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Prescription Reviews of Hospitalized and Discharged Patients to Assess and Improve Polypharmacy Management

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Although some studies have described deprescribing polypharmacy during hospitalization, no study has reviewed outpatient prescriptions after discharge. This study aimed to determine how polypharmacy management could be improved even after discharge. Seventy-two patients who had a record of a polypharmacy fee（for receiving prescription review and deprescribing）during hospitalization were selected as the study population. Deprescribing situations during hospitalization and in outpatient settings after discharge were analyzed to assess whether polypharmacy management was conducted appropriately. The mean numbers of medications at admission and discontinued during hospitalization were 9.79 and 4.88, respectively. The common reasons for deprescribing were serious dysphagia（31.1%）, followed by other symptoms or complaints（22.2%）and laboratory values（15.7%）. The medications frequently discontinued during hospitalization were antidiabetic agents（88.2%）and antipyretic analgesic anti-inflammatory agents（73.1%）, and antacids（60.7%）. Of the 72 patients, 19 had outpatient visits and four of them had re-prescriptions. All medications discontinued due to a lack of benefit as indicated by laboratory values were not re-prescribed. In contrast, 42.9% of medications discontinued due to adverse effects as indicated by laboratory values were re-prescribed. All medications discontinued due to serious dysphagia were not re-prescribed. Among vasodilators, 42.9% were re-prescribed, and no antihypertensive drugs were re-prescribed. Even if medications are discontinued due to adverse effects, as indicated by laboratory values in polypharmacy management, it is necessary to adequately monitor laboratory values because re-prescribing of the discontinued medications might be necessary. Furthermore, to discontinue medications with multiple effects, it is necessary to properly understand the intention of prescription.

Key words: polypharmacy, prescription review, deprescribing, re-prescription, hospitalization

Introduction

The use of multiple medications, commonly referred to as polypharmacy, is a worldwide issue. Polypharmacy includes the use of potentially inappropriate medications, therapeutic duplications, and medication under/overuse[1, 2)] , and is not defined based on the number of medications[3)] . Previous studies have shown that receiving five to six or more medications is associated with weakness, dysfunction, falls, and adverse drug reactions, and death in the elderly[4-6)] . The risk of adverse drug reactions is approximately twice as high for patients receiving five to seven medications compared to that for those receiving four or fewer medications[7)] . Multiple morbidities and visits to multiple medical institutions are known as the causes of polypharmacy[8)] .

Countermeasures for polypharmacy are employed in several countries. For example, a study in the United Kingdom showed that medication reviews are useful for reducing polypharmacy and increasing the appropriateness of prescribing[9)] . In Japan, since 2016, a new medical treatment fee has been added for prescription reviews and deprescribing（as a polypharmacy fee[10)]）, whereby when a patient receiving six or more medications is admitted to a hospital and two or more medications are discontinued during the hospitalization, the patients is charged US$25（using an exchange rate of 1 US$ = 100 yen）

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as a polypharmacy fee. In recent years, various efforts have been made to manage polypharmacy in Japan. Previous studies have shown that the Screening Tool of Older Persons' potentially inappropriate Prescriptions criteria（STOPP criteria）is useful for modifying prescriptions including potentially inappropriate medications[11]. Japanese pharmacists contribute by making proposals to doctors because they do not have prescription privilege. Pharmacists have been shown to contribute toward reducing unnecessary medications or therapeutic duplications by revising medication plans at admission[12], and reducing unnecessary medications, therapeutic duplications, or medications suspected to cause side effects with prescription review services during hospitalization[13]. In addition, pharmacists have been shown to reduce medication and adjust doses by assessing renal function and electrolyte abnormalities[14]. However, the studies that reported these contributions considered only pharmacists' interventions during hospitalization and not outpatient prescriptions after discharge. It is unknown whether medications discontinued during hospitalization remained discontinued or were re-prescribed after discharge. If a patient's condition worsens due to deprescribing, the medications discontinued during hospitalization should be resumed. We hypothesized that there is a difference between patients whose medications are re-prescribed and patients whose medications are not re-prescribed at outpatient visit. We further hypothesized that medications re-prescribed at outpatient visit have a tendency. If these hypotheses are proved, inappropriate deprescribing is avoided and polypharmacy management is improved. In this study, therefore, we investigated deprescribing situations in terms of factors such as the type of patient, reasons for medication discontinuation, type of medications, and number of medications in a hospital. Furthermore, we reviewed medications for outpatients to assess whether deprescribing status could be maintained even after discharge and examined whether polypharmacy management was appropriate by ensuring that the discontinued medications were not re-prescribed. If the discontinued medications are re-prescribed, polypharmacy management might not be appropriate. Finally, we aimed to reveal how to improve polypharmacy management based on the knowledge obtained in this study.

Methods

1. Study design and setting

We performed a retrospective observational study in a hospital（238 beds and 25 clinical departments）located in a suburb of Tokyo, Japan（IMS Miyoshi General Hospital）. In this hospital, all prescription changes（such as additions, discontinuations, and dosage adjustments）and the underlying reasons are documented in a pharmacists' recording system. When this study was initiated, neither doctors and pharmacists had received specific training for polypharmacy management and did not use any tools for deprescribing such as the STOPP criteria. Patients for whom a record of polypharmacy fee between April 2016 to March 2017 was available were selected as the study population. The study was approved by the ethics committee of Meiji Pharmaceutical University（reference No. 3028）.

Data collection

1. Deprescribing situations during hospitalization

We reviewed electronic medical records and pharmacists' records retrospectively to investigate deprescribing situations during hospitalization. All patients with a record of a polypharmacy fee were selected. The data included age, sex, length of hospital stay, medications at admission, medications at discharge, medications discontinued during hospitalization, reasons for discontinuation, and medications added during hospitalization. We defined "discontinued medications" as medications discontinued by a doctor during the hospitalization and not restarted until discharge. Furthermore, by referring to previous studies involving prescription modifications, we classified the reasons for medication discontinuation during hospitalization into nine categories: symptoms or complaints, laboratory values, blood pressure or heart rate, patient's or family's needs for deprescribing, unclear prescription intention,

drug-drug interaction, contraindications or careful administration due to morbidity, serious dysphagia（difficulty swallowing oral medications）, and other[14, 15]（Figure 1a）. We slightly modified this classification because the perspective about reasons for medication discontinuation is a little different in the hospital. Furthermore, if the reason for discontinuation was "symptoms or complaints," "laboratory values," or "blood pressure or heart rate," the reason was further classified as adverse effects（suspected side effects/excessive effects）or not beneficial（Figure 1b）. These reasons were evaluated by two blinded pharmacists because in classifying a reason as adverse effects or not beneficial, it is necessary to make a judgment pharmaceutically. Discrepancies were resolved by a third pharmacist. All pharmacists who evaluated the reasons had been clinical pharmacists for more than 5 years. They only accessed the collected data and did not access electronic medical records and pharmacists' records. Medications used by the patients at admission were classified by therapeutic categories.

2. Prescription review after discharge

We retrospectively reviewed electronic medical records and pharmacist records to investigate whether deprescribing status could be maintained even after discharge. Patients with a record of a polypharmacy fee and who visited the hospital as outpatients within 3 months after discharge were selected. The data collected included age, sex, length of hospital stay, medications at admission, medications at discharge, medications discontinued during hospitalization, the period from discharge to the first outpatient visit after discharge, outpatient prescription at the first visit, and the reasons for re-prescription.

We checked for each patient whether medications discontinued during hospitalization were re-prescribed at outpatient visit. Patients for whom re-prescription occurred were classified as the "re-prescribed group"; if re-prescription did not occur, the patients were classified as the "non-re-prescription group." Background characteristics of the patients were compared between the two groups to identify factors associated with re-prescription.

Medications that were discontinued during hospitalization were analyzed according to whether they were re-prescribed at outpatient visit. This analysis was conducted based on the reasons for medication discontinuation during hospitalization and their therapeutic categories to reveal the association with re-prescription. Medications prescribed at another hospital before hospitalization were excluded from the review.

Data analysis

All continuous variables pertaining to the characteristics of the study population are shown as mean and standard deviation values. Ratios of the reasons for discontinuation to all reasons, of "adverse effects," and of "not beneficial" were calculated. The ratio of medications discontinued during hospitalization to medications that patients used at admission was calculated by therapeutic categories. The statistical significance of the difference between the two groups was analyzed with the statistical software EZR[16]. For comparing characteristics, proportions were compared by Fisher's exact test and continuous variables were compared by Mann–Whitney U test. A P value of < 0.05 was considered to indicate significance.

Results

1. Deprescribing situations during hospitalization

The characteristics of the study population are shown in Table 1. A total of 72 patients were included in this study（mean age: 81.6 years, 38.9% males）. Of them, 87.5% were aged 75 years or older. The mean numbers of medications at admission and those discontinued during hospitalization were 9.79 and 4.88, respectively（total 705 and 351）. The reasons for medication discontinuation are shown in Figure 1A. The most common reasons were serious dysphagia（31.1%）, followed by symptoms or complaints（22.2%）, laboratory values（15.7%）, and blood pressure or heart rate（11.1%）. Because the classifications by two blinded pharmacists were identical, a third pharmacist was not involved. Among the medications discontinued due to "symptoms or complaints," 92.3% were classified as not beneficial

（Figure 1B）. In contrast, all medications discontinued due to “blood pressure or heart rate” were classified under adverse effects. The most frequent category of the discontinued medications was antidiabetic agents（88.2%）, followed by antipyretic analgesic anti-inflammatory agents（73.1%）, antacids（60.7%）, and anti-diarrhea drugs and probiotics（55.0%）（Figure 1C）.

Table 1. Characteristics of the study population（n = 72）

	Value
Age (years), mean (SD)	81.6 (9.00)
≥75, n (%)	63 (87.5)
Male, n (%)	28 (38.9)
Length of hospital stay, day (SD)	28.1 (16.6)
Medications at admission, n (SD)	9.79 (3.47)
Medications at discharge, n (SD)	5.88 (3.76)
Medications discontinued during the hospitalization, n (SD)	4.88 (2.54)
Medications added during the hospitalization, n (SD)	0.96 (1.26)
Patients who had outpatient visits after discharge, n (%)	19 (26.4)

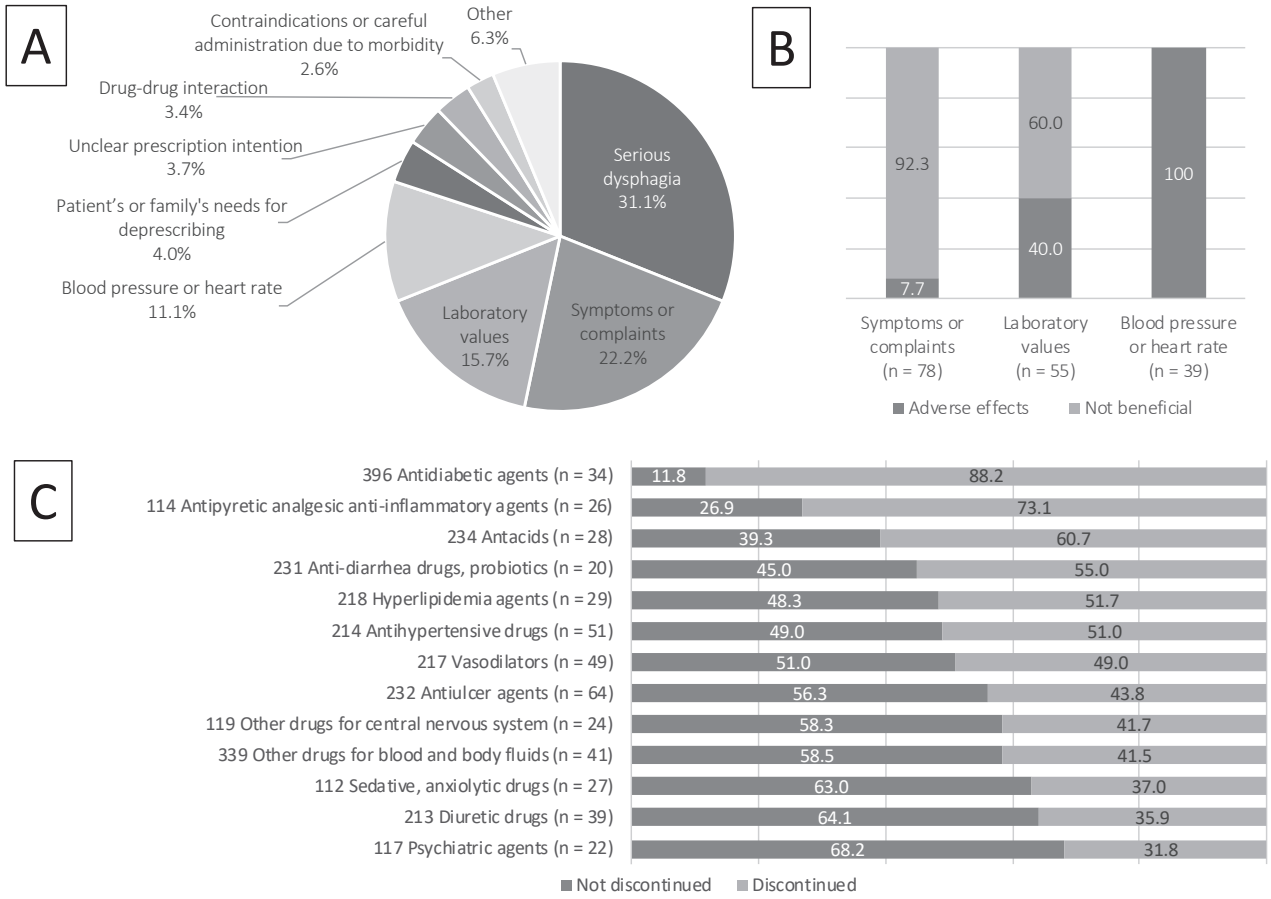

Figure 1. Discontinued medications（n = 351）

A）Reasons for medication discontinuation, B）Adverse effects or not beneficial,
C）Categories of the discontinued medications（n ≥ 20）

2. Prescription review after discharge

The characteristics of the patients who had outpatient visits after discharge are summarized in Table 2. Of the 72 patients, 19 had outpatient visits and four of these 19 had re-prescriptions（Figure 2）. Comparison of background characteristics revealed no significant differences between patients with and without re-prescription at the first outpatient visit. The numbers of medications at admission and discharge were considerably higher in the “re-prescribed group”; however, the intergroup difference was not significant（p =0.27, 0.39）. There was almost no intergroup difference in the number of discontinued medications during hospitalization（non-re-prescription group: 5.27, re-prescribed group: 4.50）. The remaining 53 patients did not use the hospital outpatient services.

Table 2. Characteristics of the patients who had outpatient visits after discharge

	Total (n = 19)	Non-re-prescription group (n = 15)	Re-prescribed group (n = 4)	*P* value
Age (years), mean (SD)	79.3 (9.65)	79.5 (10.9)	78.3 (2.75)	0.51 [b]
Male, n (%)	9 (47.4)	8 (53.3)	1 (25.0)	0.58 [a]
Length of hospital stay, day (SD)	21.3 (15.0)	20.2 (14.6)	25.5 (18.1)	0.62 [b]
Medications at admission, n (SD)	10.4 (4.66)	9.47 (2.80)	14.0 (8.49)	0.27 [b]
Medications at discharge, n (SD)	6.68 (5.19)	5.73 (3.08)	10.3 (9.78)	0.39 [b]
Medications discontinued during the hospitalization, n (SD)	5.11 (2.90)	5.27 (3.13)	4.50 (2.08)	0.72 [b]
Medications added during the hospitalization, n (SD)	1.37 (1.77)	1.53 (1.92)	0.75 (0.96)	0.53 [b]
Period from discharge to outpatient visits, day (SD)	12.9 (9.00)	13.3 (10.2)	11.8 (1.50)	0.84 [b]

[a] Fisher's exact test, [b] Mann–Whitney U test

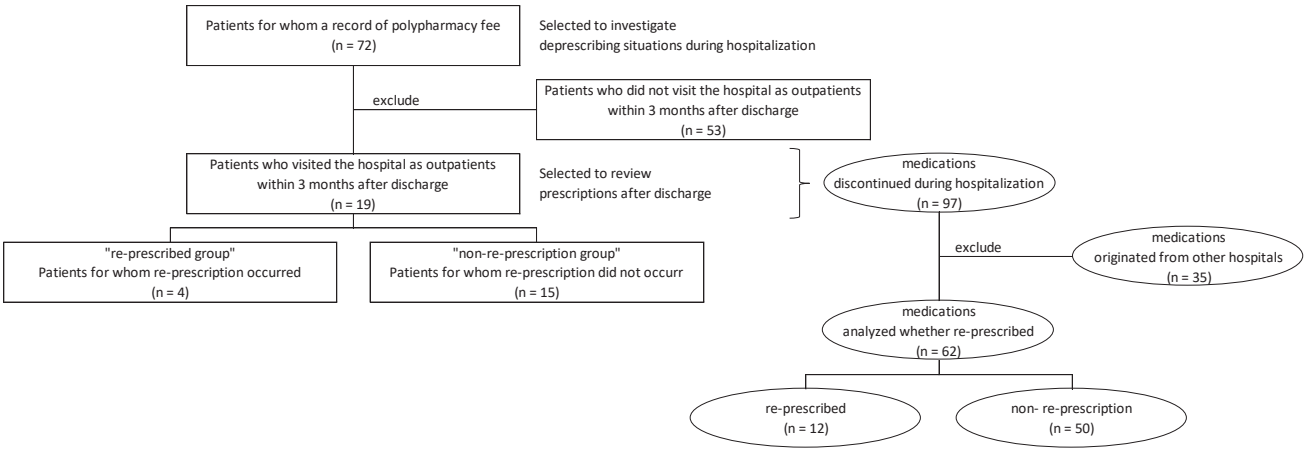

Figure 2. Flowchart of the patients included in the study and medications analyzed whether re-prescribed

For the 19 patients with outpatient visits, a total of 97 medications were discontinued during hospitalization. Thirty-five medications originated from other hospitals were excluded from the analysis（Figure 2）. Of the remaining 62 medications, 12 were re-prescribed at outpatient visits. Figure 3 shows whether medications were re-prescribed or not based on the reasons for medication discontinuation during hospitalization（Figure 3A）and their therapeutic categories（Figure 3B）. All medications discontinued due to “laboratory values（not beneficial）” were not re-prescribed. In contrast, 42.9% of medications discontinued due to “laboratory values（adverse effects）” were re-prescribed. All medications discontinued due to “serious dysphagia” were not

re-prescribed. Among vasodilators, 42.9% were re-prescribed. In contrast, no antihypertensive drugs were re-prescribed.

Re-prescribed Case 1 comprised a patient taking a total of 26 medications including alfacalcidol and flunitrazepam. Alfacalcidol was discontinued due to “laboratory values（adverse effects）” during hospitalization and re-prescribed for hypocalcemia at outpatient visit. Flunitrazepam was discontinued due to “symptoms or complaints” and the reason for re-prescription could not be investigated.

Re-prescribed Case 2 comprised a patient taking a total of six medications including furosemide and dilazep. Furosemide was discontinued due to “laboratory values（adverse effects）” during hospitalization and re-prescribed for edema at outpatient visit. Dilazep was discontinued due to “other reasons” and the reason for re-prescription could not be investigated.

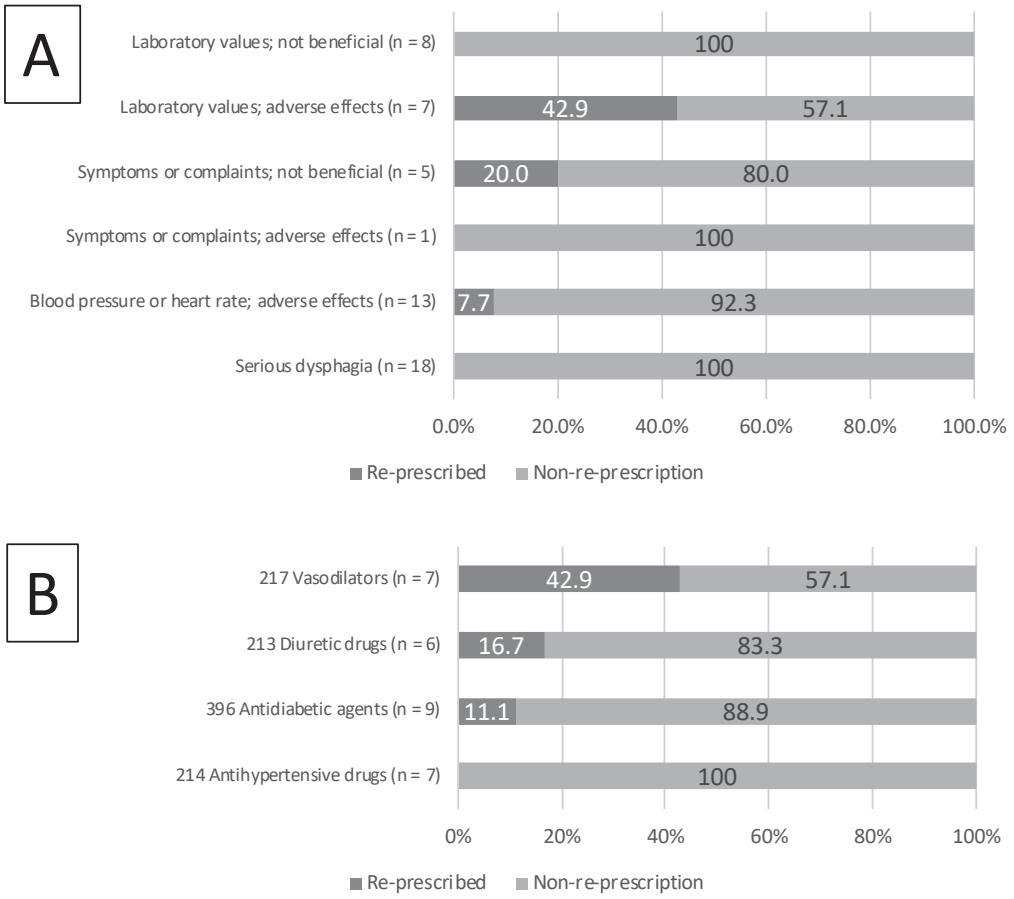

Figure 3. Re-prescribing at outpatient visits（n = 62）

A）Reasons for discontinuation during hospitalization（n > 5）, B）Therapeutic categories（n > 5）

Discussion

Since our study included patients for whom a record of polypharmacy fee was available, discontinuation of two or more medications was observed for all patients. Our study revealed that the main reasons for medication discontinuation during hospitalizations were “serious dysphagia,” “symptoms or complaints,” “laboratory values,” and “blood pressure or heart rate.” The main categories of discontinued medications were antidiabetic agents, antipyretic analgesic anti-inflammatory agents, and antacids. Since only 19 patients（26%）had outpatient visits at the hospital after discharge, factors associated with re-prescribing were not identified. However, approximately 80% of the discontinued medications were not re-prescribed at the outpatient visits and it could be suggested that polypharmacy management during the hospitalization was appropriate. Medications discontinued due to adverse effects as indicated by

laboratory values during hospitalization tended to be re-prescribed at outpatient visits. Furthermore, vasodilators discontinued during hospitalization tended to be re-prescribed at outpatient visits as well. Therefore, pharmacists should repeatedly consider whether medications were not really needed during hospitalization if medications were discontinued due to adverse effects as indicated by laboratory values or if vasodilators were discontinued, because those medications are more likely to be re-prescribed at outpatient visits.

Regarding deprescribing in the hospital, the average number of medications at admission (9.79) reduced by 4.88 medications on average during hospitalization. This was because more and closer attention could be paid to the use of and need for medications in inpatients compared to those among outpatients. For example, inpatients frequently receive interventions, such as medical examinations, blood tests, and vital checks, provided by medical staff during hospitalization; if inpatient medication is discontinued, medical staff can easily follow-up with the patient. Such follow-up would be very difficult or not feasible if medication discontinuation occurs in outpatients. Therefore, inpatient medication can be easily discontinued. In addition, polypharmacy fee may have facilitated deprescribing. Approximately one-third of the medications discontinued during hospitalization were due to serious dysphagia and finally judged not necessary. By comparing reference studies, we slightly modified discontinuation reasons and did not consider dose reduction; however, the reasons for medication discontinuation were almost the same across studies and included “symptoms or complains,” “laboratory values,” and “blood pressure or heart rate” [14, 15].

Among the medications discontinued due to “symptoms or complaints,” more than 90% were considered as not beneficial in our study. Similarly, medications discontinued due to “laboratory values” were associated with both adverse effects and a lack of benefit. Antiulcer agents were often considered as unnecessary medications because many patients may be prescribed these agents despite having no symptoms[17], and in the hospital, approximately half of these medications were discontinued. It should be noted however that a previous study suggested that approximately 10% of the patients experienced symptom relapse and careful monitoring is needed after discontinuation[15]. Moreover, antidiabetic agents and antipyretic analgesic anti-inflammatory agents listed as drugs to be used carefully among the elderly in the guideline for safe drug therapy for the elderly, 2015[8] were found to be the major discontinued medications (about 70%) even though few patients used these medications. These findings are really important in that they revealed unnecessary or inappropriate medication use commonly occurred in the hospital and suggested that prescription reviews are important during hospitalization to avoid aimless long-term use and polypharmacy.

Regarding medication use in the outpatient setting after deprescribing during hospitalization, 19 out of the 72 patients used hospital outpatient services within 13 days of discharge on average and only four had re-prescriptions. No difference could be found between patients whose medications were re-prescribed and patients whose medications were not re-prescribed at outpatient visit. In order to improve polypharmacy management, it is necessary to consider why medications are re-prescribed. Medications might be re-prescribed, first, because of a lack of information sharing between doctors in inpatient and outpatient services; second, because of changes in the patient condition after discharge; and third, inappropriate discontinuation or some other reasons. If re-prescription occurs because of a lack of information sharing, the method of information sharing between inpatient and outpatient staff members should be improved. This issue was not addressed in the prescription process during outpatient visits. If the cause of re-prescription is a change in the patient’s condition after discharge, patient education including prescription changes should be provided before discharge. For example, a patient whose blood pressure increases after discharge might need to be aware of salty foods. If the discontinuation was inappropriate, all medical staff including

doctors and pharmacists should work together by consulting with family doctors who originally prescribed medications to clarify the prescription intention. The remaining 53 patients did not use the hospital outpatient services because some of them were transferred to a nursing home or used family doctor services. Thus, their post-discharge prescriptions were unknown.

Regarding deprescribing during hospitalization to improve polypharmacy management, medications at hospitals and those after discharge were compared. We have found that there is a slight tendency for medications to be re-prescribed at outpatient visits. Except for the medications discontinued due to serious dysphagia, almost all medications discontinued for other reasons were re-prescribed. Especially, nearly half of the medications discontinued due to laboratory values (adverse effects) were re-prescribed at the outpatient visit. Therefore, it is important to manage laboratory values appropriately after changing medications. In fact, Case 1 was a case wherein a medication discontinued due to laboratory values during hospitalization was re-prescribed due to laboratory values at the outpatient visit. Further, medications are often discontinued due to serious dysphagia, which might be indicated in various ways such as patient complaints or laboratory values. Since a previous study suggested approximately 6.5% of the discontinued or reduced medications were related to the occurrence of adverse events[15], re-prescription must be considered to avoid unnecessary adverse events, although there were no such cases in our study. With regard to the categories of the medications discontinued, vasodilators tended to be re-prescribed while antihypertensive drugs were not. Because both categories of medications have pharmacological actions other than antihypertensive action, discontinuation should be decided not only by considering blood pressure but also by understanding the intention of prescription properly. In Case 2, diuretic drugs were discontinued due to laboratory values during hospitalization. However, it was re-prescribed due to edema rather than laboratory values. It is possible that the doctor who examined the patient during hospitalization did not properly understand the intention of the prescription.

This study has some limitations. First, since we investigated only patients who visited the hospital after discharge, the prescription changes after discharge were only partially evaluated. In the case of a patient who used the outpatient service in the hospital after discharge, the doctor who examined the patient during hospitalization would attend to the patient. If not, another doctor easily could obtain the patient's clinical information from medical records. However, too much information can confuse doctors and distract from prescribing. In contrast, if the patient sought outpatient services outside the hospital, doctors could rely on the patient referral document prepared at discharge by our doctor. Because shared patient information differed between doctors in the hospital and community clinics, our findings cannot be extended to all discharged patients. Second, we could not investigate all reasons for re-prescription retrospectively. The method should be modified to comprise a prospective design. Third, the study was conducted in a medium-sized general hospital where some clinical departments did not provide inpatient services, such as rheumatology and gynecology. For these reasons, there may be a bias in the reasons for discontinuation and the findings cannot be generalized. However, to our knowledge, this is the first study to assess polypharmacy management by reviewing outpatient prescriptions.

In summary, our findings suggested that confirmation of the patient's symptoms, complaints, and laboratory values was effective in discovering and avoiding aimless long-term medication. It is necessary to manage laboratory values appropriately after changing medications due to adverse effects. To discontinue medications with multiple effects, it is also necessary to properly understand the intention of prescription. There is currently no clear information such as guidelines for improving polypharmacy management, and our findings could be useful in enhancing polypharmacy management during both hospitalization and after discharge.

Conflict of Interest

There is no conflict of interest to report.

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