Patient Preference and Adherence

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ORIGINAL RESEARCH

Risk Factors for Non-Adherence to Pharmacist or Non-Pharmacist Explanations on Preoperative Medication Discontinuation: A Retrospective Japanese Study

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Purpose: The risk factors for non-adherence to pharmacist or non-pharmacist explanations of preoperative medication discontinuation are unknown. The primary outcome of this study was to determine whether the final explainer's occupation was a risk factor for non-adherence. The secondary outcomes were to determine the risk factors for non-adherence after limiting the departments or adjusting for age.

Patients and Methods: We retrospectively examined the data (including patient age, sex, prescription medications, comorbidities, presence of roommate, and number of days between receiving explanation and surgery) of 1132 patients on medications that could affect surgery at a Japanese university hospital between April 1, 2017, and March 31, 2020. The primary endpoint was whether the occupation of the last person explaining medication discontinuation to the patient was an independent risk factor for non-adherence (age ≥65 years vs <65 years). Secondary endpoints included subgroup analyses in urological, gastrointestinal, and otolaryngological areas, as well as a sensitivity analysis (age as a continuous variable) to confirm the validity of the primary endpoint results. A multivariate binary logistic regression identified independent non-adherence risk factors.

Results: The main analysis showed that discontinuing two or more medications was a risk factor for non-adherence (adjusted odds ratio (AOR): 1.67; 95% confidence interval (CI): 1.13–2.47; p = 0.01). However, in analyses coordinated by department (urological, gastrointestinal, and otolaryngological), ≥65 (versus <65) years of age was determined as a risk factor for increased nonadherence (AOR: 2.27, 95% CI: 1.11–4.63; p=0.024). Age-adjusted analysis (continuous variables) showed similar results to the primary endpoint (AOR: 1.68, 95% CI: 1.14–2.49, p = 0.009).

Conclusion: Two or more medications, and not the final explainer's occupation, were associated with pre-surgery medication non-adherence. To prevent non-adherence, pharmacists and non-pharmacists should educate patients about preoperative medication discontinuation. These findings could help identify high-risk non-adherence patients.

Plain Language Summary: At Kitasato University Hospital, pharmacists and non-pharmacists explain before surgery that patients scheduled for surgery should discontinue medications that could affect surgery. However, there are patients who fail to follow these explanations precisely, but the risk factors have not yet been identified. This study examined risk factors for patients who failed to comply with explanations from a pharmacist or non-pharmacist regarding the use of medications that could affect surgery. Risk factors were examined using a statistical method for identifying risk factors by considering patients' age ≥65 (versus <65) years, sex, the job title that explained the instructions to the patient, number of medications to be discontinued before surgery, and number of days between instructions and surgery as risk factors. Based on pharmacist/non-pharmacist explanations, the statistical analysis revealed that patients taking two or more medications that could affect surgery may be a risk factor for non-adherence to medications that should be discontinued before surgery. To improve medication adherence, pharmacists and non-pharmacists should be aware of the patient's non-adherence risk factors, repeatedly explain them to the patient, and help the patient understand that failure to comply with the explanation increases surgical cancelation and intraoperative bleeding risks.

Received: 19 October 2023
Accepted: 20 January 2024
Published: 31 January 2024

Keywords: medication adherence, hematologic agents, pharmaceutical service

Introduction

In Japan, a lack of instructions for preoperative medication discontinuation resulted in seven cases of canceled surgery between January 1, 2014, and February 28, 2019.[1] Inappropriate anticoagulant medication management can lead to canceled surgeries and prolonged inpatient stays, which place patient–hospital reliability at risk. Perioperative management of anticoagulant medications should be individualized to prevent bleeding complications while continuing existing treatment.[2,3]

Since September 1, 2013, Kitasato University Hospital in Minami-ku, Kanagawa, Japan, has begun perioperative medication management, with doctors and pharmacists checking patients' medications preoperatively and explaining to patients that take continuing medications (such as anticoagulants) that these could affect surgical outcomes. However, patients did not adhere to instructions in some cases, and surgery was canceled. Furthermore, institutional and patient-related reasons for scheduled surgical cancelations have been reported in Asia.[4] A systematic review revealed that a preoperative consultation with an internist effectively prevented surgical cancelations.[5] Moreover, factors related to patient non-adherence have been reported.[6–11] However, only a few studies have reported non-adherence to preoperative medication management. Our previous study showed that the rate of non-adherence was 11.4% depending on the final pharmacist's explanation of medication management affecting surgery at a Japanese university hospital and that patient age of ≥65 years was a risk factor.[12] However, it had the following limitations: (i) the study included only groups of patients who received explanations from a pharmacist; thus, there were no data on occupational differences of individuals who ultimately provided the explanation to the patients; (ii) the number of patients was not large enough to adjust for all confounding factors; and (iii) there was an insufficient adjustment for confounding factors.[12] Nevertheless, a non-pharmacist may be the final healthcare provider who explains preoperative medication management. Pharmacist intervention has improved adherence;[13–18] however, an investigation is required to determine whether occupational differences in individuals providing a final explanation to patients is a risk factor for non-adherence. In addition, there are no studies demonstrating an association between patient non-adherence and the duration of medication discontinuation that could potentially affect surgery. The patient and hospital burden caused by non-adherence can be prevented by identifying and addressing risk factors for non-adherence.

The aims of this study were to investigate whether the occupation of the individual explaining medication management was a risk factor for patient non-adherence after increasing the number of patients compared with that in our previous study[12] and identify risk factors for non-adherence after adjusting for confounding factors.

Materials and Methods

Study Design

A retrospective, cross-sectional study was performed (level III evidence) following the STROBE statement[19] among all patients who received an explanation from a pharmacist or non-pharmacist of preoperative medication discontinuation between April 1, 2017 and March 31, 2020 at Kitasato University Hospital in Kanagawa, Japan. The hospital comprises 1135 beds and 31 departments. Patient data were collected from electronic medical records for the period July 1, 2021 to March 31, 2023. All data were anonymized. Two researchers (YN and AA) conducted independent reviews for data confirmation. Researcher disagreements were resolved through discussions, and another senior research associate (AT) was consulted when necessary.

Patients and Eligibility Criteria

Patients who were preoperatively explained by pharmacists or non-pharmacists to continue or discontinue medications affecting surgery were included. All patients had their medications checked by a pharmacist before admission for urological, gastrointestinal, otolaryngological, respiratory, plastic, breast, or gynecology surgery. Here, surgery included operations performed after a planned hospitalization, examinations and biopsies that involved bleeding; outpatient surgeries were excluded. If a patient underwent two or more surgeries during the study period, the data from the first

surgery were included without any exclusion. Patients eligible for pharmacist interviews were those scheduled to undergo surgery at Kitasato University Hospital after consultation with the pharmacy department and each surgical department, regardless of the hospitalization status. Examinations and biopsies that involved bleeding for which pharmacist interviews were conducted were agreed upon in advance between the respective departments and the pharmacy department.

Pre-Surgical Decision Protocol

During consultation, a physician reviewed the patient's medication use and explained whether the medication would be discontinued or continued. If a surgery date was determined, the date to discontinue the medication was explained and the explanation was recorded in the electronic medical record. If a surgery date had not been determined, the medications to be discontinued and the approximate duration of discontinuation prior to surgery were explained. Subsequently, the pharmacist interviewed the patient and double-checked the medications being used and the record of the physician's instructions. The pharmacists checked the records for discrepancies, such as missing explanations of medication discontinuation or inconsistencies in the agreed-upon time of discontinuation, to provide accurate explanations to the patients, and if necessary, contacted the physicians to correct the instructions. The pharmacist explained medication discontinuation or continuation verbally and with documentation. If a surgery date was confirmed, the pharmacist also explained the date of discontinuation. If the surgery was not yet confirmed, the pharmacist also explained the approximate date of discontinuation. The physician and pharmacist explained that medications affecting surgery would be discontinued, whereas unmentioned medications would be continued. Finally, the pharmacists recorded their explanations to patients in the electronic medical records. The physician explained the final date to discontinue medication during the pre-admission consultation once the surgery date was determined for patients whose surgery date had not yet been determined. For patients who did not have a consultation before surgery, the explanation was provided to the patient by a non-pharmacist, such as a physician or a medical staff member assigned by the physician, over the phone to the patient. All interviewed pharmacists were trained by senior pharmacists to standardize the explanation methods. The explanation was attributed to a pharmacist if their job title could be identified from the final record; otherwise, it was assigned to an individual with a different job title.

Surgery-Affecting Medications

Medications potentially affecting surgery were defined as follows: (i) antiplatelets, (ii) anticoagulants, (iii) coagulation factor X inhibitors, (iv) thrombin formation inhibitors, and medications to improve (v) cerebral blood circulation and (vi) coronary blood flow. Medications potentially affecting surgery at Kitasato University Hospital and the required approximate duration (days) of medication discontinuation before surgery, examination, or biopsy are shown in Table S1.

Non-Adherence Definition

Non-adherence was defined as failing to follow the instructions given by pharmacists or non-pharmacists prior to surgery when admitted. The ward pharmacist confirmed the pre-admission explanation by pharmacists or non-pharmacists regarding medication discontinuation to the patient in the electronic medical record on the day of admission to ensure that the instructions were followed. Patients were divided into "adherence" and "non-adherence" groups based on whether or not they stopped taking their medications as instructed at the time of admission. The decision to cancel surgery owing to non-adherence was made by the primary doctor and anesthesiologist.

Sample Size

The number of patients required for multiple binary logistic regression analysis was calculated using a method that included at least 10 times the number of patients for the explanatory variables used in this study.[20] Multiple binary logistic regression analysis with five explanatory variables, 8% non-adherence rate, and 50% dropout rate was conducted for 1250 patients (50 in the non-adherent group).

Main Analysis

The main aim of the study was to identify whether the last explainer's occupation was a risk factor for non-adherence. The effect of independent variables on non-adherence was analyzed using multivariate binary logistic regression models. The risk factors assumed for the primary outcome were as follows: (i) age at hospitalization (≥65 or <65 years), (ii) sex, (iii) explainer (pharmacist or non-pharmacist), (iv) number of medications to be discontinued (one, two or more), and (v) number of days from the receipt of instructions until surgery (≥15 or <15 days). Variables that were considered clinically important were prioritized for independent variables, followed by variables identified in previous studies.[6–11] The proportion of individuals aged ≥65 years is expected to increase in Japan.[21,22] Furthermore, age was used as a categorical variable with a 65-year threshold as older age has been identified as a risk factor for non-adherence in several studies.[6,10] The number of patients taking three or more medications potentially affecting surgery was smaller than that of patients taking two or fewer medications. Medications potentially affecting surgery were used as a categorical variable, with a threshold of two medications.[12] The longest discontinuation period for medications potentially affecting surgery was 14 days. Therefore, a discontinuation period of ≥15 days was considered clinically significant.

Secondary Analysis

Secondary aims of the study were to examine risk factors for non-adherence limited to department or after adjusting for the effect of age. A subgroup analysis using a binary logistic regression model was performed to examine the effect of departments on the primary outcome. Risk factors were set as follows: (i) age at hospitalization (≥65 or <65 years), (ii) sex, (iii) explainer (pharmacist or non-pharmacist), (iv) number of medications to be discontinued (one, two or more), and (v) number of days from the receipt of instructions until surgery (≥15 or <15 days). To ensure a sufficient sample size for the analysis, the analysis targeted urology, gastroenterology, and otolaryngology departments, which had the largest number of patients.

A sensitivity analysis was performed using a binary logistic regression model to examine the effect of age on the primary outcome. Risk factors were set as follows: (i) age at hospitalization (a continuous variable), (ii) sex, (iii) explainer (pharmacist or non-pharmacist), (iv) number of medications to be discontinued (one, two or more), and (v) number of days from the receipt of instructions until surgery (≥15 or <15 days). As a continuous variable, the effect of age was confirmed as age was treated as a binary categorical variable (≥65 or <65 years) for the primary aim.

Statistical Analyses

Fisher's exact test was used to compare categorical variables between the adherence and non-adherence groups. The Shapiro–Wilk test was used to test the normality of age, number of medications, medications that affect surgery, and number of days to surgery, which were treated as continuous variables. Continuous variables were expressed as medians and means, whereas categorical data are expressed as absolute value and percentage. Welch's *t*-test was used to analyze the means of continuous variables, and Mann–Whitney's *U*-test was used to analyze the medians.[23,24] Patients with missing study data were excluded from the univariate and multivariate analyses. However, multiple imputations were planned using chained equations to create 100 sets of multiple imputation data if the missing data accounted for ≥5% of the data. All statistical analyses were performed using EZR version 1.36 software (Saitama Medical Center, Jichi Medical University, Saitama, Japan). A graphical user interface for R version 4.2.3 (The R Foundation for Statistical Computing, Vienna, Austria) was used, which is a modified R Commander version designed to add statistical functions frequently utilized in biostatistics.[25] All tests were two-tailed. Statistical significance was set at $p < 0.05$. Sample size calculations were performed only for the primary outcome, and p-values for non-primary outcomes were nominal to account for multiplicity.

Results

Patient Characteristics

Clinical information was obtained for 1225 patients, of whom 1132 (92.4%) were eligible for the study (Figure 1). The results of the Shapiro–Wilk test showed no normality in age ($p < 0.001$), number of medications ($p < 0.001$), medications

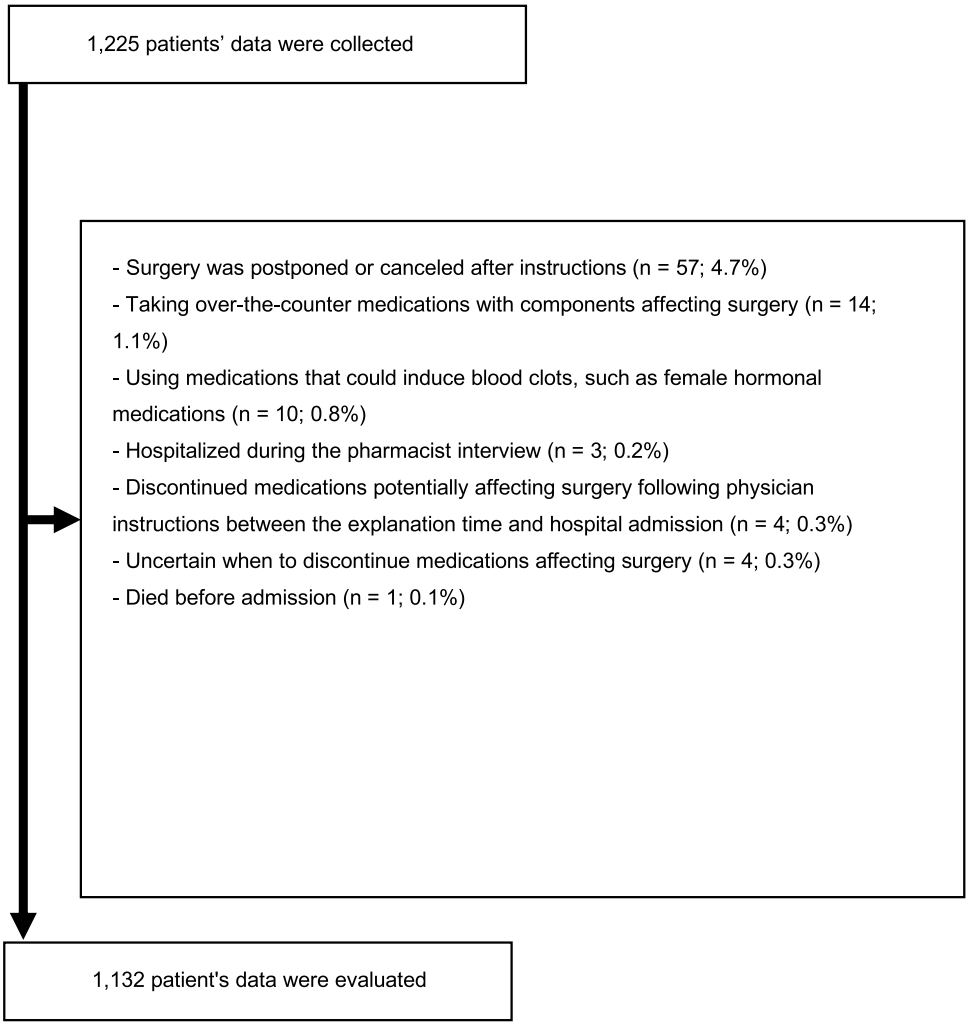

Figure 1 Patient inclusion flowchart. The following patients were excluded: those (i) whose surgery was postponed or canceled after instructions; (ii) taking over-the-counter medications with components affecting surgery; (iii) using medications that could induce blood clots, such as female hormonal medications; (iv) hospitalized during the pharmacist interview; (v) who had discontinued medications potentially affecting surgery following physician instructions between explanation time and hospital admission; (vi) who were uncertain when to discontinue medications affecting surgery; and (vii) who died before admission.

that affect surgery ($p < 0.001$), or number of days to surgery ($p < 0.001$), which are treated as continuous variables. There were significant differences in the mean age ($p = 0.036$), sex ($p < 0.001$), median number of days to surgery ($p < 0.001$), mean number of days to surgery ($p < 0.001$), and distribution of days to surgery ($p < 0.001$) between the pharmacist and non-pharmacist groups (Table 1). The non-adherence rates to the pharmacist and non-pharmacist explanations at admission were 11.1% (n = 87) and 15.4% (n = 54), respectively, with no statistically significant differences between the two groups ($p = 0.051$). There was one surgical cancelation (0.13%) in the pharmacist group and one (0.29%) in the non-pharmacist group.

The percentage of total non-adherence counts included 50.0% of patients (n = 73) who discontinued medications potentially affecting surgery earlier than explained and 19.9% of patients (n = 29) who discontinued later. Urology had the highest proportion of patients (n = 379, 33.4%), followed by gastroenterology (n = 321, 28.4%) and otolaryngology (n = 124, 11.0%). The percentage of missing values was 2% (n = 23) and 2% (n = 22) for the dementia and roommate variables, respectively. All variables had <5% missing values; therefore, multiple imputations were not performed.

Table 1 Baseline Patient Characteristics (n = 1132)

Characteristic	Total (n = 1132)	Pharmacist Group (n = 782)	Non-Pharmacist Group (n = 350)	p
Age				
Median (IQR), years	73 (68–79)	73 (67–78)	74 (68–79)	0.076
Mean (SD), years	71.2 (11.1)	70.8 (11.4)	72.2 (10.1)	0.036[a]
Distribution, No. (%)				0.050
<65 years	218 (19.3)	163 (20.8)	55 (15.7)	
≥65 years	914 (80.7)	619 (79.2)	295 (84.3)	
Sex, No. (%)				<0.001[a]
Male	768 (67.8)	563 (72.0)	205 (58.6)	
Female	364 (32.2)	219 (28.0)	145 (41.4)	
Non-adherence, No. (%)	141 (12.5)	87 (11.1)	54 (15.4)	0.051
Number of non-adherence [b], No. (%)	146 (100)	89 (61.0)	57 (39.0)	0.595
Discontinued earlier	73 (50.0)	42 (47.2)	31 (54.4)	
Discontinued later	29 (19.9)	17 (19.1)	12 (21.1)	
Influenced other medications	16 (11.0)	11 (12.4)	5 (8.8)	
Discontinued on the same day	10 (6.8)	8 (9.0)	2 (3.5)	
Discontinued medications that should not have been discontinued	17 (11.6)	11 (12.4)	6 (10.5)	
Did not discontinue	1 (0.7)	0 (0)	1 (1.8)	
Dementia, No. (%)	30 (2.7)	16 (2.1)	14 (4.0)	0.075
Roommate, No. (%)	891 (80.3)	604 (79.4)	287 (82.2)	0.291
Number of medications				
Median (IQR)	7 (5–9)	7 (5–10)	7 (5–9)	0.135
Mean (SD)	7.4 (3.5)	7.6 (3.6)	7.2 (3.2)	0.065
Medications that affect surgery				
Median (IQR)	1 (1.0–1.0)	1 (1.0–1.0)	1 (1.0–1.8)	0.171
Mean (SD)	1.3 (0.5)	1.2 (0.5)	1.3 (0.5)	0.289
Distribution, No. (%)				0.165
One	878 (77.6)	616 (78.8)	262 (74.9)	
Two or more	254 (22.4)	166 (21.2)	88 (25.1)	
Type of medication				0.397
Distribution, No. (%)				
Antiplatelet medication	1053 (74.3)	723 (74.5)	330 (74.0)	
Activated coagulation factor X inhibitor	181 (12.8)	119 (12.3)	62 (13.9)	
Anticoagulant medication	106 (7.5)	71 (7.3)	35 (7.8)	
Improved coronary blood flow	32 (2.3)	27 (2.8)	5 (1.1)	
Thrombin inhibitor	29 (2.0)	21 (2.2)	8 (1.8)	
Improved cerebral blood circulation	16 (1.1)	10 (1.0)	6 (1.3)	
Number of days until surgery				
Median (IQR), days	22 (14–34)	18 (12–27)	35 (23.3–53)	<0.001[a]
Mean (SD), days	27 (20.1)	21 (14.4)	41 (24)	<0.001[a]
Distribution, No. (%)				
<15 days	317 (28.0)	285 (36.4)	32 (9.1)	<0.001[a]
≥15 days	815 (72.0)	497 (63.6)	318 (90.9)	
Department				0.595
Distribution, No. (%)				
Urology	379 (33.4)	361 (46.2)	18 (5.1)	
Gastrointestinal surgery	321 (28.4)	161 (20.6)	160 (45.7)	
Otolaryngology	124 (11.0)	110 (14.1)	14 (4.0)	
Respiratory surgery	93 (8.2)	12 (1.5)	81 (23.1)	
Plastic surgery	89 (7.9)	81 (10.4)	8 (2.3)	
Breast surgery	75 (6.6)	25 (3.2)	50 (14.3)	
Gynecology	51 (4.5)	32 (4.0)	19 (5.5)	

Notes: *For age, number of medications, medications that affect surgery, and number of days until surgery, Welch's *t*-test was used for analysis of means and Mann–Whitney's *U*-test for analysis of medians; those for distributions (age and number of days until surgery), sex, non-adherence, number of non-adherences, dementia, roommate, medications that affect surgery, type of medication, and department were calculated using Fisher's exact test. [a]Significant difference ($p < 0.05$). [b]Total number.
Abbreviations: IQR, interquartile range; SD, standard deviation.

Primary Outcome

The multivariate binary logistic regression analysis showed that the number of medications to be discontinued was an independent risk factor for preoperative medication non-adherence (adjusted odds ratio: 1.67; 95% confidence interval: 1.13–2.47; p = 0.01) (Table 2).

Secondary Outcomes

Multivariate binary logistic regression analysis of patients in the urology, gastroenterology, and otolaryngology department showed that age (≥65 years) was an independent risk factor for preoperative medication non-adherence (adjusted odds ratio: 2.27; 95% confidence interval: 1.11–4.63; p = 0.024) (Table 3). Adjusting for department in the subgroup analysis confirmed findings that differed from those in the primary analysis.

Sensitivity Analysis Results

The number of medications to be discontinued was an independent risk factor for preoperative medication non-adherence (adjusted odds ratio: 1.68; 95% confidence interval: 1.14–2.49; p = 0.009) (Table 4). Additionally, the sensitivity analysis results, where age was redefined from a binary categorical variable (≥65 or <65 years) to a continuous variable, aligned with the findings of the primary outcome analysis.

Discussion

We previously identified age ≥65 years as a risk factor for non-adherence to medications affecting surgery in an observational study of 887 patients.[12] However, it is unknown whether the job title of the final explainer of medications affecting surgery is a risk factor for non-adherence. Systematic reviews have shown different risk factors for non-adherence based on distinct definitions of target diseases and medications,[6–11] with age, sex, and number of medications taken per day.[6,7,9–11] The study used multivariate binary logistic regression analysis to examine risk factors for medication non-adherence in patients explained by pharmacists or non-pharmacists to discontinue medications that would affect surgery. The univariate analysis showed that the pharmacist and non-pharmacist groups differed in mean age, sex, and number of days to surgery. Additionally, the multivariate binary logistic regression analysis revealed the number of medications to be discontinued is a risk factor for non-adherence. Furthermore, the sensitivity analysis (with

Table 2 Multivariate Binary Logistic Regression Analysis of Risk Factors for Medication Non-Adherence Affecting Surgery (n = 1132)

Risk factor	Odds Ratio (95% CI)	p
Age		
<65 years	1 (ref)	
≥65 years	1.50 (0.90–2.51)	0.119
Sex		
Male	1 (ref)	
Female	0.77 (0.52–1.16)	0.210
Explainer		
Pharmacist	1 (ref)	
Non-pharmacist	1.33 (0.90–1.96)	0.147
Medications		
One	1 (ref)	
Two or more	1.67 (1.13–2.47)	0.010 [a]
Days until surgery		
<15	1 (ref)	
≥15	1.41 (0.90–2.20)	0.131

Note: [a]Significant (p < 0.05).
Abbreviations: CI, confidence interval; ref, reference.

Table 3 Subgroup Analysis of Multivariate Binary Logistic Regression Analysis of Risk Factors for Non-Adherence to Medications Affecting Surgery. Adjusted for Departmental Effects (n = 824)

Risk Factor	Odds Ratio (95% CI)	p
Age		
<65 years	1 (ref)	
≥65 years	2.27 (1.11–4.63)	0.024[a]
Sex		
Male	1 (ref)	
Female	0.73 (0.42–1.25)	0.251
Explainer		
Pharmacist	1 (ref)	
Non-pharmacist	0.99 (0.60–1.62)	0.955
Medications		
One	1 (ref)	
Two or more	1.48 (0.93–2.36)	0.101
Days until surgery		
<15	1 (ref)	
≥15	1.34 (0.82–2.20)	0.237

Note: [a]Significant ($p < 0.05$).
Abbreviations: CI, confidence interval; ref, reference.

Table 4 Sensitivity Analysis of Multivariate Binary Logistic Regression Using Age-Adjusted Risk Factors for Non-Adherence to Medications Affecting Surgery (n = 1132)

Risk Factor	Odds Ratio (95% CI)	p
Age	1.01 (0.99–1.03)	0.266
Sex		
Male	1 (ref)	
Female	0.76 (0.51–1.14)	0.188
Explainer		
Pharmacist	1 (ref)	
Non-pharmacist	1.34 (0.91–1.97)	0.141
Medications		
One	1 (ref)	
Two or more	1.68 (1.14–2.49)	0.009 [a]
Days until surgery		
<15	1 (ref)	
≥15	1.42 (0.91–2.21)	0.124

Note: [a]Significant ($p < 0.05$).
Abbreviations: CI, confidence interval; ref, reference.

age as a continuous variable) showed that risk factors were the number of medications to be discontinued. However, the subgroup analysis, in which limited to medical departments revealed that the risk factor was the patient's age (≥65 years). Systematic reviews have reported that a preoperative consultation with an internist reduced the frequency of surgical cancelations and unnecessary hospitalizations after admission for surgery.[5] However, there are limited data identifying risk factors for non-adherence to advance directives for medications potentially affecting surgery. Previous studies have shown that pharmacists' interventions in medication treatment improve patient adherence.[13–18] A retrospective study of

258 patients taking direct oral anticoagulants has shown that patient adherence improved when pharmacists co-managed patients' medications with their doctors.[15] Contrarily, patient adherence was not significantly different from usual care in patients with type 2 diabetes after pharmacist interventions for new statin use.[26] This study demonstrated that the occupation of the ultimate explainer of medication discontinuation was not associated with patient non-adherence. Furthermore, the percentage of pharmacist explanations in different departments varied from 95.3% in urology surgery to 12.9% in respiratory surgery. Future research should be based on specific departments owing to this bias in departmental patient selection.

A nationwide study examining non-adherence to antiretroviral therapy found that non-adherence was significantly higher among Asians aged 0–19 years and 50 years and older than among those aged 30–39 years.[10] Moreover, systematic reviews have shown an association between non-adherence and age.[7,9,11] We also previously reported age ≥65 years as an independent risk factor for non-adherence to medications potentially affecting surgery, and the results of the subgroup analysis in this study showed similar results (Table 3).[12] However, other analyses in this study did not show aged ≥65 years as a risk factor for non-adherence. (Tables 2, 4 and S2–S4). One possible reason is that the final explainer with a non-pharmacist job title was an exclusion criterion in the previous study.[12] However, this was not an exclusion criterion in the current study, and the proportion of included departments varied. Various factors, including patient characteristics, specific to each department, could have contributed to the different study results. The association between age and non-adherence (including factors not examined in the present study) should be further investigated.

We also examined the association between non-adherence and the number of days between explanation and surgery. The number of days between a pharmacist's explanation and surgery (categorized as more or less than 30 days) was unrelated to non-adherence in our retrospective study.[12] The present results are consistent with those of our previous study. However, confounding factors (such as the patients' annual income, educational background, living arrangements [alone or with others], and health literacy)[7–9] were not adjusted for in our study. Therefore, future prospective investigations adjusting for these factors should be conducted.

Herein the association between non-adherence and sex was examined. Systematic reviews have yielded inconclusive results regarding whether sex is a risk factor for non-adherence owing to differences in medications and other investigated factors.[6,9,10,27] Our study showed that sex was not significantly related to non-adherence. This could be attributed to the fact that 33.4% of the study participants were from the urology department and 67.8% were male individuals. Hence, sex- or patient-selection bias was possible. The number of eligible patients was higher in the urology department than in other departments as patients in this department underwent examinations and biopsies involving bleeding. Therefore, future analyses of the relationship between sex differences and non-adherence to medications potentially affecting surgery should be performed with an equal number of patients per department.

Analysis of the relationship between the number of medications affecting surgery and non-adherence in this study revealed the number of medications affecting surgery as a risk factor for non-adherence. Multivariate binary logistic regression analysis was performed after adjusting for age as a continuous variable as a sensitivity analysis. The results were identical to those for the primary outcome, indicating the robustness of the main analysis. A systematic review examining non-adherence in patients with end-stage kidney disease reported the number of medications taken per day as a risk factor for non-adherence.[7] A post-hoc Cochran–Armitage analysis showed that the percentage of non-adherence tended to increase with the number of medications affecting surgery (Figure S1). Considering the multiplicity of analyses, 668 patients in each group were needed to analyze the number of medications and non-adherence rates, an insufficient sample size for this study. Consequently, caution should be taken when interpreting the results. However, the findings were considered clinically significant because they were consistent in the main and sensitivity analyses in this study, and taking two or more medications affecting surgery was identified as a risk factor for non-adherence.

Here, the surgical cancelation rates were 0.13% (n = 1) and 0.29% (n = 1) in the pharmacist and non-pharmacist groups, respectively. To the best of our knowledge, this is the first retrospective study on whether explanation by individuals of different occupations is a risk factor for non-adherence to medications that affect surgery, and a comparison with the findings of previous studies was not possible.

A systematic review on improving patient adherence for secondary prevention of acute coronary syndromes found that text message interventions were ineffective.[28] However, text messaging interventions, interventions explained by pharmacists through face-to-face interviews, and interventions using mobile apps are effective.[29–31] Kimura et al developed a scientifically based preoperative medication discontinuation management database and an app and reported that discontinuation forgetfulness was reduced by approximately 50%.[32] Additionally, a clinically significant increase in adherence was reported for the artificial intelligence intervention group in an open-label, randomized, controlled trial evaluating whether artificial intelligence interventions improve statin adherence.[33]

The preoperative discontinuation of over two medications affecting surgery was identified as a risk factor for non-adherence in this study; however, the relationship between risk factors for non-adherence is complex and probably cannot be determined by simple individual patient factors alone. In the future, pharmacists should use text messages, apps, and artificial intelligence to educate patients about medications that should be discontinued preoperatively. To our knowledge, this is the first study to examine the non-adherence rate in different explanatory occupations using a cohort of >1000 patients and identify the number of medications to be discontinued as an independent risk factor for non-adherence. Future research could further elucidate risk factors for non-adherence to discontinuation of medications affecting surgery and use digital tools to examine strategies to improve medication adherence tailored to patient characteristics.

Limitations

This study has some limitations. The bias in the number of patients per department may have contributed to patient selection bias. Differences in the patient sex ratio, age, and time between the explanation of preoperative medication withdrawal and surgery in each department impeded randomization. Moreover, statistical analyses were only performed on restricted risk factors. Therefore, caution should be exercised when interpreting the results. Second, this was a retrospective single-center study. Our findings are not generalizable as only a priori assumed risk factors were examined, and unadjusted factors were not analyzed. Generalizable results require prospective, multicenter, global studies. Finally, the study's non-adherence rate indicated that a cohort of 1022 patients per group was needed for analysis, with a post-hoc power of 44.5%. A future prospective study with a higher number of patients is required to identify the association between the explainer's occupation and non-adherence that could not be identified in our investigation.

Conclusion

This study showed that the number of medications to be discontinued (and not the occupation of individuals who ultimately explained discontinuation to patients) was a risk factor for non-adherence to preoperative medication discontinuation. Physicians and pharmacists should understand risk factors for non-adherence to surgery-related medications and proactively educate patients to improve adherence. Finally, ongoing patient education should underscore the importance of adherence to reduce the potential non-adherence burden on patients and hospitals.

Data Sharing Statement

The data that support the findings of this study are openly available in "Dataset Akamine Akihiko4" at https://data.mendeley.com/datasets/dw2993xm2n/1.

Ethics Approval and Informed Consent

The study was approved by the Institutional Review Board for Observation and Epidemiological Study at the University of Kitasato (Approval No. KMEO B22-176; Date: January 23, 2023). Additionally, this research involved the secondary use of data from a previous study, which had also been approved by the same board (Approval No. KMEO B21-013; Date: June 11, 2021). The secondary use was authorized by the Institutional Review Board for Observation and Epidemiological Study at the University of Kitasato. Both studies were conducted in strict adherence to the ethical guidelines outlined in the Declaration of Helsinki and Good Clinical Practice. Informed consent was acquired through an opt-out method, which was clearly detailed on the Kitasato University School of Medicine's website.

Consent for Publication

We have obtained ethical approval from the Institutional Review Board for Observation and Epidemiological Study at the University of Kitasato (KMEO B22-176) to conduct the research and permission to use the information in the database for research purposes. There were no requests for non-participation by the studied patients in the conduct of this study. We have ensured that all acquired data and patient information have been anonymized.

Acknowledgments

The authors thank Hiroki Yoshida for advice on the statistical analysis. We would like to thank Editage (www.editage.jp) for English language editing.

Author Contributions

All authors have substantially contributed to various aspects of this research, including its conception, design, execution, data collection, analysis, and interpretation. Additionally, all authors have been actively involved in drafting the manuscript or critically revising it for important intellectual content. They have also given their final approval for the version to be published and have collectively agreed upon the journal to which the article is being submitted. Throughout the process, all authors have reviewed and consented to all versions of the article—prior to submission, during revisions, the final version accepted for publication, and even any significant changes made during the proofing stage. Moreover, each author has agreed to take responsibility and be accountable for the study's content, ensuring the integrity and accuracy of the work presented.

Funding

The authors declare that no funds, grants, or other support were received during the preparation of this manuscript.

Disclosure

The authors report no conflicts of interest in this work.

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