Received: 22 December 2022 | Revised: 20 July 2023 | Accepted: 29 July 2023

DOI: 10.1002/pcn5.133

ORIGINAL ARTICLE

PCN Reports Psychiatry and Clinical Neurosciences Open Access

Association between psychotropics use and occurrence of falls in hospitalized patients: A matched case–control study

Chihiro Morishita MD, PhD[1] | Jiro Masuya MD, PhD[1] | Yoshitaka Ishii MD, PhD[1] | Tomoteru Seki MD, PhD[1] | Ayaka Deguchi MD, PhD[1] | Yoshio Iwata MD[1] | Yu Tamada MD, PhD[2] | Yota Fujimura MD, PhD[2] | Mina Honyashiki MD, PhD[1] | Kazuharu Harada PhD[3] | Masataka Taguri PhD[3] | Takeshi Inoue MD, PhD[1]

[1]Department of Psychiatry, Tokyo Medical University, Tokyo, Japan

[2]Department of Psychiatry, Tokyo Medical University Hachioji Medical Center, Tokyo, Japan

[3]Department of Health Data Science, Tokyo Medical University, Tokyo, Japan

Correspondence

Chihiro Morishita, MD, PhD, Department of Psychiatry, Tokyo Medical University, 6-7-1 Nishishinjuku, Shinjuku-ku, Tokyo 160-0023, Japan.
Email: mchihiro@tokyo-med.ac.jp

Funding information
None

Abstract

Aim: Understanding the appropriate prescription of psychotropics for hospitalized patients in terms of preventing falls is an important issue. The aim of this study was to assess the associations between the occurrence of falls and the use of various individual psychotropics in hospitalized patients.

Methods: A retrospective matched case–control study was conducted on adult patients admitted to every department of Tokyo Medical University Hospital, with the outcome being in-hospital falls. A total of 447 hospitalized patients who had had in-hospital falls at some point in their hospitalization between January 2016 and December 2016 were included as cases. A total of 447 hospitalized patients who did not have in-hospital falls, and were individually matched to the cases by sex, age, and clinical department, were included as controls. All data were extracted from electronic medical records. Conditional logistic regression analyses were conducted to assess the association between the exposure to 16 psychotropic medications and the occurrence of in-hospital falls. The multivariable logistic regression model adjusted sex, age, clinical department, body mass index, fall risk score on the fall risk assessment measure, and use of psychotropic medications.

Results: The multivariable conditional logistic regression model showed a significant association between the use of risperidone (odds ratio [OR] = 3.730; 95% confidence interval [CI] = 1.229–11.325) and flunitrazepam (OR = 4.120; 95% CI = 1.105–15.364) and an increased OR of falls among hospitalized patients.

Conclusion: The use of risperidone and flunitrazepam were identified as risk factors for falls among hospitalized patients.

KEYWORDS

falls, hospitalized patients, matched case–control study, psychotropics, risk factor

INTRODUCTION

Falls in hospitalized patients are common and serious accidents. A previous study on adult hospitalized patients in the United States reported that the fall rate was presumed to be 3.56 per 1000 persons per day, and approximately one in four falls resulted in injury.[1] Furthermore, both falls with and without injuries were found to lead to a decline in an individual's activities of daily living over a long period of time.[2] From the viewpoint of medical safety management, falls in hospitalized patients have been associated with increased length and cost of hospitalization,[3] and furthermore, some medical negligence suits associated with falls in hospitals have also been reported.[4] In other words, the prevention of in-hospital falls is a crucial issue in medical safety management.

To reduce the rate of in-hospital falls, medical staff are required to assess the fall risk of hospitalized patients, and prevent hospitalized patients from exposure to the risk factors for falls.[5] The use of psychotropics is considered to be strongly associated with falls in terms of their mechanism of action, and hence it is expected that understanding the appropriate prescription of psychotropics would lead to the prevention of falls in hospitalized patients.[6] Many randomized control trials have investigated the efficacy and safety of individual psychotropic drugs; however, the frequency of the occurrence of falls is low, and therefore, it was difficult to statistically evaluate the fall risk associated with each psychotropic drug.[7,8] On the other hand, some previous studies investigated the association of the use of psychotropics with falls as the main outcome, and the use of hypnotics has been suggested to be most strongly associated with an increased risk of falls.[9–27] However, most previous studies analyzing falls as the main outcome determined the fall risk associated with the use of each class of psychotropics (i.e., antipsychotics, antidepressants, anxiolytics, and hypnotics) or the use of benzodiazepines and non-benzodiazepines.[9–17,19–22,24–27] To the best of our knowledge, there have been no clinical reports to date that have simultaneously assessed the associations between in-hospital falls and various individual medications within multiple classes of psychotropics. In other words, the following unanswered question that has troubled physicians in the clinical setting remains: whether or not each individual psychotropic medication is an independent risk factor for falls among hospitalized patients. To clarify this important issue, we hypothesized that each individual psychotropic would be a risk factor for falls in hospitalized patients, and aimed to assess the associations between falls and the use of various individual psychotropics in hospitalized patients, by performing a matched case–control study.

PARTICIPANTS AND METHODS

Study design and participants

A retrospective matched case–control study was conducted on adult patients admitted to every department of Tokyo Medical University Hospital, which is a 904-bed general hospital. In the case–control study, the outcome was in-hospital falls. First, all in-hospital falls between January 2016 and December 2016 were identified from incident reports. In our hospital, nurses are required to register all in-hospital falls in incident reports, after informing doctors of the incident. A fall is defined as a sudden, unintended descent of a person's body to a lower level or the ground. The in-hospital fall rate was 1.9 per 1000 persons per day during the abovementioned period for inpatients in our hospital. All adult hospitalized patients who experienced in-hospital falls at some point in their hospitalization during the abovementioned period were included in the case group. There were no exclusion criteria for the case group. The presence of in-hospital falls in cases during their hospitalization was confirmed from the electronic medical records. If a case was identified to have experienced two or more in-hospital falls, only the first in-hospital fall was included in the study analyses, considering that a previous fall is a potential risk factor for subsequent falls.[28] For the controls, among the adult patients who were admitted at the same time as the cases but who did not experience in-hospital falls, one patient was randomly matched to each case by sex, age (plus or minus 3 years and closest), and clinical department (i.e., 1:1 matching). There were no exclusion criteria for the control group. The absence of in-hospital falls in the controls during their hospitalization was confirmed from their electronic medical records. Regarding controls who had been admitted to Tokyo Medical University Hospital two or more times during the study period, the data of the first hospitalization was included in the analyses. Finally, 447 matched cases and controls without missing data were included in the analyses.

Ethics review

The study was designed in compliance with the Declaration of Helsinki (as revised in Brazil in 2013), and was approved by the Institutional Review Board of Tokyo Medical University (approval number: SH3612). The anonymity of the participants was assured. The study was a retrospective observational study using data collected from electronic medical record surveys, and hence was considered to pose no risk to participants. Therefore, information regarding the study and the way to decline participation were presented on the hospital homepage, and patients were assumed to be willing to participate in the study unless they took action to decline participation (the so-called opt-out approach).

Data extraction

All data regarding patient characteristics and administered psychotropics were extracted from electronic medical records. The index date for each case was defined to be the day when the case experienced the fall. The index date for each control was defined as the hospital day corresponding to the days from admission to the fall of the corresponding case. For example, for a case who had fallen on

the 11th hospital day, the index date of this case was considered to be the 11th hospital day, and the index date of the corresponding control was considered to be the 11th day of hospitalization of the control.

Psychotropic medications administered to participants on the day before the index date were investigated, and the following 16 psychotropics, which were used by 10 or more participants on the day before the index date, were analyzed as exposure for falls: olanzapine, quetiapine, risperidone, duloxetine, mirtazapine, alprazolam, ethyl loflazepate, etizolam, brotizolam, estazolam, eszopiclone, flunitrazepam, suvorexant, triazolam, zolpidem, and zopiclone. Data regarding the following characteristics of the patients at the time of admission in the case and control groups were extracted: body mass index, and total fall risk score measured using the fall risk assessment measure,[29] in addition to the matching variables of sex, age, and clinical department. For patients who used any psychotropic medication on the day before the index date, their diagnoses of mental disorders were also extracted, in accordance with the 10th Revision of the International Classification of Diseases. The fall risk assessment measure used at Tokyo Medical University Hospital consists of the following items: age, history of falls, elimination status, medications, sensory dysfunction, gait/balance, mobility, and cognitive status, and is routinely administered by nurses to patients on admission to assess their fall risk. The full total score is 36; a total score of 7 to 15 indicates a moderate risk for falls, and a total score of 16 or higher indicates a high risk for falls.

Statistical analyses

Data regarding patient characteristics were initially compared between the case and control groups. The *t*-test was used for continuous variables, and the chi-squared test was used for categorical variables. Subsequently, to assess the association between the exposure to 16 psychotropic medications and the occurrence of in-hospital falls, conditional logistic regression analyses were conducted, and odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. The dependent variable was the occurrence of in-hospital falls. In the multivariable conditional logistic regression model, in addition to the matching variables (sex, age, and clinical department), body mass index, fall risk score, and use of psychotropic medications were adjusted. In addition, to investigate the risk of falls associated with the exposure to 16 psychotropic medications among older hospitalized patients, analyses were conducted excluding those under 65 years of age. All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 28.0 (IBM Corp, Armonk, NY, USA), and a *p*-value of <0.05 was considered to indicate a statistical significance.

RESULTS

Table 1 summarizes the comparison of patient characteristics at the time of admission between the case and control groups. Regarding matching variables (i.e., sex, age, and clinical department), significant differences were not detected between the case and control groups. The details of the clinical departments of the patients are presented in Supporting Information: Supplementary Table 1. Regarding body mass index and total fall risk score, significant differences were detected between the two groups. The body mass index of the case group was significantly lower than that of the control group ($p = 0.002$), and the total fall risk score of the case group was significantly higher than that of the control group ($p < 0.001$). The major psychiatric diagnoses for patients who had been exposed to any psychotropic medication on the day before the index date are summarized in Supporting Information: Supplementary Table 2. In a few patients, psychotropic medications were administered for the purpose of improving nausea and vomiting associated with chemotherapy, or chronic musculoskeletal pain.

Table 2 shows the results of conditional logistic regression analyses for the occurrence of the outcome of in-hospital falls according to psychotropic medication exposure on the day before the index date. Details of the number and proportion of patients who had been exposed to each psychotropic medication on the day before the

TABLE 1 Characteristics of the patients in the case and control groups.

	Case group (n = 447)	Control group (n = 447)	Statistical difference (p)
Age (years), mean (SD)[a]	68.7 (14.1)	68.7 (14.1)	0.983
Sex (male), n (%)[b]	241 (53.9)	241 (53.9)	1.000
Inpatient department (Supplementary Table 1)[b]			1.000
Body mass index (kg/m^2), mean (SD)[a]	21.2 (3.9)	22.0 (3.8)	0.002
Fall risk score,[c] mean (SD)[a]	6.6 (4.1)	4.6 (3.7)	<0.001

Abbreviation: SD, standard deviation.

[a]Analyzed by the *t*-test.

[b]Analyzed by the χ^2-test.

[c]Evaluated by the fall risk assessment tool.

TABLE 2 Univariable and multivariable conditional logistic regression analyses for the occurrence of falls.

	Univariable analyses			Multivariable analysis[a]		
Variables	OR	95% CI	*p*-value	OR	95% CI	*p*-value
Body mass index (kg/m^2)	0.939	0.904–0.975	0.001*	0.931	0.892–0.972	0.001*
Fall risk score[b]	1.215	1.156–1.277	<0.001*	1.205	1.144–1.269	<0.001*
Olanzapine	0.571	0.167–1.952	0.372	0.328	0.066–1.628	0.173
Quetiapine	1.333	0.463–3.843	0.594	0.565	0.140–2.291	0.424
Risperidone	3.000	1.191–7.558	0.020*	3.730	1.229–11.325	0.020*
Duloxetine	1.750	0.512–5.978	0.372	1.255	0.275–5.725	0.769
Mirtazapine	2.667	0.707–10.052	0.147	5.712	0.719–45.369	0.099
Alprazolam	1.400	0.444–4.411	0.566	2.039	0.433–9.608	0.368
Ethyl loflazepate	1.667	0.606–4.586	0.323	1.846	0.505–6.741	0.354
Etizolam	1.824	1.009–3.295	0.047*	1.451	0.725–2.906	0.293
Brotizolam	1.167	0.676–2.012	0.579	0.929	0.477–1.808	0.828
Estazolam	3.333	0.917–12.112	0.067	1.423	0.299–6.781	0.658
Eszopiclone	2.000	0.807–4.955	0.134	1.458	0.491–4.332	0.497
Flunitrazepam	3.600	1.337–9.696	0.011*	4.120	1.105–15.364	0.035*
Suvorexant	5.000	1.096–22.820	0.038*	2.736	0.482–15.526	0.256
Triazolam	2.000	0.602–6.642	0.258	2.294	0.486–10.831	0.294
Zolpidem	1.500	0.930–2.420	0.097	1.250	0.707–2.209	0.443
Zopiclone	3.857	1.680–8.857	0.001*	2.524	0.958–6.651	0.061

Note: Matching variables are not presented in the table.

Abbreviations: CI, confidence interval; OR, odds ratio.

[a]The multivariable logistic regression model adjusted age, sex, inpatient department, body mass index, fall risk score, and the use of olanzapine, quetiapine, risperidone, duloxetine, mirtazapine, alprazolam, ethyl loflazepate, etizolam, brotizolam, estazolam, eszopiclone, flunitrazepam, suvorexant, triazolam, zolpidem, and zopiclone.

[b]Evaluated by the fall risk assessment tool.

*Statistically significant difference ($p < 0.05$).

index date in the case and control groups are presented in Supporting Information: Supplementary Table 3. In univariable logistic regression models, a significantly increased OR of in-hospital falls was observed for the exposure to risperidone, etizolam, flunitrazepam, suvorexant, and zopiclone, but not for the exposure to olanzapine, quetiapine, duloxetine, mirtazapine, alprazolam, ethyl loflazepate, brotizolam, estazolam, eszopiclone, triazolam, and zolpidem. Multivariable logistic regression model, which adjusted sex, age, clinical department, body mass index, fall risk score, and use of psychotropic medications, found risperidone (OR = 3.730; 95% CI = 1.229–11.325; $p = 0.020$) and flunitrazepam (OR = 4.120; 95% CI = 1.105–15.364; $p = 0.035$) as remaining significantly associated with an increased OR of in-hospital falls. On the other hand, regarding etizolam, suvorexant, and zopiclone, as well as medications that were nonsignificant in univariable logistic regression models, multivariable analysis showed that the exposure to each medication was not significantly associated with an increased OR of in-hospital falls. Regarding characteristics of the patients, a low body mass index and a high total fall risk score were significantly associated with an increased OR of in-hospital falls in both univariable and multivariable logistic regression models. Regarding the analyses of older hospitalized patients, in which 129 cases and controls under 65 years of age were excluded, the results are shown in Supporting Information: Supplementary Table 4. In the multivariable conditional logistic regression model, a significantly increased OR of in-hospital falls was observed for the exposure to mirtazapine, in addition to risperidone and flunitrazepam, which were significantly associated with an increased OR of in-hospital falls in the main multivariable analysis (including all cases and controls). On the other hand, the calculated CIs, particularly that of mirtazapine, were wide.

DISCUSSION

The summary of our main findings are as follows. We observed a significant association between the use of risperidone and flunitrazepam and an increased OR of falls among hospitalized patients in multivariable conditional logistic regression analysis. On the other

hand, we observed no significant association of an increased OR of falls with the use of olanzapine, quetiapine, duloxetine, mirtazapine, alprazolam, ethyl loflazepate, etizolam, brotizolam, estazolam, eszopiclone, suvorexant, triazolam, zolpidem, and zopiclone, although these findings might not indicate the absence of a risk for falls. To the best of our knowledge, this study is the first to simultaneously evaluate the association of in-hospital falls with the use of individual medications within multiple classes of psychotropics, by collecting data including actual medication use from medical records.

As we mentioned in the Introduction section, many previous studies investigating the risk of falls have focused on the use of each class of psychotropics[9,13,15–17,19,22,24,25] or the use of each type of benzodiazepine receptor agonists,[10–14,20,21,23,26,27,30–33] although the psychotropic classes or types identified as risk factors for falls were partially inconsistent among the studies. The main reason for these discrepancies might be that various medications were grouped together into each class or type of psychotropics. Furthermore, these discrepancies might be explained by the design of previous studies. Namely, many previous studies focused on community-dwelling persons or nursing home residents,[10–17,19–22,24,25,27,31–33] and collected data using administrative databases.[10–17,20–22,24,25,27,30,33] Therefore, there might be the possibility of a lack of information regarding the time interval between drug administration and the occurrence of falls, that is, the medication data might include medications that had already been discontinued at the time of the fall or were initiated after the fall.[10–17,20–22,24,25,27,30–33] Additionally, there might be the possibility of differences between actual medication use and prescriptions, owing to medication nonadherence.[10–17,20–22,24,25,27,31–33] Furthermore, there is the possibility that the outcome of falls was not identified accurately, because validation studies were not conducted or poor accuracy was found for the case-identification algorithms.[10–17,20–22,24,25,27,30–33] On the other hand, only a few previous studies simultaneously investigated the association between several individual hypnotic medications and falls among hospitalized patients.[18] Obayashi et al. reported that the use of brotizolam, estazolam, and zopiclone was significantly associated with an increased risk for falls among hospitalized patients, whereas the use of flunitrazepam, nitrazepam, triazolam, and zolpidem was not, although they did not investigate the associations between falls and individual medications within each class of psychotropics, except for hypnotics.[18] Their findings regarding hypnotics were inconsistent with our findings that the use of flunitrazepam was the most strongly associated with falls in hospitalized patients among hypnotics. The main reason for the discrepancy might be that they categorized patients who used hypnotics at some point during their hospital stay into the exposure group, which means that the exposure group included patients who started using hypnotics after they fell.

The strength of our present study is that we collected the data of hospitalized patients from medical records. The study design enabled us to obtain reliable data regarding patient characteristics, in addition to data regarding psychotropic medications that were actually being used at the time of the falls, with consideration of the timing of drug administration and medication adherence. Furthermore, we were able to avoid outcome misclassification bias, confirming the presence/absence of in-hospital falls in subjects during their hospitalization. Another strength is that we controlled for some potential risk factors in our multivariable conditional logistic regression analysis. Therefore, the nature of this study enabled us to suggest independent risk factors for falls. Additionally, the results of the analysis in older hospitalized patients (Supporting Information: Supplementary Table 4) were similar to the results of the main analysis (Table 2), although uncertainty might still exist, considering the calculated CIs.

Our findings that both the use of flunitrazepam and risperidone are independent risk factors for in-hospital falls appear reasonable, considering the mechanism of action of these medications. The significant association of flunitrazepam use with falls might be explained by the duration and severity of the carry-over effect of flunitrazepam, which has a long half-life of 15–20 h.[34,35] Additionally, this significant association might be explained by the profound muscle relaxant action of flunitrazepam.[35,36] The significant association of risperidone use with falls might be explained by the high frequency of extrapyramidal side-effects (EPSs), based on its binding to dopamine D_2 receptors. A previous systematic review and meta-analysis of 54 studies showed that risperidone was associated with more frequent use of antiparkinson medications than olanzapine and quetiapine, suggesting that risperidone might induce more EPSs, which clinicians consider treating with antiparkinson medications, than olanzapine and quetiapine.[37]

There are several limitations to this study. First, there might be bias in the selection of the controls, although we controlled for patient characteristics in the main multivariable analysis. Second, the participants who used two or more psychotropics were included in our data, and therefore, the influence of the use of multiple psychotropics, including drug–drug interactions, on falls remains unclear, although the use of other psychotropic medications was adjusted for in the multivariable analysis. Third, although significant differences were not detected between the case and control groups for the doses of risperidone and flunitrazepam (data not shown), we did not conduct a conditional logistic regression analysis considering the doses of the psychotropic medications because a large variety of types and doses of psychotropics were prescribed for patients with different diseases, and hence it was difficult to reflect the dose of each psychotropic in the analyses. Finally, the associations of the exposure to some psychotropics with the occurrence of in-hospital falls might not have reached statistical significance because of the relatively small sample sizes of the participants using these psychotropics. Further planned prospective studies of a large number of hospitalized patients are warranted in the future.

Conclusion

In this study, we found that the use of flunitrazepam and risperidone was associated with an increased OR of falls. On the other hand, the use of olanzapine, quetiapine, duloxetine, mirtazapine, alprazolam,

ethyl loflazepate, etizolam, brotizolam, estazolam, eszopiclone, suvorexant, triazolam, zolpidem, and zopiclone was not associated with an increased OR of falls. In other words, our results suggest that a risk of falls exists for the use of psychotropic medications, particularly, risperidone and flunitrazepam. These findings provide useful information, namely that physicians should avoid administering flunitrazepam to hospitalized patients, and furthermore, physicians should administer risperidone to hospitalized patients with great caution after assessing the patients' characteristics. These approaches might lead to a reduction in the occurrence of falls in hospitalized patients.

AUTHOR CONTRIBUTIONS

Chihiro Morishita: Conceptualization, data curation, formal analysis, investigation, methodology, project administration, supervision, writing—original draft, writing—review and editing. **Jiro Masuya**: Data curation, writing—review and editing. **Yoshitaka Ishii**: Data curation, writing—review and editing. **Tomoteru Seki**: Data curation, writing—review and editing. **Ayaka Deguchi**: Data curation, writing—review and editing. **Yoshitaka Ishii**: Data curation, writing—review and editing. **Yu Tamada**: Data curation, writing—review and editing. **Yota Fujimura**: Data curation, writing—review and editing. **Mina Honyashiki**: Data curation, writing—review and editing. **Kazuharu Harada**: Formal analysis, writing—review and editing. **Masataka Taguri**: Formal analysis, writing—review and editing. **Takeshi Inoue**: Conceptualization, formal analysis, methodology, supervision, writing—original draft, writing—review and editing. All authors have read and approved the final article.

ACKNOWLEDGMENTS

We thank Dr. Helena Popiel of the Center for International Education and Research, Tokyo Medical University, for editorial review of the manuscript. This research did not receive any funding from agencies in the public, commercial, or not-for-profit sectors.

CONFLICT OF INTEREST STATEMENT

Jiro Masuya has received personal fees from Otsuka Pharmaceutical, Eli Lilly, Astellas, MSD, Janssen Pharmaceutical, Takeda Pharmaceutical, Shionogi Pharmaceutical, and Meiji Yasuda Mental Health Foundation, as well as grants from Pfizer, and Mitsubishi Tanabe Pharma. Yu Tamada has received honoraria from Otsuka Pharmaceutical, Dainippon Sumitomo Pharma, and Eisai. Yota Fujimura has received honoraria and a research grant from Sumitomo Pharma, and research grants from Otsuka Pharmaceutical, and Shionogi. Takeshi Inoue is a member of the advisory boards of Pfizer, Novartis Pharma, and Mitsubishi Tanabe Pharma, and has received personal fees from Mochida Pharmaceutical, Takeda Pharmaceutical, Eli Lilly, Janssen Pharmaceutical, MSD, Taisho Toyama Pharmaceutical, Yoshitomiyakuhin, and Daiichi Sankyo; grants from Shionogi, Astellas, Tsumura, and Eisai; and grants and personal fees from Otsuka Pharmaceutical, Dainippon Sumitomo Pharma, Mitsubishi Tanabe Pharma, Kyowa Pharmaceutical Industry, Pfizer, Novartis Pharma, and Meiji Seika Pharma. The other authors have no actual or potential conflicts of interest to declare.

DATA AVAILABILITY STATEMENT

Data cannot be shared publicly because of Ethics Committee restrictions. Data are available from the Internal Review Board of the Department of Psychiatry, Tokyo Medical University (Japan) (contact via email: seisinka@tokyo-med.ac.jp) for researchers who meet the criteria for access to confidential data.

ETHICS APPROVAL STATEMENT

The study was approved by the Institutional Review Board of Tokyo Medical University (approval number: SH3612).

PATIENT CONSENT STATEMENT

The study was a retrospective observational study using data collected from electronic medical record surveys, and hence was considered to pose no risk to participants. Therefore, information regarding the study and the way to decline participation were presented on the hospital homepage, and patients were assumed to be willing to participate in the study unless they took action to decline participation (the so-called opt-out approach).

CLINICAL TRIAL REGISTRATION

Not applicable.

ORCID

Chihiro Morishita http://orcid.org/0000-0002-8480-9303
Tomoteru Seki http://orcid.org/0000-0003-2593-7118
Takeshi Inoue http://orcid.org/0000-0001-5248-1289

REFERENCES

1. Bouldin ELD, Andresen EM, Dunton NE, Simon M, Waters TM, Liu M, et al. Falls among adult patients hospitalized in the United States: prevalence and trends. J Patient Saf. 2013;9:13–7.
2. Tinetti ME, Williams CS. The effect of falls and fall injuries on functioning in community-dwelling older persons. J Gerontol A Biol Sci Med Sci. 1998;53:M112–9.
3. Bates DW, Pruess K, Souney P, Platt R. Serious falls in hospitalized patients: correlates and resource utilization. Am J Med. 1995;99:137–43.
4. Oliver D, Killick S, Even T, Willmott M. Do falls and falls-injuries in hospital indicate negligent care – and how big is the risk? A retrospective analysis of the NHS Litigation Authority Database of clinical negligence claims, resulting from falls in hospitals in England 1995 to 2006. Qual Saf Health Care. 2008;17:431–6.
5. Panel on Prevention of Falls in Older Persons, American Geriatrics Society and British Geriatrics Society. Summary of the Updated American Geriatrics Society/British Geriatrics Society clinical practice guideline for prevention of falls in older persons. J Am Geriatr Soc. 2011;59:148–57.
6. Campbell AJ, Robertson MC, Gardner MM, Norton RN, Buchner DM. Psychotropic medication withdrawal and a home-based exercise program to prevent falls: a randomized, controlled trial. J Am Geriatr Soc. 1999;47:850–3.

7. Herring WJ, Connor KM, Ivgy-May N, Snyder E, Liu K, Snavely DB, et al. Suvorexant in patients with insomnia: results from two 3-month randomized controlled clinical trials. Biol Psychiatry. 2016;79:136–48.
8. Ancoli-Lsrael S, Krystal AD, McCall WV, Schaefer K, Wilson A, Claus R, et al. A 12-week, randomized, double-blind, placebo-controlled study evaluating the effect of eszopiclone 2 mg on sleep/wake function in older adults with primary and comorbid insomnia. Sleep. 2010;33:225–34.
9. Morishita C, Ichiki M, Shimura A, Ishibashi Y, Inubuse A, Masuya J, et al. Psychotropics use and occurrence of falls in hospitalized patients: a matched case-control study. Psychiatry Clin Neurosci. 2022;76:71–6.
10. Saarelainen L, Tolppanen AM, Koponen M, Tanskanen A, Sund R, Tiihonen J, et al. Risk of hip fracture in benzodiazepine users with and without alzheimer disease. J Am Med Dir Assoc. 2017;18:87e15–e21.
11. Yu NW, Chen PJ, Tsai HJ, Huang CW, Chiu YW, Tsay WI, et al. Association of benzodiazepine and Z-drug use with the risk of hospitalisation for fall-related injuries among older people: a nationwide nested case-control study in Taiwan. BMC Geriatr. 2017;17:140.
12. Chang CM, Wu ECH, Chang IS, Lin KM. Benzodiazepine and risk of hip fractures in older people: a nested case-control study in Taiwan. Am J Geriatr Psychiatry. 2008;16:686–92.
13. Wang PS, Bohn RL, Glynn RJ, Mogun H, Avorn J. Hazardous benzodiazepine regimens in the elderly: effects of half-life, dosage, and duration on risk of hip fracture. Am J Psychiatry. 2001;158:892–8.
14. Wagner AK, Zhang F, Soumerai SB, Walker AM, Gurwitz JH, Glynn RJ, et al. Benzodiazepine use and hip fractures in the elderly: who is at greatest risk? Arch Intern Med. 2004;164:1567–72.
15. Bolton JM, Metge C, Lix L, Prior H, Sareen J, Leslie WD. Fracture risk from psychotropic medications: a population-based analysis. J Clin Psychopharmacol. 2008;28:384–91.
16. Thorell K, Ranstad K, Midlöv P, Borgquist L, Halling A. Is use of fall risk-increasing drugs in an elderly population associated with an increased risk of hip fracture, after adjustment for multimorbidity level: a cohort study. BMC Geriatr. 2014;14:131.
17. Woolcott JC, Richardson KJ, Wiens MO, Patel B, Marin J, Khan KM, et al. Meta-analysis of the impact of 9 medication classes on falls in elderly persons. Arch Intern Med. 2009;169:1952–60.
18. Obayashi K, Araki T, Nakamura K, Kurabayashi M, Nojima Y, Hara K, et al. Risk of falling and hypnotic drugs: retrospective study of inpatients. Drugs R D. 2013;13:159–64.
19. Sterke CS, van Beeck EF, van der Velde N, Ziere G, Petrovic M, Looman CWN, et al. New insights: dose-response relationship between psychotropic drugs and falls: a study in nursing home residents with dementia. J Clin Pharmacol. 2012;52:947–55.
20. Xing D, Ma XL, Ma JX, Wang J, Yang Y, Chen Y. Association between use of benzodiazepines and risk of fractures: a meta-analysis. Osteoporos Int. 2014;25:105–20.
21. Berry SD, Lee Y, Cai S, Dore DD. Nonbenzodiazepine sleep medication use and hip fractures in nursing home residents. JAMA Intern Med. 2013;173:754–61.
22. Seppala LJ, Wermelink AMAT, de Vries M, Ploegmakers KJ, van de Glind EMM, Daams JG, et al. Fall-risk-increasing drugs: a systematic review and meta-analysis: II. psychotropics. J Am Med Dir Assoc. 2018;19:371e11–e17.
23. Ishibashi Y, Nishitani R, Shimura A, Takeuchi A, Touko M, Kato T, et al. Non-GABA sleep medications, suvorexant as risk factors for falls: case-control and case-crossover study. PLoS One. 2020;15:e0238723.
24. Leipzig RM, Cumming RG, Tinetti ME. Drugs and falls in older people: a systematic review and meta-analysis: I. Psychotropic drugs. J Am Geriatr Soc. 1999;47:30–9.
25. Johnell K, Jonasdottir Bergman G, Fastbom J, Danielsson B, Borg N, Salmi P. Psychotropic drugs and the risk of fall injuries, hospitalisations and mortality among older adults. Int J Geriatr Psychiatry. 2017;32:414–20.
26. Passaro A, Volpato S, Romagnoni F, Manzoli N, Zuliani G, Fellin R. Benzodiazepines with different half-life and falling in a hospitalized population. J Clin Epidemiol. 2000;53:1222–9.
27. Treves N, Perlman A, Kolenberg Geron L, Asaly A, Matok I. Z-drugs and risk for falls and fractures in older adults-a systematic review and meta-analysis. Age Ageing. 2018;47:201–8.
28. Frels C, Williams P, Narayanan S, Gariballa SE. Iatrogenic causes of falls in hospitalised elderly patients: a case-control study. Postgrad Med J. 2002;78:487–9.
29. Morita E, Iijima S, Hirai S, Kazawa M, Anzai Y. Revision of an assessment score sheet for fall prediction and examination on inter-rater agreement among the nurse evaluators (*in Japanese*). J Jpn Acad Nurs Admin Policies. 2010;14:51–8.
30. Tamiya H, Yasunaga H, Matusi H, Fushimi K, Ogawa S, Akishita M. Hypnotics and the occurrence of bone fractures in hospitalized dementia patients: a matched case-control study using a national inpatient database. PLoS One. 2015;10:e0129366.
31. Diem SJ, Ewing SK, Stone KL, Ancoli-Israel S, Redline S, Ensrud KE, et al. Use of non-benzodiazepine sedative hypnotics and risk of falls in older men. J Gerontol Geriatr Res. 2014;3:158.
32. de Vries OJ, Peeters G, Elders P, Sonnenberg C, Muller M, Deeg DJH, et al. The elimination half-life of benzodiazepines and fall risk: two prospective observational studies. Age Ageing. 2013;42:764–70.
33. Vestergaard P, Rejnmark L, Mosekilde L. Anxiolytics and sedatives and risk of fractures: effects of half-life. Calcif Tissue Int. 2008;82:34–43.
34. Vermeeren A. Residual effects of hypnotics: epidemiology and clinical implications. CNS Drugs. 2004;18:297–328.
35. Higuchi T, Koyama T, Kanba S, Ohmori T, Kato T. *Clinical psychopharmacology handbook* (in Japanese). 2nd ed. Tokyo: Igaku-Shoin Ltd.; 2009.
36. Griebel G, Perrault G, Letang V, Granger P, Avenet P, Schoemaker H, et al. New evidence that the pharmacological effects of benzodiazepine receptor ligands can be associated with activities at different BZ (ω) receptor subtypes. Psychopharmacology. 1999;146:205–13.
37. Rummel-Kluge C, Komossa K, Schwarz S, Hunger H, Schmid F, Kissling W, et al. Second-generation antipsychotic drugs and extrapyramidal side effects: a systematic review and meta-analysis of head-to-head comparisons. Schizophr Bull. 2012;38:167–77.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Morishita C, Masuya J, Ishii Y, Seki T, Deguchi A, Iwata Y, et al. Association between psychotropics use and occurrence of falls in hospitalized patients: a matched case–control study. Psychiatry Clin Neurosci Rep. 2023;2:e133. https://doi.org/10.1002/pcn5.133