factors associated with excessive polypharmacy in older people. Arch Public Health 2015; 73: 50. [Medline] [CrossRef]
29. Jano E, Aparasu RR. Healthcare outcomes associated with beers criteria: a systematic review. Ann Pharmacother 2007; 41: 438–447. [Medline] [CrossRef]
30. Sköldunger A, Fastbom J, Wimo A, *et al*. Impact of Inappropriate Drug Use on Hospitalizations, Mortality, and Costs in Older Persons and Persons with Dementia: Findings from the SNAC Study. Drugs Aging 2015; 32: 671–678. [Medline] [CrossRef]
31. Floroff CK, Slattum PW, Harpe SE, *et al*. Potentially inappropriate medication use is associated with clinical outcomes in critically ill elderly patients with neurological injury. Neurocrit Care 2014; 21: 526–533. [Medline] [CrossRef]