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Original Article

# Deterioration of Postoperative Daily Living Activities in Elderly Patients: Incidence and Associated Factors

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SUMMARY

*Background:* Postoperative functional status is a concern in elderly patients. Previously, we reported that administration of non-steroidal anti-inflammatory drugs (NSAIDs) was associated with maintenance of activities of daily living (ADL) scores in elderly patients after hip fracture surgery. The aim of the present study was to investigate whether perioperative NSAIDs administration is related to ADL scores in other age groups after a wide range of surgeries.
*Methods:* The medical records of 368,859 patients aged ≥ 15 years who underwent surgery under general anesthesia were reviewed.
*Results:* The ADL deterioration ratios of patients aged 70 years or older were significantly higher than those of the younger cohort. NSAIDs administration was associated with postoperative ADL maintenance in elderly patients who underwent various surgeries. However, administration of NSAIDs was not related to ADL maintenance in the younger patients.
*Conclusions:* Postoperative ADL deterioration incidences were higher in elderly patients than in younger patients. Perioperative administration of NSAIDs was associated with postoperative ADL maintenance in various surgeries in elderly patients but not in younger patients. The mechanisms of postoperative ADL deterioration are likely different in elderly and younger patients.



## 1. Introduction

The global growth of the elderly population is expected to increase the frequency of surgeries on the elderly.[1] Some researchers have reported that only a few elderly patients show a protracted decline in activity of daily living (ADL) and that most patients exhibit better quality of life (QOL) after elective surgery;[2,3] however, other investigators have suggested that the functional decline risk is high or the functional status is vulnerable in elderly patients after surgery.[4,5] Functional impairment is a risk factor of mortality in elderly patients.[6,7]

We previously reported that perioperative administration of non-steroidal anti-inflammatory drugs (NSAIDs) was associated with the maintenance of ADL scores in the elderly after hip fracture surgery.[8] The aim of the present study was to investigate whether administration of NSAIDs during the three days after surgery affected the postoperative ADL scores in different age groups after a wide range of surgeries.

## 2. Materials and methods

This study was approved by the ethics review boards of our hospital and National Hospital Organization (NHO). Following the Japanese ethics guidelines for human medical research, this study protocol was open to the general public via our hospital and NHO websites to obtain patient objections. To protect patient privacy, all types of personal identification were encrypted in a security room of the NHO databank. The requirement for individual informed consent was waived due to the anonymous nature of the data.

### *2.1. Data sources*

The study period was from April 1, 2014, to March 31, 2018. We used data from the Japanese DPC (diagnosis procedure combination) administrative claims database that was obtained from 69 hospitals in the NHO group. The DPC database is a diagnosis-dominant, case-mix system administered by the Ministry of Health, Labor, and Welfare of Japan, and linked with a lump sum payment system.

### *2.2. Selection of patients and variables*

The inclusion criteria were that all patients had to be 15 years or older and have undergone surgery under general anesthesia during the study period. Patients administered a combination of general and another type of anesthesia were also included. We excluded 4707 cases of patients who died after surgery, 16,164 cases of patients who were fully dependent at the time of admission to the

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hospital, and 34,743 cases with missing baseline characteristics data. The data of the remaining 313,245 patients of the initial 368,859 were analyzed. We divided the 313,245 patients into elderly (70 years or older) and younger (less than 70 years old) patients based on an analysis of the ADL deterioration ratios (Figure 1).

Data from the DPC database included age, sex, height, weight, diagnoses, surgical procedure, anesthetic type, medications during hospitalization, comorbidities before hospitalization, and ADL scores at both admission and discharge. The evaluation items for the ADL score are basically the same as those for the Barthel Index, except that the maximum value for the former is 20.[9] Body mass index (BMI) was calculated from the height and weight. The change in ADL was determined by deducting the baseline ADL score (at admission) from the ADL score at hospital discharge. A negative number indicated deterioration, zero indicated no change, and a positive number was indicative of amelioration.

A modified Charlson Comorbidity Index (CCI) was calculated for each patient based on the Quan coding algorithms.[10] Of the analgesics, 20 types of NSAIDs were included: aspirin, celecoxib, diclofenac, dimetotiazine mesilate, emorfazone, etodolac, flurbiprofen, ibuprofen, indomethacin, isopropylantipyrine, ketoprofen, lornoxicam, loxoprofen, mefenamic acid, meloxicam, naproxen, salicylate, sulindac, tiaramide, and zaltoprofen. Patients who were administered the above-mentioned NSAIDs within three days after surgery were considered to be a part of the NSAIDs group. The postoperative hospital length of stay (LOS) was defined as the number of calendar days from operation to discharge.

### *2.3. Propensity score matching*

Propensity score-matched analysis was used to reduce selection bias and potential baseline differences between the NSAID and the non-NSAID groups. We analyzed the elderly and younger patients separately. Propensity scores were calculated using a binary logistic regression analysis, with administration of NSAIDs as the dependent variable and 15 perioperative factors as predictor variables. The independent variables were age, sex, BMI, the modified CCI, length of hospital stay after surgery, ADL dependency at hospital admission, surgery types, and baseline comorbidities (anemia, diabetes mellitus, mental, neurologic, circulatory, respiratory, digestive, and renal/urinary). These selected variables were based on prior subject matter knowledge and empirical observations.[11–13] The score was defined as the probability of a patient receiving NSAIDs based on covariates. After adjustment with the scores, none of the perioperative variables remained statistically different between the two groups. The multivariate regression model of propensity for an elderly patient given NSAIDs had a C-statistic of 0.621, while that for a younger patient was 0.604.

### *2.4. Statistical analysis*

Patient characteristics were compared between the NSAID and the non-NSAID groups using the chi square test. The change of ADL score was assessed using the Pearson chi square test after propensity score matching. Multivariate logistic regression analysis was performed between the deterioration and the maintenance (no change and amelioration) groups to analyze the effects of various factors. In addition to NSAIDs, the following were selected for the model: age, sex, BMI, modified CCI, ADL dependency at admission, surgery type, and LOS. These variables have been previously suggested to affect the prognosis. Odds ratios and 95% confidence intervals were determined. A p value of < 0.05 was considered significant for all statistical tests. All statistical analyses were carried out using SPSS software version 24 (IBM, Armonk, New York).

## 3. Results

Of the 313,245 patients aged 15 years old or older, 18,067 (5.8%) had decreased ADL scores during their hospital stay. The percentages of postoperative ADL deterioration at each generation are shown in Figure 2. The ADL deterioration ratios of elderly patients (70 years or older) were significantly higher than those of the younger patients (p < 0.01).

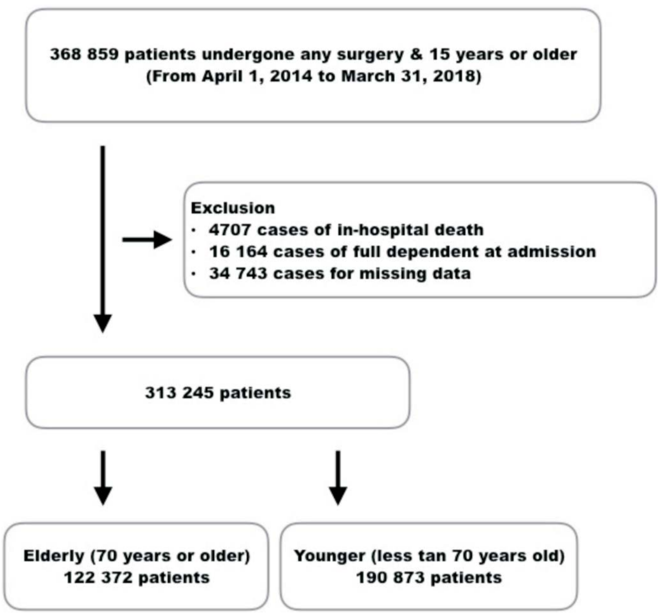


**Figure 1.** Characteristics of excluded and eligible patients in the analytical data set.

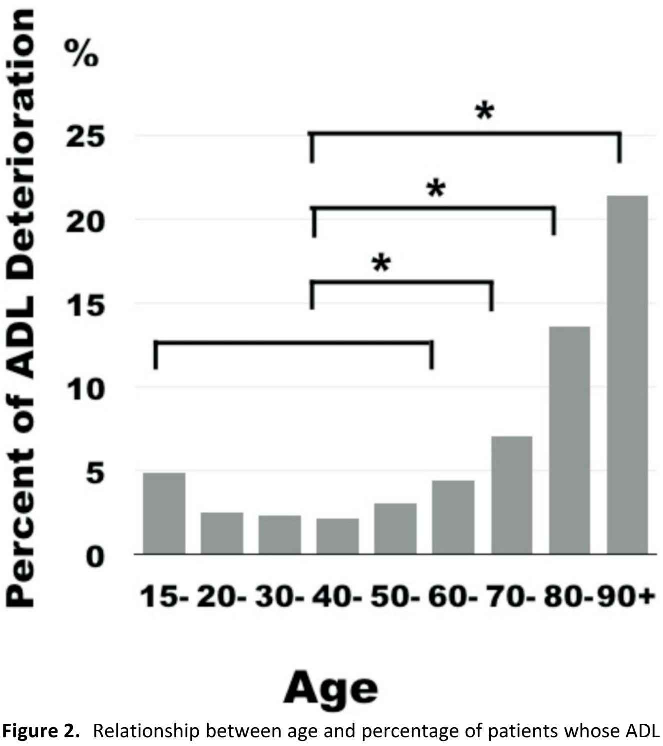


**Figure 2.** Relationship between age and percentage of patients whose ADL scores decreased during their hospital stay. ADL: activities of daily living. Note: The ADL deterioration ratios of patients aged 70 years or older were significantly higher than those of younger than 70 (p < 0.01).

Of the 122,372 elderly patients, 82,124 (67.1%) received NSAIDs and 40,248 (32.9%) did not. Results of the multivariate analysis in the elderly patients showed that advanced age, female sex, lower BMI, higher CCI, prehospital dependency, orthopedic surgeries, longer LOS, and no administration of NSAIDs were associated with deterioration of ADL scores (Table 1). Table 2 compares the characteristics of the NSAID and non-NSAID groups. Before propensity score matching, all of the 15 baseline factors differed significantly between the two groups. After 1:1 matching, a total of 36,527 patients in each group showed no significant baseline differences. After the propensity score matching, administration of NSAIDs was associated with maintenance of the ADL score during the hospital stay in the elderly patients ($p < 0.01$) (Table 3).

Of the 190,873 younger patients (less than 70 years old),

**Table 1**
Multivariate analysis: Factors affecting ADL deterioration during hospital stay.

| Variable | | Younger patients (n = 190,873) | | | | | Elderly Patients (n=122,372) | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | B | OR | 95% CI | p value | | B | OR | 95% CI | p value |
| Age | 15–19 | | 1 | | | 70–79 | | 1 | | |
| | 20–49 | -0.381 | 0.683 | 0.603 to 0.774 | < 0.001 | 80–89 | 0.561 | 1.753 | 1.682 to 1.828 | < 0.001 |
| | 50–59 | -0.283 | 0.753 | 0.661 to 0.858 | < 0.001 | 90+ | 0.866 | 2.377 | 2.166 to 2.609 | < 0.001 |
| | 60–69 | 0.011 | 1.011 | 0.893 to 1.144 | 0.865 | | | | | |
| Sex | Male | 0.083 | 1.087 | 1.032 to 1.144 | 0.001 | Female | 0.057 | 1.059 | 1.017 to 1.103 | 0.006 |
| BMI | < 21 | 0.162 | 1.176 | 1.112 to 1.244 | < 0.001 | < 21 | 0.088 | 1.092 | 1.046 to 1.139 | < 0.001 |
| CCI | 1+ | 0.282 | 1.326 | 1.251 to 1.405 | < 0.001 | 1+ | 0.254 | 1.289 | 1.228 to 1.352 | < 0.001 |
| Dependency | (+) | 0.618 | 1.855 | 1.739 to 1.978 | < 0.001 | (+) | 0.351 | 1.421 | 1.358 to 1.487 | < 0.001 |
| Orthopedic | | 1.355 | 3.877 | 3.652 to 4.116 | < 0.001 | | 0.480 | 1.615 | 1.539 to 1.695 | < 0.001 |
| LOS (day) | < 10 | | 1 | | | < 10 | | 1 | | |
| | 10–30 | 0.042 | 1.043 | 0.980 to 1.109 | 0.183 | 10–30 | 0.416 | 1.516 | 1.440 to 1.597 | < 0.001 |
| | 31+ | 0.884 | 2.420 | 2.246 to 2.608 | < 0.001 | 31+ | 1.027 | 2.794 | 2.632 to 2.966 | < 0.001 |
| NSAIDs | (-) | 0.112 | 1.119 | 1.053 to 1.189 | < 0.001 | (-) | 0.136 | 1.146 | 1.100 to 1.195 | < 0.001 |

ADL: activity of daily living; OR: odds ratio; CI: confidence interval; BMI: body mass index; CCI: Charlson Comorbidity Index; Dependency: pre-hospital ADL dependency; LOS: length of hospital stay; NSAIDs: non-steroidal anti-inflammatory drugs.

**Table 2**
Demographic and clinical characteristics of elderly patients.

| | | Before propensity score matching | | | | After propensity score matching | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | NSAIDs (+) | NSAIDs (-) | p value | Standardized difference | NSAIDs (+) | NSAIDs (-) | p value | Standardized difference |
| n | | 82,124 | 40,248 | | | 36,527 | 36,527 | | |
| Age | 70–79 | 56,996 (69.4%) | 24,863 (61.8%) | 0.000 | 0.16 | 23,451 (64.2%) | 23,530 (64.4%) | 0.829 | < 0.01 |
| | 80–89 | 23,423 (28.5%) | 13,798 (34.3%) | | 0.13 | 12,095 (33.1%) | 12,020 (32.9%) | | < 0.01 |
| | 90+ | 1705 (2.1%) | 1587 (3.9%) | | 0.11 | 981 (2.7%) | 977 (2.7%) | | 0 |
| Sex | Male | 39,739 (48.4%) | 21,771 (54.1%) | 0.000 | 0.11 | 19,916 (54.5%) | 19,891 (54.5%) | 0.853 | 0 |
| | Female | 42,385 (51.6%) | 18,477 (45.9%) | | | 16,611 (45.5%) | 16,636 (45.5%) | | |
| BMI | < 21 | 22,540 (27.4%) | 12,663 (31.5%) | 0.000 | 0.09 | 10,805 (29.6%) | 10,868 (29.8%) | 0.610 | < 0.01 |
| | 21+ | 59,584 (72.6%) | 27,585 (68.5%) | | | 25,722 (70.4%) | 25,659 (70.2%) | | |
| CCI | 0 | 26,056 (31.7%) | 9372 (23.3%) | 0.000 | 0.19 | 8755 (24.0%) | 8708 (23.8%) | 0.683 | < 0.01 |
| | 1+ | 56,068 (68.3%) | 30,876 (76.7%) | | | 27,772 (76.0%) | 27,819 (76.2%) | | |
| Pre-hospital ADL | (-) | 64,579 (78.6%) | 29,698 (73.8%) | 0.000 | 0.11 | 28,113 (77.0%) | 28,081 (76.9%) | 0.779 | < 0.01 |
| Dependency | (+) | 17,545 (21.4%) | 10,550 (26.2%) | | | 8414 (23.0%) | 8446 (23.1%) | | |
| Orthopedic surgery | | 24,543 (29.9%) | 7733 (19.2%) | 0.000 | 0.25 | 6869 (18.8%) | 6905 (18.9%) | 0.733 | < 0.01 |
| Other surgery | | 57,581 (70.1%) | 32,515 (80.8%) | | | 29,658 (81.2%) | 29,622 (81.1%) | | |
| Length of hospital | < 10 | 30,605 (37.3%) | 13,961 (34.7%) | 0.000 | 0.05 | 13,420 (36.7%) | 13,307 (36.4%) | 0.533 | 0.01 |
| Stay (day) | 10–30 | 40,249 (49.0%) | 19,218 (47.7%) | | 0.03 | 17,767 (48.6%) | 17,789 (48.7%) | | < 0.01 |
| | 31+ | 11,270 (13.7%) | 7069 (17.6%) | | 0.11 | 5340 (14.6%) | 5431 (14.9%) | | 0.01 |
| Mental | (-) | 78,865 (96.0%) | 38,353 (95.3%) | 0.000 | 0.03 | 35,250 (96.5%) | 35,271 (96.6%) | 0.671 | 0.01 |
| | (+) | 3359 (4.1%) | 1895 (4.7%) | | | 1277 (3.5%) | 1256 (3.4%) | | |
| Anemia | (-) | 79,325 (96.6%) | 37,937 (94.3%) | 0.000 | 0.11 | 35,152 (96.2%) | 35,141 (96.2%) | 0.831 | 0 |
| | (+) | 2799 (3.4%) | 2311 (5.7%) | | | 1375 (3.8%) | 1386 (3.8%) | | |
| Diabetes mellitus | (-) | 68,008 (82.8%) | 32,447 (80.6%) | 0.000 | 0.06 | 29,658 (81.2%) | 29,621 (81.1%) | 0.726 | < 0.01 |
| | (+) | 14,116 (17.2%) | 7801 (19.4%) | | | 6869 (18.8%) | 6906 (18.9%) | | |
| Neurologic | (-) | 74,592 (90.8%) | 36,980 (91.9%) | 0.000 | 0.04 | 33,966 (93.0%) | 33,964 (93.0%) | 0.977 | 0 |
| | (+) | 7532 (9.2%) | 3268 (8.1%) | | | 2561 (7.0%) | 2563 (7.0%) | | |
| Circulatory | (-) | 47,836 (58.2%) | 21,183 (52.6%) | 0.000 | 0.11 | 19,610 (53.7%) | 19,558 (53.5%) | 0.700 | < 0.01 |
| | (+) | 34,288 (41.8%) | 19,065 (47.4%) | | | 16,917 (46.3%) | 16,969 (46.5%) | | |
| Respiratory | (-) | 75,922 (92.4%) | 36,926 (91.7%) | 0.000 | 0.03 | 33,760 (92.4%) | 33,823 (92.6%) | 0.376 | 0.01 |
| | (+) | 6202 (7.6%) | 3322 (8.3%) | | | 2767 (7.6%) | 2704 (7.4%) | | |
| Digestive | (-) | 64,203 (78.2%) | 30,546 (75.9%) | 0.000 | 0.05 | 28,046 (76.8%) | 28,081 (76.9%) | 0.759 | < 0.01 |
| | (+) | 17,921 (21.8%) | 9702 (24.1%) | | | 8481 (23.2%) | 8446 (23.1%) | | |
| Renal/urinary | (-) | 78,285 (95.3%) | 36,706 (91.2%) | 0.000 | 0.16 | 34,142 (93.5%) | 34,175 (93.6%) | 0.620 | < 0.01 |
| | (+) | 3839 (4.7%) | 3542 (8.8%) | | | 2385 (6.5%) | 2352 (6.4%) | | |

NSAIDs: non-steroidal anti-inflammatory drugs; BMI: body mass index; CCI: Charison Comorbidity Index; ADL: activity of daily living.

**Table 3**
Effects of NSAIDs on the ADL change.

| | NSAIDs (+) | NSAIDs (-) | p value |
|---|---|---|---|
| Elderly | | | < 0.01 |
| (n) | 36,527 | 36,527 | |
| ADL deterioration | 3259 (8.9%) | 3534 (9.7%) | |
| ADL maintenance | 33,268 (91.1%) | 32,993 (90.3%) | |
| Younger | | | < 0.01 |
| (n) | 39,060 | 39,060 | |
| ADL deterreration | 1423 (3.6%) | 1279 (3.3%) | |
| ADL maintenance | 37,637 (96.4%) | 37,781 (96.7%) | |

Data are number (%), p values by chi square test, NSAIDs: non-steroidal anti-inflammatory drugs; ADL: activity of daily living.

149,887 (78.5%) received NSAIDs and 40,986 (21.5%) did not. The results of the multivariate analysis in the younger patients showed that age (teens and 60s), male sex, lower BMI, higher CCI, prehospital ADL dependency, orthopedic surgeries, longer LOS, and no administration of NSAIDs were associated with deterioration of the ADL score (Table 1). However, after the propensity score matching, data from the younger patients indicated that administration of NSAIDs was associated with deterioration of the ADL score after surgery ($p < 0.01$) (Table 3).

The major surgery types in the elderly cohort included general surgery (29%), orthopedic surgery (26%), and urological surgery (10%). Additionally, a total of 9005 (7%) brain and cardiovascular surgeries were performed. In the younger generation, major surgery types included general surgery (23%), orthopedic surgery (19%), and obstetrics and gynecological surgery (18%). Additionally, a total of 9274 (5%) brain and cardiovascular surgeries were performed on this age group. Flurbiprofen (37%), loxoprofen (35%), diclofenac (20%), celecoxib (6%), and others (2%) were the types of NSAIDs used during the three postoperative days.

## 4. Discussion

The present study showed that the incidents of ADL deterioration in patients in their 70s, 80s, or older than 90 years were 7.1%, 13.6%, and 21.4%, respectively. These incidents were two- to six-fold higher than those in younger patients (3.4%). Of the patients in their 90s or older, one in five experienced ADL deterioration at hospital discharge.

Most of the previous studies evaluating the outcome of elderly surgeries have investigated mortality and morbidity;[14,15] however, to our knowledge, few reports have focused on the functional status decline after operation. Watt et al. reviewed six studies that investigated risk factors associated with functional decline among older adults who received elective surgery.[16] In the review, the pooled incidence of ADL deterioration was 21.03%. In a subgroup of patients undergoing general surgery, the pooled incidence of ADL deterioration was 15.25%. Although the reviewed studies involved patients in their 60s, our results were consistent with their pooled incidences.

This study assessed 122,372 elderly patients and demonstrated that the administration of NSAIDs was associated with postoperative ADL maintenance. Contrarily, the administration of NSAIDs was associated with deterioration of the ADL scores in the younger age group. This result may indicate that the mechanisms of ADL deterioration were different between the elderly and younger patients.

We speculated that NSAIDs have two primary effects on elderly patients. The first is the pain-relieving effect. The proportion of orthopedic surgeries in elderly patients was much higher than that in the younger population (26% vs. 19%, $p < 0.01$). Most elderly patients who underwent orthopedic surgery were speculated to have restricted motion before surgery which led to muscle weakness, articular contracture, and pain. The pain relief effects of NSAIDs might promote rehabilitation and decrease ADL deterioration in the elderly patients. The second is the anti-inflammatory effect. Some investigations have reported that blood brain barrier permeability is greater in the aging central nervous system.[17] This permeability effect is associated with increased tissue cytokine levels. Furthermore, aged microglia had deficits in phagocytosis at baseline and after stimulus-induced activation.[18] Since microglia maintain homeostasis of the central nervous system environment, its functional decline might easily facilitate neuroinflammation. These phenomena are speculated causes of age-dependent neuroinflammation and cognitive impairment when the level of inflammatory cytokines increase following peripheral surgical wounding.[19] Postoperative cognitive dysfunction disturbs rehabilitation and recovers the former ADL status. Since NSAIDs are reported to prevent postoperative cognitive dysfunction in human and animal studies,[20,21] the anti-inflammatory effects of NSAIDs might reduce the risk of poor functional recovery.

NSAIDs, however, are risky for elderly patients,[22] even if they have positive effects. Particularly after surgery, NSAIDs are reported to cause negative effects, including anastomotic leaks, necrotizing soft tissue infections, bleeding complications, and delay of bone healing.[23] Because acetaminophen, unlike NSAIDs, does not affect platelet function, it is useful throughout the surgical procedure. The safety and efficacy of acetaminophen are demonstrated in numerous studies. Furthermore, acetaminophen is reported to inhibit neuronal inflammation and attenuate cognitive impairment in animal and in vitro studies.[24,25] Further studies on the relationship between acetaminophen administration and postoperative ADL changes are needed. Investigation of perioperative medications, which although have minor effects, is worthwhile, because it is a modifiable factor. All other risk factors,[26,27] including advanced age, stroke, lower extremity function limitation, and vision impairment, are difficult to change or control before surgery.

This study presents some limitations due to its retrospective design and the lack of data after hospital discharge. We were unable to investigate the mechanisms of the ADL deterioration due to the lack of precise data on postoperative problems, including delirium, fever, pain, anemia, malnutrition, and loss of muscle. Since we checked only if NSAIDs were administered or not, it was unknown whether the relationship between the NSAIDs and ADL scores was dose-dependent. Further studies are required to determine whether the ADL maintenance was a consequence of NSAIDs administration or the absence of other factors that restricted NSAID administration. Additionally, not all our results may be generalizable to other races and countries, because this study population was mainly Japanese.

The incidence of postoperative ADL deterioration in patients aged 70 years or older was higher than that of younger patients. Perioperative administration of NSAIDs was associated with ADL maintenance in the elderly patients who underwent various surgeries. However, a similar relationship was not observed in the younger cohort. Mechanisms of ADL deterioration after surgery were speculated to be different between the elderly and younger patients. This study provides insights for further investigation of postoperative ADL deterioration in elderly patients.

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