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Original Paper

The Negative Association between Psychotropics and Hospital Stay in Older Patients with Osteoarthritis: A Retrospective Study

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Abstract

Background: As the population ages, the number of patients with osteoarthritis also rises. Patients with end-stage osteoarthritis often undergo surgery, including total joint replacement, in the hospital. In those cases, the length of hospital stay is problematic for both patients and hospitals. This study aimed to determine the factors that influenced the length of stay in older patients with osteoarthritis treated at our hospital.

Methods: We performed a retrospective chart review. The study included 253 patients with osteoarthritis aged ≥ 65 years who underwent surgery and were admitted to our hospital between January 2017 and December 2019. A total of 247 patients were included in the final analysis. The objective variable was length of stay. Factors with a p value <0.05 in the univariate analysis were further analyzed via multiple regression analysis to determine independent risk factors for prolongation of length of stay. Multivariate analysis of factors associated with length of stay was performed, adjusting for confounding factors.

Results: Of 42 variables analyzed by univariate analysis, 22 were significantly correlated. Furthermore, the results of the multiple regression analysis showed that length of stay was significantly associated with the use of psychotropics. Users of psychotropics had a significantly longer length of stay than nonusers did.

Conclusions: Psychotropics are negatively associated with the length of stay in older patients with osteoarthritis.

Key words: osteoarthritis, length of stay, older patients, psychotropics

Introduction

Osteoarthritis (OA) is a degenerative disease of the articular cartilage and other joint components[1]. The number of patients with OA increases as the population ages[2]. Patients with OA are restricted in activities of daily living (ADLs) because of pain[2]. Treatments for OA can be divided into conservative and surgical treatments. Surgical procedures, including total joint replacement, are typically performed in hospitals, and surgical patients stay for several days in the hospital for rehabilitation to improve ADLs.

The hospital length of stay (LOS) for surgical treatment has been well discussed[3]. An extended stay in the hospital can cause several problems for both patients and society at large, in terms of cost and ADLs[4,5]. Although patients should aim to recover their ADL abilities after surgery, an extended hospital stay for treatment is associated with a risk of decreased ADL ability, especially in older adults[4]. Moreover, prolonged treatment of inpatients incurs a higher cost to society[5]. Perhaps reflecting on this concern, the LOS for surgical patients undergoing knee OA treatment is generally just a few days, typically 3–7 days in the United States and European Union[6–9]. However, the average LOS for such patients is much longer in Japan. Ishii et al.[10] reported that the average LOS for patients receiving total knee arthroplasty for knee OA is 37 days in Japan. This might be because of the use of a universal health insurance system and relatively low premiums in Japan, and patients and their relatives may believe that it is safer to extend the hospital stay until recovery is complete.

Previous literature has suggested several factors as

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affecting the LOS of patients with OA, such as low exercise capacity[11], chronic kidney disease, advanced age[12], high body mass index (BMI), female[13], and polypharmacy[14,15]. However, only a limited number of studies have comprehensively investigated the factors associated with LOS, including drugs.

In the present study, we aimed to identify the factors that affect the LOS in patients aged ≥65 years who were hospitalized for surgery for OA by assessing data regarding their medical history, drugs received, adverse events, and clinical laboratory values during hospitalization.

Materials and Methods

Participants

This retrospective observational study included 253 patients with OA aged ≥65 years who were admitted to our hospital from January 2017 to December 2019 for surgery. An experienced orthopedic surgeon made the diagnosis of OA. We excluded patients with missing data, no surgery, and death.

Investigation items

We collected patient background data including sex, age, BMI, current medical history, comorbidities, Charlson Comorbidity Index[16], adverse events occurring during hospitalization, number of drugs at admission, number of drugs at discharge, five or more drugs at admission, increase in drugs during hospitalization, and Functional Independence Measure (FIM) score[17].

The drugs were classified based on the Ministry of Internal Affairs and Communications classification system[18]. After classification, we evaluated the top 12 drugs with the most users.

Laboratory data included the levels of albumin (Alb), aspartate aminotransferase, alanine aminotransferase, γ-glutamyl transferase, serum creatinine (SCr), creatinine clearance (Ccr), and estimated glomerular filtration rate (eGFR). Each variable was assessed at the time of admission. We collected the data from the patients' medical charts. Ccr was calculated using the Cockcroft-Gault equation[19]. The eGFR was calculated using the below equations, which are used commonly in Japan[20]:

Male eGFR creatinine (mL/min/1.73 m^2) $= 194 \times SCr^{-1.094} \times age^{-0.287}$

Female eGFR creatinine (mL/min/1.73 m^2) $= 194 \times SCr^{-1.094} \times age^{-0.287} \times 0.739$

Assessing ADLs

To evaluate ADLs in the present study, we used the FIM score, which is one of the most common measurement tools used for assessing ADL[17]. The FIM score was used to assess the patient's level of disability as well as a change in his or her status in response to rehabilitation. It has been validated for use in older patients as well[21]. The FIM score includes 13 lower-order items regarding motor function (FIM-M) and 5 lower-order items regarding cognitive function (FIM-C). Each item on the FIM is scored on a scale ranging from 1 (*total assistance*) to 7 (*complete independence*). The total score (FIM-T) ranges from 18 to 126 points. The FIM score was assessed at admission and discharge by a physiotherapist who had a long experience of working in our hospital and was familiar with the FIM tool. On the basis of the judgment provided by our physiotherapist, appropriate rehabilitation was offered to all participants, regardless of their FIM scores or LOS.

Statistical analysis

All statistical analyses were performed using JMP Pro version 1 (SAS Institute, Cary, NC, USA). First, we performed the Shapiro-Wilk test to evaluate whether the numerical data were normally or nonnormally distributed. In the case of normal distribution, the data were presented as mean ± standard deviation, and in the case of nonnormal distribution, the data were presented as median (interquartile range, 25th–75th percentiles). For the univariate analysis to research the correlation factors with LOS, the following statistical methods were used, depending on the type of background data. When the numerical data showed a normal distribution, we performed Pearson's rank correlation test. If the data did not show a normal distribution, we used Spearman's rank correlation test. Wilcoxon's rank-sum test was used for comparison between two groups. Multiple linear regression analysis was conducted to determine the effect of the factors on LOS. The least-squares method of multiple linear regression analysis was used as the model-building method. Factors that were significantly associated with LOS in the univariate and single-correlation analyses were used as explanatory variables in the multiple regression analysis. Multicollinearity among the factors was assessed using the variance inflation factor (VIF) coefficient. When the VIF was >4 between explanatory variables, only variables that were more reasonable from a medi-

cal/pharmacologic perspective were used in the multiple regression analysis. To compare the LOS between the two groups, we created a Kaplan-Meier curve and performed a log-rank test. In all of the statistical analyses, a p value of <0.05 was considered statistically significant.

Ethics approval and consent to participate

The present study was performed according to the Declaration of Helsinki and was approved by the institutional review board (IRB) of the authors' affiliated institutions. Participants were presented with an opt-out option. We informed participants that they could withdraw from the study at any time. The patients and/or their families were informed that the data from the research would be submitted for publication, and they provided their consent.

Results

Descriptive and univariate analyses

A total of 253 patients who met the study's inclusion criteria were screened in the present retrospective study. OA included shoulders (1.6%), ankles (2.0%), hips (38.9%), and knees (57.5%). In total, 247 patients (38 men and 209 women; mean age: 76.6 ± 6.1 years) were included in the final analysis; six patients were excluded for no surgery (n = 5), missing data (n = 1), and death (n = 0; Fig. 1).

Table 1 shows the results of the univariate analysis between patient background items and LOS. Among the 42 variables, 22 were significantly correlated. In terms of patient background, we found significant differences in LOS for sex, ankle OA, hip OA, knee OA, hypertension, diabetes, deep vein thrombosis, postoperative infection, and the use of five or more drugs. There were significant positive correlations with LOS for age, BMI, number of drugs at admission, and number of drugs at discharge. Significant negative correlations with LOS were found for FIM-M score and FIM-T score. Among the 12 drug classes, a significant difference was noted in the LOS of patients with the following four drug types: peptic ulcer drugs, vasodilators, psychotropics, and antidiabetic drugs. In the univariate analysis of laboratory data, we observed significant negative correlations between LOS and Alb, Ccr, and eGFR. There were no significant differences or correlations with LOS and the other items (Table 1).

Multiple linear regression analysis

To determine how much each factor contributes to the LOS, we performed multiple linear regression analysis. Factors that were found to be significantly different or correlated in the univariate and single-correlation analyses were used as explanatory variables, as follows: female, age, ankle OA, knee OA, deep vein thrombosis, postoperative infection, the use of five or more drugs at admission, FIM-M score, drugs for peptic ulcer, vasodilators, psychotropics, antidiabetic drugs, and eGFR. The objective variable was LOS. Table 2 shows that significant associations were found for LOS and ankle OA, postoperative infection, age, deep vein thrombosis, psychotropics, and FIM-M score. These factors were independent of each other, and no multicollinearity was observed (Table 2).

Effect of psychotropics on LOS

Interestingly, the results of the univariate and multi-

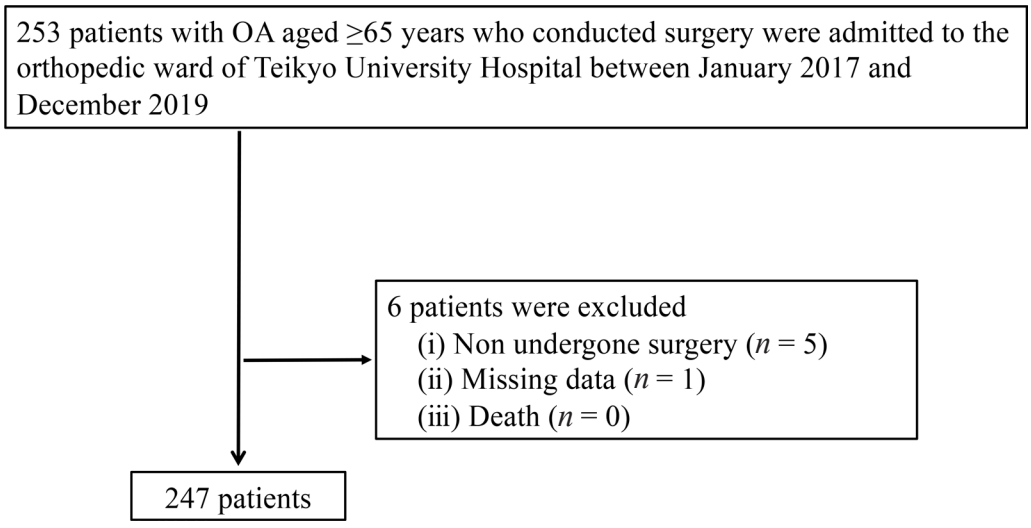

Fig. 1　Flow chart of patient extraction.

Table 1　Association between demographic characteristics and LOS.

Characteristics	All patients (n = 247)	Correlation coefficient	p value
Gender, n (%)			0.0090¶
Male	38 (15.4)		
Female	209 (84.6)		
Age (y)	77 (72–84)	0.2811	＜0.0001‡
BMI (kg/m^2)	25.0 (22.6–28.3)	0.2126	0.0008‡
Current medical history, n (%)			
Shoulder OA	4 (1.6)		0.1318¶
Ankle OA	5 (2.0)		0.0382¶
Hip OA	96 (38.9)		0.0001¶
Knee OA	142 (57.5)		0.0004¶
Comorbidities, n (%)			
Hypertension	168 (68.0)		0.0446¶
Dyslipidemia	104 (42.1)		0.8582¶
Osteoporosis	55 (22.3)		0.8396¶
Diabetes	42 (17.0)		0.0391¶
Cancer	26 (10.5)		0.9560¶
Charlson Comorbidity Index	0 (0–1)	0.0686	0.2831‡
Adverse events, n (%)			
Delirium	13 (5.3)		0.2849¶
Deep vein thrombosis	14 (5.5)		0.0009¶
Postoperative infection	2 (0.8)		0.0401¶
No. of drugs at admission	5 (3–8)	0.1916	0.0025‡
No. of drugs at discharge	6 (4–9)	0.1388	0.0292‡
≥5 drugs at admission, *n* (%)	135 (54.7)		0.0067¶
Increase in drugs during hospitalization, *n* (%)	159 (64.4)		0.4009¶
FIM			
FIM-M	89 (85–90)	−0.2340	0.0002‡
FIM-C	35 (35–35)	−0.1171	0.0662‡
FIM-T	124 (120–125)	−0.2358	0.0002‡
Drugs, n (%)			
Antihypertensives	151 (61.1)		0.1047¶
Drugs for peptic ulcer	133 (53.8)		0.0300¶
Drugs for hyperlipidemias	95 (38.5)		0.3793¶
Antipyretic analgesic drugs	95 (38.5)		0.2393¶
Other drugs relating to blood and body fluides	53 (21.5)		0.1599¶
Vitamins A and D	51 (20.6)		0.9991¶
Puragatives and clysters	49 (19.8)		0.0552¶
Hypnotics and anxiolytics	45 (18.2)		0.3463¶
Vasodilators	42 (17.0)		0.0305¶
Psychotropics	36 (14.6)		0.0031¶
Antidiabetic drugs	33 (13.4)		0.0058¶
Drugs for treatment of gout	25 (10.1)		0.4611¶
Clinical laboratory date			
Alb (g/dL)	4.1 (3.9–4.3)	−0.1283	0.0466‡
AST (U/L)	22 (18–26)	0.0006	0.9931‡
ALT (U/L)	16 (12–22)	−0.0425	0.5057‡
γ-GTP (U/L)	23 (16.25–38.5)	−0.1294	0.1455‡
SCr (mg/dL)	0.7 (0.6–0.9)	0.0106	0.8687‡
Ccr (mL/min)	52.2 ± 15.3	−0.2571	＜0.0001‡
eGFR (mL/min)	54.4 (45.0–63.1)	−0.1808	0.0044‡

Values are mean ± standard deviation or median (interquartile range) where appropriate.
Alb, albumin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; Ccr, creatinine clearance; eGFR, estimated glomerular filtration rate; FIM, Functional Independence Measure; FIM-C, Functional Independence Measure-Cognitive; FIM-M, Functional Independence Measure-Motor; FIM-T, Functional Independence Measure-Total; γ-GTP, γ-glutamyl transferase; LOS, length of stay; OA, osteoarthritis; SCr, serum creatinine.
P values indicate the association with LOS.
¶: Wilcoxon's rank-sum test.
‡: Spearman's rank correlation test.

Table 2　Multiple regression analysis for LOS.

Variable	Unstandardized coefficient				t	Standard coefficient	VIF	p value
	β	Standard error	95% CI of β					
Ankle OA	15.361	3.585	8.298	22.426	4.28	0.252	1.140	<0.0001
Postoperative infection	19.257	5.410	8.598	29.916	3.56	0.201	1.052	0.0005
Age	0.607	0.174	0.264	0.951	3.48	0.217	1.278	0.0006
Deep vein thrombosis	7.272	2.138	3.059	11.486	3.40	0.196	1.094	0.0008
Psychotropics	3.987	1.495	1.042	6.932	2.73	0.164	1.244	0.0082
FIM-M	−0.205	0.964	−0.395	−0.015	−2.13	−0.124	1.117	0.0345
Knee OA	1.869	1.024	−0.147	3.886	1.83	0.108	1.146	0.0691
Female	2.028	1.433	−0.794	4.809	1.42	0.085	1.195	0.1582
eGFR	−0.040	0.070	−0.180	0.098	−0.58	−0.366	1.333	0.5656
Antidiabetic drugs	0.572	1.492	−2.368	3.512	0.38	0.023	1.153	0.7017
≥5 drugs at admission	0.231	1.222	−2.176	2.637	0.19	0.013	1.655	0.8505
Vasodilators	−0.144	1.345	−2.795	2.506	−0.11	−0.006	1.143	0.9144
Drugs for peptic ulcer	−0.013	1.160	−2.300	2.273	0.01	−0.001	1.497	0.9905
Constant	51.521	18.852	14.379	88.664	2.73			0.0068

CI, confidence interval; eGFR, estimated glomerular filtration rate; FIM-M, Functional Independence Measure-Motor; LOS, length of stay; OA, osteoarthritis; VIF, variance inflation factor.
$R^2 = 0.2920$, $p < 0.0001$.

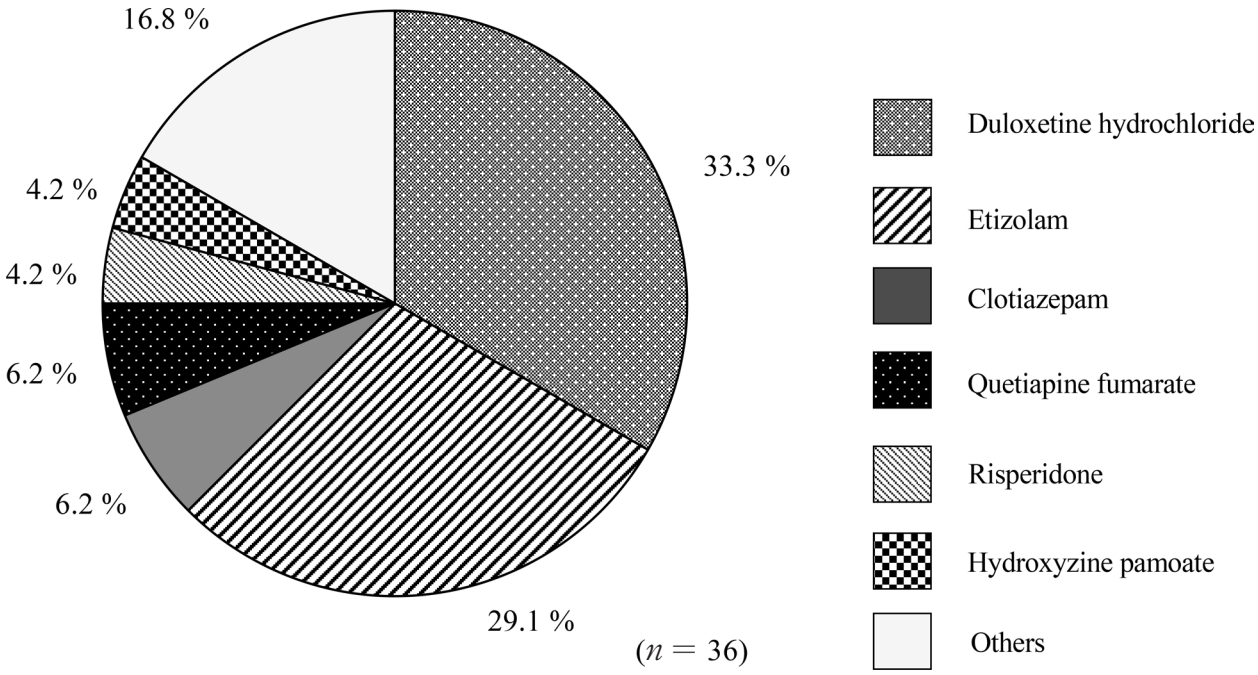

Fig. 2　Breakdown of psychotropics.

ple linear regression analyses revealed that the use of psychotropics was significantly associated with LOS. The overall rate of psychotropics use was 14.6%. Fig. 2 displays the types of psychotropics administered. Because few previous studies have suggested that the use of psychotropics may affect the LOS in OA, our results are very important. Furthermore, we performed a log-rank test to compare the LOS between patients who used psychotropics and those who did not. As shown in Fig. 3, psychotropic users had a significantly longer LOS than nonusers did (hazard ratio: 1.469, 95% confidence interval: 1.029–2.096; $p = 0.028$).

Discussion

Because of the functional decline in older patients and the increasing burden of medical costs, the prolon-

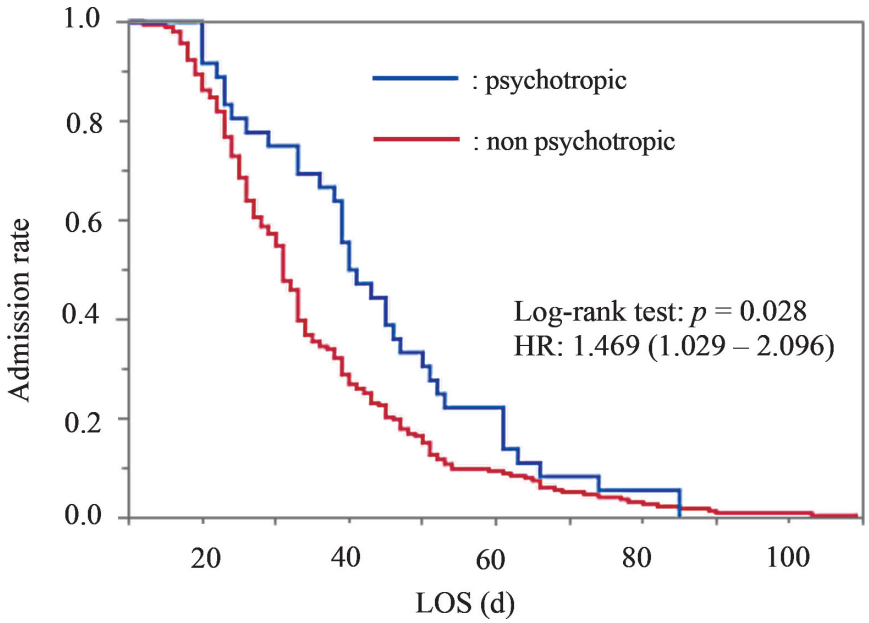

Fig. 3　Effect of psychotropics on LOS.
A Kaplan-Meier curve was created and log-rank tests were performed to compare the length of stay.
LOS, length of stay; HR, hazard ratio.

gation of LOS is problematic[4,5]. Therefore, it is very important to identify the risk factors associated with LOS prolongation. The most important and novel finding of the present study was that use of psychotropics was negatively associated with LOS in older patients undergoing surgery for OA, independently of ankle OA, postoperative infection, age, deep vein thrombosis, and FIM-M score. Log-rank tests showed that the use of psychotropics could extend LOS by 46%.

Duloxetine hydrochloride was the most common psychotropic (33.3%) used by the patients in our study. Duloxetine hydrochloride has not only antidepressant effects but also analgesic effects[22] and is used to manage chronic low-back pain and chronic pain due to OA, for which nonsteroidal anti-inflammatory drugs are not adequately effective. Today, duloxetine hydrochloride is widely used as a first-choice drug for pain associated with neuropathy. In the present study, more than 80% of the patients who used duloxetine hydrochloride used it as an analgesic. However, the medicine's label clearly states that side effects may frequently occur, including somnolence (24.3%), nausea (22.4%), and serotonin syndrome (frequency unknown). Generally, these side effects prevent improvement in ADLs. Older patients are especially more susceptible to adverse drug events because of a general decline in their physiological function[23]. Although duloxetine hydrochloride was prescribed before admission, it may no longer be required after surgery if the pain subsides. Some patients, however, continue to take it after surgery. This is because they are dependent on it owing to anxiety about pain. Medical staff should assess the patient's postoperative pain and side effects of duloxetine hydrochloride and consider reducing or discontinuing it or switching to another analgesic.

In addition, benzodiazepines comprised 35.4% of the psychotropics assessed in the present study. Drugs containing benzodiazepines have been reported to cause motor dysfunction, such as falls[24], and cognitive dysfunction, such as anterograde amnesia[25]. In this study, benzodiazepines were prescribed for anxiety disorders or insomnia not due to OA; therefore, it may be difficult for patients to stop using them. However, it has been reported that with appropriate education (e.g., regarding side effects and drug interactions) and a proposal of alternative therapy, benzodiazepines can be stopped in 27% of patients[26]. Medical staff members should assess the necessity of benzodiazepines and, if alternative therapies are available, suggest reducing or stopping these drugs. To prevent adverse events such as rebound insomnia and pain relapse, benzodiazepines should be reduced according to clinical guidelines for proper usage and tapering of hypnotics, for example, a 25% reduction in dose every 1–2 weeks over 4–8 weeks.

Because psychotropics are prescribed for behavioral

and psychological symptoms of dementia (BPSD) and/or strong pain, it is possible that the prolonged LOS was caused by not adverse events with psychotropics but rather the conditions of the patient who were taking them, such as pain or BPSD. First, the FIM-C score and delirium were not associated with LOS in this study (Table 1), so it is unlikely that BPSD contributed to prolonged LOS. Second, although we assessed pain using a numerical rating scale, it is difficult to determine whether pain affected LOS because of the inconsistent timing of the assessments. Therefore, further research is needed to determine why the use of psychotropics affects LOS.

In addition to psychotropics, ankle OA, postoperative infection, age, deep vein thrombosis, and FIM-M score were significantly associated with LOS in the present study. Univariate analysis showed that LOS was significantly prolonged in those with postoperative infection (80 vs. 32 days, $p = 0.0401$). Similarly, it was also significantly prolonged in those with deep vein thrombosis (45 vs. 31 days, $p = 0.0009$). Moreover, there was a positive correlation between age and LOS and a negative correlation between FIM-M score and LOS.

Chona et al.[27] reported that postoperative infection was the most influential factor for LOS in patients who underwent surgery, and the postoperative onset of deep vein thrombosis and age might also have been associated with prolongation of LOS. Our results supported these previous reports. A previous study reported that low albumin level, age, obesity, smoking, and diabetes were risk factors for postoperative infection[28]. It was also reported that the risk of deep vein thrombosis increases with age[29]. Medical staff must be particularly careful when managing patients with these risks.

Our study has several limitations. First, this was a single-center, retrospective, observational study. Therefore, it is not possible to determine the causal relationships between psychotropics and LOS. Second, we did not consider drug doses and interactions in this study. Finally, we were unable to adequately consider the occurrence of adverse events during hospitalization, which might affect LOS, such as falls and the development of nerve damage.

In conclusion, our results indicate that psychotropics are independently associated with LOS in older patients with OA. Therefore, whether or not deprescribing psychotropics affects the reduction of LOS should be examined.

Statements & Declarations

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Competing Interests

The authors have no relevant financial or nonfinancial interests to disclose.

Ethics Approval

The present study was performed according to the Declaration of Helsinki and was approved by the IRB of the authors' affiliated institutions.

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