

[ORIGINAL ARTICLE]

Multidisciplinary Team Deprescribing Intervention for Polypharmacy in Elderly Orthopedic Inpatients: A Propensity Score-matched Analysis of a Retrospective Cohort Study

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Abstract:

Objective This study evaluated the effectiveness of a multidisciplinary team deprescribing intervention to reduce polypharmacy and potentially inappropriate medications (PIMs) in elderly orthopedic inpatients.

Methods In this single-center retrospective observational study, orthopedic inpatients ≥ 75 years old and prescribed ≥ 6 different medications were enrolled as participants. Interventions comprised multidisciplinary team-led polypharmacy screening and suggestions regarding deprescribing any unnecessary medications during hospital stays. The primary outcome was reduction in the mean number of regular medicines and PIMs. Secondary outcomes included falls, delirium, and other adverse events during hospitalization as well as emergency department visits or unplanned hospital admissions within six months after discharge.

Results After propensity score matching, 184 patients (intervention group, $n=92$; control group, $n=92$) were included in the analysis. The mean patient age was 83 years old. The mean number of prescribed medications and PIMs at admission were similar in both groups. The mean change in the number of regular medicines was -1.4 [standard deviation (SD), 2.3] in the intervention group and $+0.2$ (SD, 1.8) in the control group ($p < 0.001$). The mean change in the number of PIMs was -0.5 (SD, 0.9) in the intervention group and $+0.1$ (SD, 0.8) in the control group ($p < 0.001$). In-hospital adverse events other than falls and delirium were significantly less common in the deprescribing intervention group than in the control group.

Conclusion Deprescribing intervention by our multidisciplinary team seems to have been effective in reducing the number of prescribed medicines and PIMs in elderly orthopedic inpatients, with some accompanying reduction in certain adverse events.

Key words: deprescription, aged, orthopedics, polypharmacy, potentially inappropriate medication

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Introduction

Hospital admission of elderly patients is increasing rapidly as the population ages. In Japan, people ≥ 65 years old, who constitute 29% of the population, account for as much as 73% of hospitalizations (1, 2). There is a known tendency toward multimorbidity and polypharmacy in elderly pa-

tients (3, 4). Approximately 40% of Japanese patients ≥ 75 years old regularly take ≥ 5 medications (5). Polypharmacy in elderly patients is associated with an increased risk of potentially inappropriate medicines (PIMs) (6) and adverse outcomes, including falls (7), delirium (8), and adverse drug events (9).

Among elderly orthopedic patients who suffer falls or hip fractures, polypharmacy is especially common (10, 11), and

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it often continues or even increases during and after hospitalization. In one observational study that included elderly patients presenting to the emergency department (ED) with falls, polypharmacy was observed in 63% of patients. It was strongly associated with PIMs [odds ratio (OR), 4.0; 95% confidence interval (CI), 3.0-5.3] (10). In addition, 53% of patients had at least one PIM defined by the Screening Tool of Older Person's Potentially Inappropriate Prescription (STOPP) criteria (12) before falling, and there were no substantial improvements in the prevalence of polypharmacy and PIMs at 12 months post-fall.

Growing evidence has shown that deprescribing intervention in elderly hospitalized patients helps improve polypharmacy (13-15). Most studies have been conducted in internal medicine or geriatric wards, although few have investigated the effectiveness of interventions specifically for orthopedic inpatients (16-19). In addition, there is inconsistency concerning whether or not patient-important outcomes, such as falls, mortality and readmission, are improved by these interventions in the inpatient setting, including within orthopedic wards (13-19). A physician-led medication review did not significantly decrease treatment with fall-risk-increasing drugs or patient-important outcomes, such as falls, in a randomized controlled trial comprising elderly hospitalized patients with hip fracture (17).

Deprescribing interventions by a multidisciplinary team (MDT) might reduce the number of drugs and PIMs and improve clinical outcomes in orthopedic inpatients. However, supporting evidence is needed, especially data specific to elderly patients. Therefore, the present study investigated whether or not deprescription by an MDT during hospitalization reduced the number of prescribed medicines and PIMs and whether or not deprescription affected clinically important outcomes in elderly orthopedic patients.

Materials and Methods

Study design and participants

This retrospective observational study was conducted at Akashi Medical Center, a 383-bed acute care hospital in Hyogo, Japan. The hospital staff does not include geriatricians or ortho-geriatricians. The study included all consecutive patients ≥ 75 years old who were discharged from the orthopedic department and prescribed ≥ 6 medications at admission between May 2017 and April 2019. The age criterion was determined based on the fact that polypharmacy is more prevalent in patients ≥ 75 years old than in younger ones (5) and the feasibility of intervention. PIMs mostly refer to medications that patients take on a regular basis. As-needed medications and those taken infrequently were therefore excluded from this study. Eye drops, ear drops, intranasal infusers, topical medications, and over-the-counter drugs were also excluded from consideration. Finally, patients were also excluded from analysis if their admission was for palliative care, if the length of the hospital stay was less

than one week, or if they died in the hospital. Enrolled subjects were then divided into a control (May 2017 to April 2018) and intervention groups (May 2018 to April 2019).

Control group

Deprescribing intervention was not conducted systematically, but a comprehensive list of prescribed medications was routinely compiled by pharmacists after admission. Pharmacists' suggestions about deprescribing medications were not given to the orthopedic surgeons unless there were contraindications or apparent adverse effects due to the medications. Orthopedic surgeons conducted both perioperative and postoperative care for patients until discharge. In addition, they provided care for non-surgical patients, such as those with compression fracture. Medication management during hospitalization was also performed by orthopedic surgeons. However, medically complicated patients, such as those with poorly controlled diabetes and heart failure, required consultation with internal medicine physicians or specialists as needed. After discharge, orthopedic physicians routinely followed up most patients for at least the first six months.

Intervention group

Beginning in May 2018, our hospital instituted a deprescribing intervention by an MDT to reduce inappropriate medications for orthopedic inpatients ≥ 75 years old as a new standard of care. Polypharmacy does not have a universal standard definition, and reported definitions range between cases prescribed ≥ 2 to ≥ 11 medicines (20). We selected ≥ 6 medications as the screening criterion because reimbursements can be applied when there is a reduction of at least two medications in patients taking six or more regular medications according to the Japanese medical insurance system. The number of medications was checked based on a comprehensive collection of the medication history by pharmacists in routine care (Fig. 1). If patients met the above eligibility criteria, pharmacists contacted the patients and their families regarding deprescription. If consent was obtained, patients received MDT intervention. If MDT intervention was refused, the MDT did not assess the appropriateness of the medications or propose deprescription.

The MDT included general internal medicine (GIM) physicians, pharmacists, ward nurses, and a nurse certified in dementia nursing. Team meetings and rounds were held once per week. The medical history was obtained from the patients themselves and their charts, and physical and neurological examinations were performed by GIM physicians as needed. Pharmacists listed prescribed medications and checked PIMs. Ward nurses checked for any changes in symptoms and findings and ascertained whether or not patients had personal preferences concerning medication. The certified nurse mainly assessed patients for changes in their cognitive function, symptoms of delirium, and the impact of the medications on these symptoms. At the weekly meeting, the MDT discussed the appropriateness of polypharmacy,

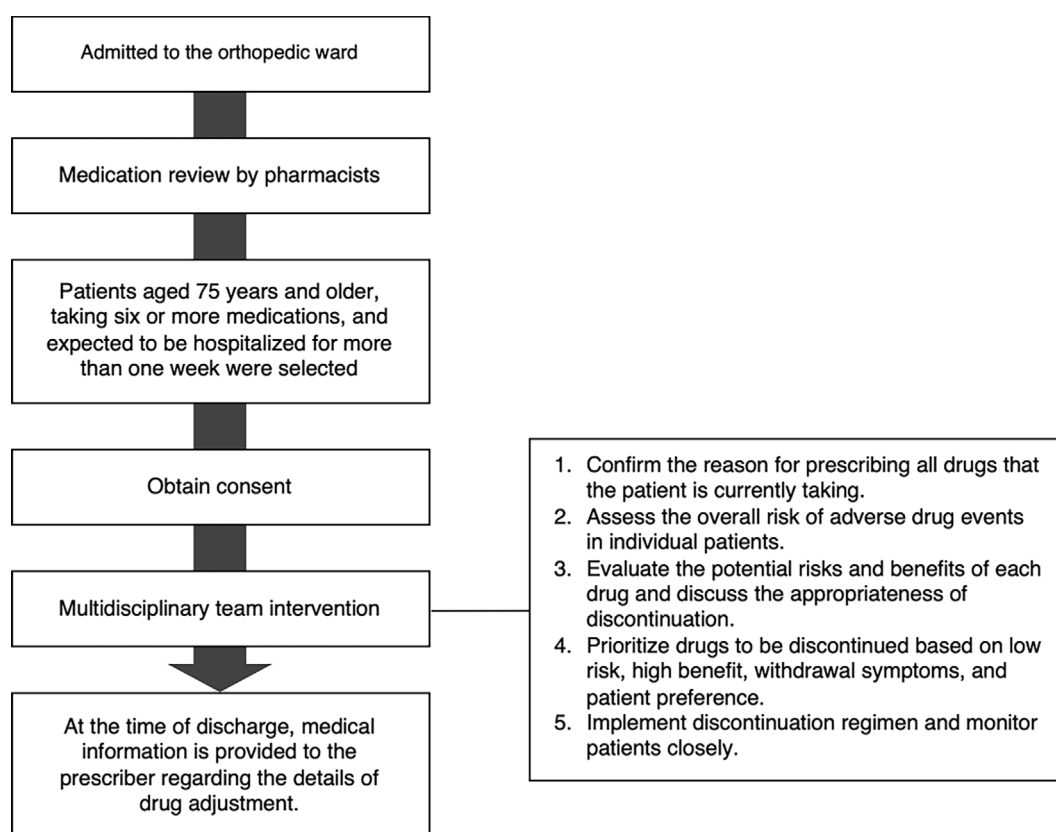


Figure 1. Flow of the deprescribing intervention performed by the multidisciplinary team.

and GIM physicians decided on whether to propose deprescription or a change in medications to orthopedic surgeons.

The appropriateness of medications was evaluated based on the deprescribing protocol (Fig. 2) (21). First, all drugs the patient was currently taking and the reasons for each of them were ascertained. To determine the required intensity of deprescribing intervention, the overall risk of drug-induced harm was considered in individual patients. Each drug was then assessed for its eligibility to be discontinued. Drugs were prioritized for discontinuation, and then the drug discontinuation regimen was suggested and monitored. The final decision to stop, change, or continue medications was made based on a proposal by orthopedic doctors. The MDT followed up all eligible patients until discharge, regardless of whether or not any drugs were ceased.

Data collection

Data were collected and examined by two physicians (H. S. and J.O.) using the electronic medical records of our hospital, both of whom were involved in the MDT intervention. Parameters were selected that were associated with the prognosis and adverse events, comprising the age, sex, reason for admission, surgery or non-surgery, medical history, Charlson Comorbidity Index (22), activities of daily living measured by Barthel index (23), and medications.

Outcome measures

The primary outcome was the change in the mean number of regular medicines and reduction in PIMs. PIMs were de-

finied based on the 2015 Beers Criteria of the American Geriatric Society (24). Secondary outcomes included falls, delirium, and any other adverse events during hospitalization, as well as ED visits or unplanned hospital admissions for any reason within six months after discharge. Delirium was considered using the criteria from the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (25). Prescribed medication classes were also analyzed at both admission and discharge, with classification based on major therapeutic classes used in previous studies. These classes included angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, statins, proton-pump inhibitors (PPIs) and benzodiazepines/Z drugs (zolpidem, zopiclone, and eszopiclone) (18, 26).

Statistical analyses

Propensity score matching was used to control and balance the patients' baseline characteristics and confounders at the time of admission. Propensity scores were estimated using a logistic regression model with the following as covariates: age, sex, reason for admission (osteoarthritis, spinal stenosis, hip fracture, vertebral fracture, others), surgery, diabetes mellitus, hypertension, dyslipidemia, coronary artery disease, heart failure, atrial fibrillation, pulmonary disease, liver disease, stroke, dementia, chronic kidney disease, malignancy, Charlson comorbidity index, and Barthel index. As the propensity score matching algorithm, nearest-neighbor matching with a 1:1 ratio without replacement was performed using a caliper of 0.05 on the propensity score scale.

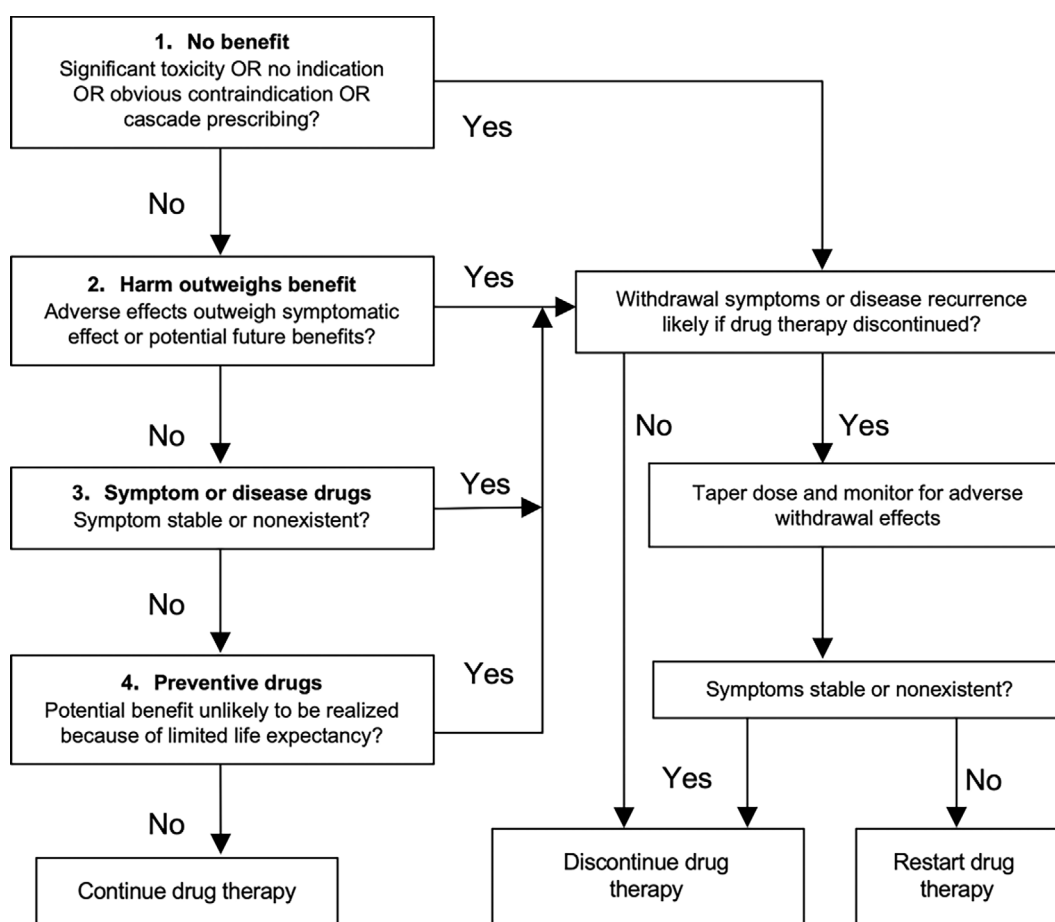


Figure 2. Deprescribing algorithm (21).

Continuous variables were reported as the mean [standard deviation (SD)] with 95% CIs, and differences were analyzed using the two-sample *t*-test. Categorical variables were reported as frequencies and percentages, and differences were analyzed using Fisher's exact test. *p* values for all tests were reported, and *p*<0.05 was considered to be significant. All statistical analyses were conducted using the JMP Pro software program, ver. 14.2.0 (SAS Institute, Cary, USA).

Ethical approval and registration

This study was approved by the Akashi Medical Center Research Ethics Committee. The need for informed consent was waived. This study was registered at the University Hospital Medical Information Network Clinical Trials Registry (UMIN-CTR) with the trial number UMIN000039920 (UMIN-CTR URL: <http://www.umin.ac.jp/ctr/index.htm>).

Results

Baseline characteristics

During the study period, 276 patients (intervention group: 123, control: 153) met the selection criteria (Fig. 3), their characteristics are shown in Table 1. In the intervention group, eight patients refused MDT intervention. The mean age of the patients was 84 years old (SD, 5.8). Patients in

the intervention group were more likely to have atrial fibrillation, respiratory disease, and chronic kidney disease than those in the control group. After propensity score matching, 184 patients (intervention group, *n*=92; control group, *n*=92) were included. The patient characteristics in the intervention and control groups were similar (Table 1). In the intervention group, seven patients refused intervention; three because of short hospital stay, two because of anxiety, one because they were satisfied with the prescription, and one without any particular reason. For the 85 patients who agreed to the intervention, 254 suggestions were made, and 230 (90.6%) were implemented by orthopedic surgeons.

Number of prescribed medications and PIMs

The mean number of prescribed medications and PIMs at admission were also similar between the groups [9.4 (SD, 2.6) and 1.5 (SD, 1.2) in the intervention group vs 9.5 (SD, 2.7) and 1.7 (SD, 1.2) in the control group, respectively] (Table 2). The mean number of prescribed medications at discharge was significantly smaller in the intervention group than in the control group [8.0 (SD, 3.2) vs 9.7 (SD, 2.7), *p*<0.001]. The mean number of PIMs at discharge was significantly smaller in the intervention group than in the control group [1.0 (SD, 1.0) vs 1.6 (SD, 1.2), *p*<0.001]. The characteristics of PIMs at admission and at discharge in each group are shown in Table 3. The most common PIMs were

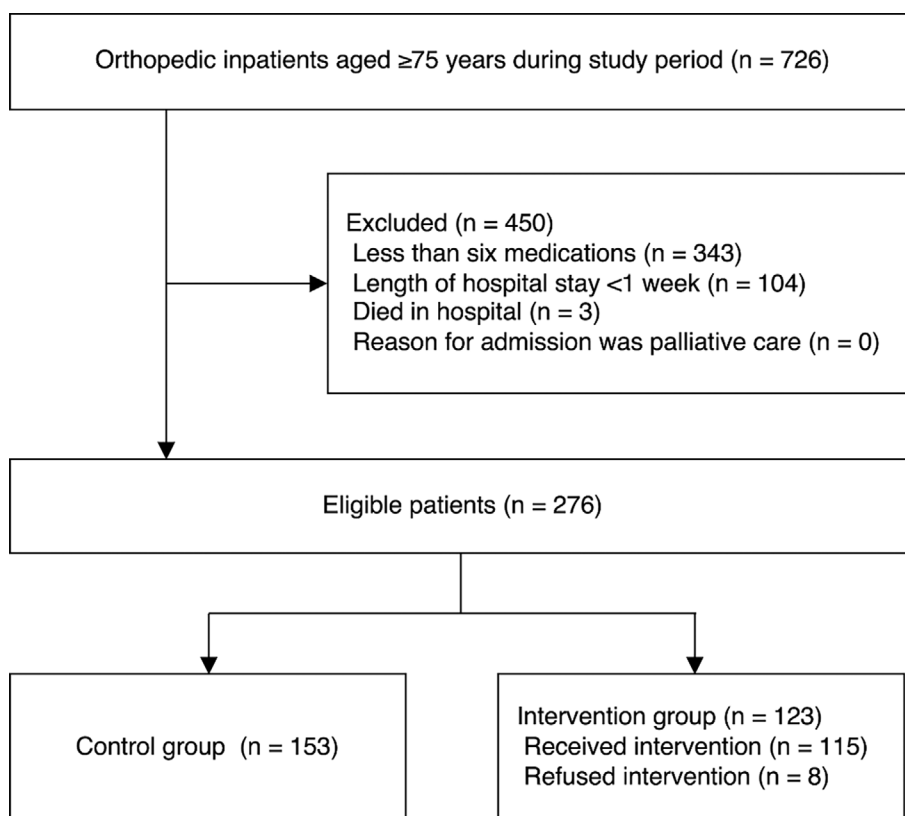


Figure 3. Flow diagram of study participants.

Table 1. Baseline Characteristics before and after 1:1 Propensity Score Matching.

Characteristics	Before matching			After matching		
	Intervention group N=123	Control group N=153	p value	Intervention group N=92	Control group N=92	p value
Age (y), mean (SD)	84 (5.8)	84 (5.9)	0.76	83 (5.6)	84 (5.8)	0.80
Female, n (%)	97 (79)	113 (74)	0.40	75 (82)	74 (80)	>0.99
Reason for admission, n (%)						
Osteoarthritis	16 (13)	20 (13)	0.89	12 (13)	11 (12)	0.92
Spinal stenosis	17 (14)	20 (13)		13 (14)	13 (14)	
Hip fracture	54 (44)	64 (42)		42 (46)	42 (46)	
Vertebral fracture	7 (5.7)	14 (9.2)		4 (4.3)	7 (7.6)	
Others	29 (24)	35 (23)		21 (23)	19 (21)	
Surgery, n (%)	107 (87)	133 (87)	>0.99	84 (91)	81 (88)	0.63
Comorbid conditions, n (%)						
Diabetes mellitus	36 (29)	36 (24)	0.34	24 (26)	21 (23)	0.73
Hypertension	98 (80)	120 (78)	0.88	78 (85)	69 (75)	0.14
Dyslipidemia	57 (46)	60 (39)	0.27	42 (46)	38 (41)	0.66
CAD	13 (11)	14 (9.2)	0.69	7 (7.6)	8 (8.7)	>0.99
Heart failure	21 (17)	22 (14)	0.62	13 (14)	14 (15)	>0.99
Atrial fibrillation	23 (19)	15 (9.8)	0.036	11 (12)	13 (14)	0.83
Pulmonary disease	12 (9.8)	30 (20)	0.028	9 (9.8)	10 (11)	>0.99
Liver disease	8 (6.5)	4 (2.6)	0.14	2 (2.2)	3 (3.3)	>0.99
Stroke	27 (22)	33 (22)	>0.99	19 (21)	19 (21)	>0.99
Dementia	31 (25)	37 (24)	0.89	23 (25)	25 (27)	0.87
CKD	90 (73)	93 (61)	0.040	61 (66)	64 (70)	0.75
Malignancy	27 (22)	27 (18)	0.45	14 (15)	14 (15)	>0.99
CCI, mean (SD)	2.0 (1.9)	1.9 (1.8)	0.73	1.6 (1.6)	1.7 (1.4)	0.81
Barthel index, mean (SD)	76 (28)	74 (29)	0.55	74 (29)	75 (28)	0.88

CAD: coronary artery disease, CCI: Charlson comorbidity Index, CKD: chronic kidney disease

Table 2. Regular Medicines and PIMs at Admission and Discharge in the Study Group.

Outcomes	Intervention group N=92	Control group N=92	p value
Number of regular medicines, mean (SD)			
Admission	9.4 (2.6)	9.5 (2.7)	0.85
Discharge	8.0 (3.2)	9.7 (2.7)	<0.001
Change from admission to discharge	-1.4 (2.3)	+0.2 (1.8)	<0.001
Number of PIMs, mean (SD)			
Admission	1.5 (1.2)	1.7 (1.2)	0.40
Discharge	1.0 (1.0)	1.6 (1.2)	<0.001
Change from admission to discharge	-0.5 (0.9)	-0.1 (0.8)	<0.001

PIMs: potentially inappropriate medications

Table 3. Characteristics of PIMs at Admission and at Discharge in the Study Group.

Drug category		Intervention group		Control group	
		at admission	at discharge	at admission	at discharge
Benzodiazepines/Z drugs ^a , n (%)	0	58 (63.0)	71 (77.2)	58 (63.0)	62 (67.4)
	1	21 (22.8)	20 (21.7)	28 (30.4)	24 (26.1)
	2	12 (13.0)	1 (1.1)	5 (5.4)	6 (6.5)
	3	1 (1.1)	0 (0.0)	1 (1.1)	0 (0.0)
NSAIDs, n (%)	0	75 (81.5)	85 (92.4)	70 (76.1)	76 (82.6)
	1	17 (18.5)	7 (7.6)	22 (23.9)	16 (17.4)
PPIs, n (%)	0	45 (48.9)	46 (50.0)	46 (50.0)	40 (43.5)
	1	47 (51.1)	46 (50.0)	45 (48.9)	52 (56.5)
	2	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
Antipsychotics, n (%)	0	83 (90.2)	84 (91.3)	78 (84.8)	79 (85.9)
	1	8 (8.7)	7 (7.6)	10 (10.9)	10 (10.9)
	2	1 (1.1)	1 (1.1)	3 (3.3)	2 (2.2)
	3	0 (0.0)	0 (0.0)	1 (1.1)	1 (1.1)
TCAs, n (%)	0	89 (96.7)	91 (98.9)	90 (97.8)	90 (97.8)
	1	3 (3.3)	1 (1.1)	2 (2.2)	2 (2.2)
Sulfonylureas, n (%)	0	87 (94.6)	89 (96.7)	85 (92.4)	85 (92.4)
	1	5 (5.4)	3 (3.3)	7 (7.6)	7 (7.6)
H2-receptor antagonists ^b , n (%)	0	90 (97.8)	91 (98.9)	86 (93.5)	86 (93.5)
	1	2 (2.2)	1 (1.1)	6 (6.5)	6 (6.5)
SSRIs, n (%)	0	88 (95.7)	89 (96.7)	91 (98.9)	91 (98.9)
	1	4 (4.3)	3 (3.3)	1 (1.1)	1 (1.1)
Digoxin, n (%)	0	91 (98.9)	92 (100.0)	88 (95.7)	88 (95.7)
	1	1 (1.1)	0 (0.0)	4 (4.3)	4 (4.3)
Peripheral alpha-1 blockers, n (%)	0	91 (98.9)	91 (98.9)	87 (94.6)	87 (94.6)
	1	1 (1.1)	1 (1.1)	5 (5.4)	5 (5.4)
Others, n (%)	0	88 (95.7)	90 (97.8)	90 (97.8)	90 (97.8)
	1	4 (4.3)	2 (2.2)	2 (2.2)	2 (2.2)

NSAIDs: non-steroidal anti-inflammatory drugs, PIMs: potentially inappropriate medications, PPIs: proton pump inhibitors, SSRIs: selective serotonin reuptake inhibitors, TCAs: tricyclic antidepressants

^aZ drugs included zopiclone, eszopiclone, zolpidem.^bOnly H2-receptor antagonists used for patients with dementia and delirium were included.

benzodiazepines/Z drugs, PPIs, and non-steroidal anti-inflammatory drugs (NSAIDs). The intervention group had a significantly higher discontinuation rate of PIMs than the control group [37/92 (40%) in the intervention group vs 19/92 (21%) in the control group; OR, 2.6; 95% CI, 1.3 to 5.3; p=0.006].

Adverse outcomes

No significant differences were found between the groups in falls (OR, 0.6; 95% CI, 0.1-3.1; p=0.72) or delirium (OR, 1.0; 95% CI, 0.5-2.0; p>0.99) (Table 4). Other adverse events were significantly less likely to occur during hospitalization in the intervention group [11/92 (12%)] than in

Table 4. Clinical Event Outcomes in the Study Group.

Outcomes	Intervention group N=92	Control group N=92	Odds ratio (95% CI)	p value
Falls ^a , n (%)	3 (3.3)	5 (5.4)	0.59 (0.09-3.13)	0.72
Delirium ^a , n (%)	24 (26)	24 (26)	1.00 (0.49-2.04)	>0.99
Other adverse events ^{a,b} , n (%)	11 (12)	24 (26)	0.39 (0.16-0.89)	0.023
ED visit ^c , n (%)	11 (12)	8 (8.7)	1.42 (0.49-4.30)	0.63
Unplanned hospital admission ^c , n (%)	9 (9.8)	5 (5.4)	1.88 (0.54-7.45)	0.41

ED: emergency department

^aOccurred during hospitalization.^bOther adverse events included infection, deep vein thrombosis, surgery-related complications, aspiration, edema, diarrhea, hypotension, hypoglycemia, hyperkalemia, hyponatremia, acute kidney injury, urinary retention, seizure, transient ischemic attack.^cWithin 6 months after discharge.**Table 5. Details of Adverse Events.**

Adverse events	Intervention group N=92	Control group N=92
Infection, n (%)	4 (4.3)	7 (7.6)
DVT, n (%)	1 (1.1)	7 (7.6)
Surgery-related complications, n (%)	2 (2.2)	3 (3.3)
Aspiration, n (%)	1 (1.1)	2 (2.2)
Edema, n (%)	2 (2.2)	0 (0)
Diarrhea, n (%)	1 (1.1)	1 (1.1)
Hypotension, n (%)	0 (0)	2 (2.2)
Hypoglycemia, n (%)	0 (0)	2 (2.2)
Hyperkalemia, n (%)	0 (0)	2 (2.2)
Hyponatremia, n (%)	0 (0)	1 (1.1)
Acute kidney injury, n (%)	0 (0)	1 (1.1)
Urinary retention, n (%)	0 (0)	1 (1.1)
Seizure, n (%)	0 (0)	1 (1.1)
Transient ischemic attack, n (%)	0 (0)	1 (1.1)

DVT: deep vein thrombosis

the control group [24/92 (26%); OR, 0.39; 95% CI, 0.16-0.89; p=0.023]. In the intervention group, 11 adverse events were observed in 11 patients, whereas in the control group, 31 adverse events were observed in 24 patients. The most common adverse events were infection, deep-vein thrombosis (DVT), and surgical complications. Hypoglycemia, hypotension, hyponatremia, hyperkalemia, acute kidney injury (AKI), urinary retention, seizures, and transient ischemic attacks were observed only in the control group (Table 5). No significant differences were observed between the two groups in the frequency of ED visits or unplanned hospital admissions within six months after discharge.

Deprescription status by medication classes

The discontinuation rates of benzodiazepines or Z drugs, probiotics, gastrointestinal drugs other than PPIs or laxatives, and of vitamins were significantly higher in the intervention group than in the control group (Table 6). No benzodiazepine withdrawal symptoms were observed in either group.

Discussion

This study investigated the outcomes of our deprescribing intervention by an MDT, including the number of prescribed medicines and PIMs, as well as clinically important outcomes in elderly orthopedic inpatients. Our deprescribing intervention by an MDT was associated with a reduction in the number of prescribed medicines and PIMs with no increase in the rate of adverse clinical events.

Deprescribing has been defined as “the systematic process of identifying and discontinuing drugs in instances in which existing or potential harms outweigh existing or potential benefits within the context of an individual patient’s goals, current level of functioning, life expectancy, values and preferences” (21). Reported methods of deprescribing interventions have included pharmacist-led medication reviews, physician-led interventions, prescriber education programs, multidisciplinary interventions, and clinical decision support systems (13). Elsewhere, deprescribing interventions in orthopedic wards have generally been safe and effective

Table 6. Discontinuation Rate by Medication Class.

Medication class	Patients in whom medication ceased/ patients receiving medication on admission (%)		Odds ratio (95% CI)	p value
	Intervention group	Control group		
ACEIs/ARBs	12/51 (24)	7/43 (16)	1.58 (0.51-5.28)	0.45
CCBs	6/57 (11)	4/61 (6.6)	1.67 (0.37-8.51)	0.52
Diuretics	13/35 (37)	11/37 (30)	1.39 (0.47-4.20)	0.62
Other antihypertensive agents	1/23 (4.3)	2/22 (9.1)	0.46 (0.01-9.52)	0.61
Anticoagulants	0/11 (0.0)	2/10 (20)	N/A	0.21
Antiplatelet agents	3/35 (8.6)	1/30 (3.3)	2.68 (0.20-147)	0.62
Statins	5/42 (12)	2/42 (4.8)	2.67 (0.41-29.7)	0.43
Oral hypoglycemic agents	8/20 (40)	2/19 (11)	5.42 (0.87-61.3)	0.065
Benzodiazepines/Z drugs ^a	20/34 (59)	7/34 (21)	5.36 (1.68-19.0)	0.003
Antidepressants	5/15 (33)	1/8 (13)	3.33 (0.28-189)	0.37
Antipsychotics	4/9 (44)	1/14 (7.1)	9.26 (0.70-548)	0.056
NSAIDs	12/17 (71)	13/22 (59)	1.64 (0.36-8.16)	0.52
Vitamins	13/45 (29)	1/33 (3.0)	12.7 (1.71-568)	0.003
Probiotics	9/13 (69)	1/11 (9.1)	19.2 (1.75-1,073)	0.005
Laxatives	15/50 (30)	9/48 (19)	1.85 (0.66-5.43)	0.24
PPIs	4/47 (8.5)	2/46 (4.3)	2.03 (0.28-23.6)	0.68
Other gastrointestinal drugs	17/31 (55)	12/45 (27)	3.28 (1.14-9.84)	0.017

ACEIs: angiotensin converting enzyme inhibitors, ARBs: angiotensin receptor blockers, CCBs: calcium channel blockers, N/A: not applicable, NSAIDs: non-steroidal anti-inflammatory drugs, PPIs: proton pump inhibitors

^aZ drugs included zopiclone, eszopiclone, zolpidem.

in reducing PIMs (16-18). Barriers to reducing polypharmacy and PIMs include a lack of problem awareness, inertia promoting continued prescription, prescriber's belief and confidence in their ability to address deprescription, and low feasibility of altering prescriptions in routine care (27). In regular practice, effort is required for orthopedic surgeons to address these issues. The number of prescribed medications is quite high, for example, after hip fractures (11). Our approach to implementing deprescribing intervention through an MDT was shown to be a valid means of reducing polypharmacy and PIMs in orthopedic inpatients.

Provided deprescription is deemed safe, the reduction of unnecessary drugs is an important outcome, as at the very least it will help reduce drug costs. However, the true goal of deprescription is to improve patient-relevant outcomes, such as drug-related adverse events, falls, fractures, ED visits, hospitalization, and mortality. There is no convincing evidence, however, that clinically important outcomes are improved by deprescription in hospitalized patients, including in the orthopedic ward (16-19). The deprescription intervention in this study was safe and associated with a reduction in adverse events other than falls and delirium. There were fewer cases of infections and DVT in the intervention group than in the control group, and electrolyte abnormalities, AKI, and hypoglycemia were not seen at all in the intervention group. One possible reason for the decrease in these adverse events might be the effectiveness of the multidisciplinary approach. In previous studies of deprescription in orthopedic wards, interventions were physician-led or pharmacist-led (16-18). In this study, however, MDT mem-

bers discussed which medicines could be potentially ceased and checked the patient's symptoms after deprescription based on the deprescription algorithm. Each team member assessed the patient's problems carefully from their own professional perspective. Deprescription discussions based on an assessment of the multifaceted problems unique to elderly people might result in effective intervention. The importance of team activities in medical care has been emphasized (28). For example, team activities in nutritional support [Nutrition Support Team (NST)], care of patients with dementia [Dementia Support Team (DST)], and appropriate use of antimicrobial agents [Antimicrobial Stewardship Team (AST)] are widely implemented in Japan. In addition, as shown in this study, organized team activities against polypharmacy and PIMs [named Support Team for Optimal Prescriptions (STOP)] might become important practices, especially in Japan, where medical and surgical co-management of patients is uncommon. Furthermore, while the present study was conducted among hospitalized orthopedic patients, it included many patients with multimorbidities, and STOP activities might also be useful for elderly medical patients.

However, this is a complex multicomponent intervention and the impact of deprescription is confounded by all other elements of the intervention. There is strong evidence supporting the efficacy of physician/geriatrician co-management of patients with hip fractures (29). Routine physician consultations may thus have had more to do with the reduction in adverse outcomes than the deprescription itself. In addition, non-improvement of clinical outcomes has been shown in

previous studies of hospitalized patients with multidisciplinary team interventions, so further research is needed to validate the results (26, 30, 31).

Limitations

Several limitations associated with the present study warrant mention. First, it was a single center study, so the results may not be easily generalized to other settings, and our team composition and approach may not be feasible in other facilities, especially those not yet using the GIM system. Second, this study was a retrospective observational study, not a randomized controlled trial. Propensity score adjustment was used in an attempt to control confounding factors, but we were unable to balance unmeasured confounding factors. Due to matching, the study included a relatively small number of patients in the analysis and was likely underpowered for the detection of significant changes in these outcomes. Further studies should attempt to replicate these results on a larger scale. There may also have been some underestimation of the true rate of adverse events owing to inadequate documentation in the charts or reporting by patients. Furthermore, the two physicians who collected the data were also members of the MDT and were not blinded to the intervention, which may have led to bias in the evaluation of the results. Third, our study focused on the deprescription of PIMs without evaluating potential prescribing omissions (12), which might be relevant to the clinical outcomes. Fourth, some clinically important outcomes were not evaluated, such as patients' quality of life and satisfaction, as the data were retrospectively collected from charts. In addition, patients who died in the hospital were excluded, and there was no evaluation of mortality. Fifth, our study did not include an analysis of the cost effectiveness, and there was no calculation of the drug costs reduced by deprescription. The balance between the cost savings and possibly prevented adverse events associated with deprescription as well as the workload incurred by the deprescribing intervention is another issue to be explored in future research. Finally, to what extent re-prescription of deprescribed medicines by primary physicians occurred after hospital discharge was unclear; future studies should evaluate re-prescription over the long term.

When frail, elderly patients are admitted to the orthopedic ward, some of their prescribed medications might be inappropriate or more than the dose actually required. This study suggests that deprescribing via protocol-led MDT intervention can safely reduce polypharmacy and PIMs in orthopedic inpatients. A large-scale randomized controlled trial with post-discharge follow-up is needed to confirm these results.

Conclusion

Deprescribing intervention by an MDT significantly reduced the number of prescribed medicines and PIMs in elderly orthopedic inpatients. The intervention was safe and did not induce any increase in falls, delirium, ED visits, or un-

planned hospital admission and was actually associated with reduced in-hospital adverse events other than falls and delirium.

The authors state that they have no Conflict of Interest (COI).

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