Mortality and Prevalence of Falls, and Their Association with Psychiatric Diagnoses and Psychotropic Medications

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ABSTRACT

Objective: Falls are a significant health problem that can affect the quality of life of older adults. This study was undertaken to study the mortality and prevalence of falls, and their associations with psychiatric diagnoses and psychotropic medications.

Methods: The study was a retrospective 10-year data analysis of a general hospital database from 2006-2015. The prevalence, odds ratio, hazard ratio, and survival analysis were analyzed to study the association with falls.

Results: The overall prevalence of falls was 3.6%. Subjects with a psychiatric diagnosis had a 3.28 times greater chance of falls. Subjects taking prescribed psychotropic medication had a 1.76 times greater chance of falls. Survival analysis revealed a mean survival of 6.84 years after falls. The average survival years after falls was age-related. Subjects with a history of falls and carrying a psychiatric diagnosis had a mean survival of 6.55 years and a hazard ratio of 0.84. Subjects with a history of falls and taking prescribed psychotropic medication had a mean survival of 6.15 years and a hazard ratio of 1.27.

Conclusion: A psychiatric diagnosis and psychotropic medication prescriptions were associated with a greater chance of falls. Subjects with a history of taking prescribed psychotropic medication had a higher risk of mortality from falls.

Keywords: Falls; prevalence; psychiatric diagnosis; psychotropic medication; survival (Siriraj Med J 2020; 72: 399-406)

INTRODUCTION

Falls are a very significant health problem for the elderly. Falls are associated with disability, death, increased medical resources utilization,[1,2] and a limited sense of well-being and reduced quality of life in the elderly.[3,4] In Thailand, from the Annual Epidemiological Surveillance Report 2015, falls, according to the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10): W00–W19, were the second most common cause of injury, second only to traffic accidents, with an increasing risk of mortality associated with falls.[5]

In falls studies, the causes of falls are mainly divided into two major categories: internal and external. One of the most significant internal causes of falls is related to the medication prescribed by physicians. Although with different methodologies, populations of study, and definitions of falls, the research findings in this field indicate

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that prescribed medications are associated with a higher risk of falls, especially psychotropic medications. The most common psychotropic medications reported to be associated with falls are antipsychotics, antidepressants, antimanics, and anxiolytic-hypnotics.[6-9] Centrally-acting psychotropic medications have been reported to have side-effects of drowsiness, dizziness, orthostatic hypotension, blurred vision, gait and balance difficulties, and also abnormal movements, which are all associated with falls.[10]

Besides the studies of the association between falls and psychotropic medications, a psychiatric diagnosis has also been reported to be related with a history of injuries, falls, and accidents more than physical diagnoses,[11] which might be explained by the nature of psychiatric illnesses. Psychiatric disorders can affect a person's behavior and judgment and might cause injuries unable to be explained only from the side-effects of psychotropic medications. In addition, mental disorders, psychotropic medications, polypharmacy, and multiple psychotropic drug use have also been reported to be associated with accidental death and all-cause mortality.[12-14]

Many newer psychotropic medications have been launched on the market over the past 20 years. In Thailand, there has been an increasing evaluation of new psychiatric cases yearly, and the trend in prescribing psychotropic medication has also been escalating. This study aimed to look into the current situation of falls in a psychiatric context; in particular, to study the prevalence of falls in a general hospital setting, the association between falls and psychotropic medications and psychiatric diagnoses, and also the survival in subjects with a history of falls.

MATERIALS AND METHODS

Study design and population

The study involved a retrospective 10-year data analysis. The protocol was approved by Siriraj Hospital IRB (Si 375/2015). The study population consisted of all subjects included in Siriraj Hospital's database during the 10-year period from 2006 to 2015 as well as cases in the Siriraj Hospital Death Registry, which was updated and matched with the Thai National Death Registry (Fig 1).

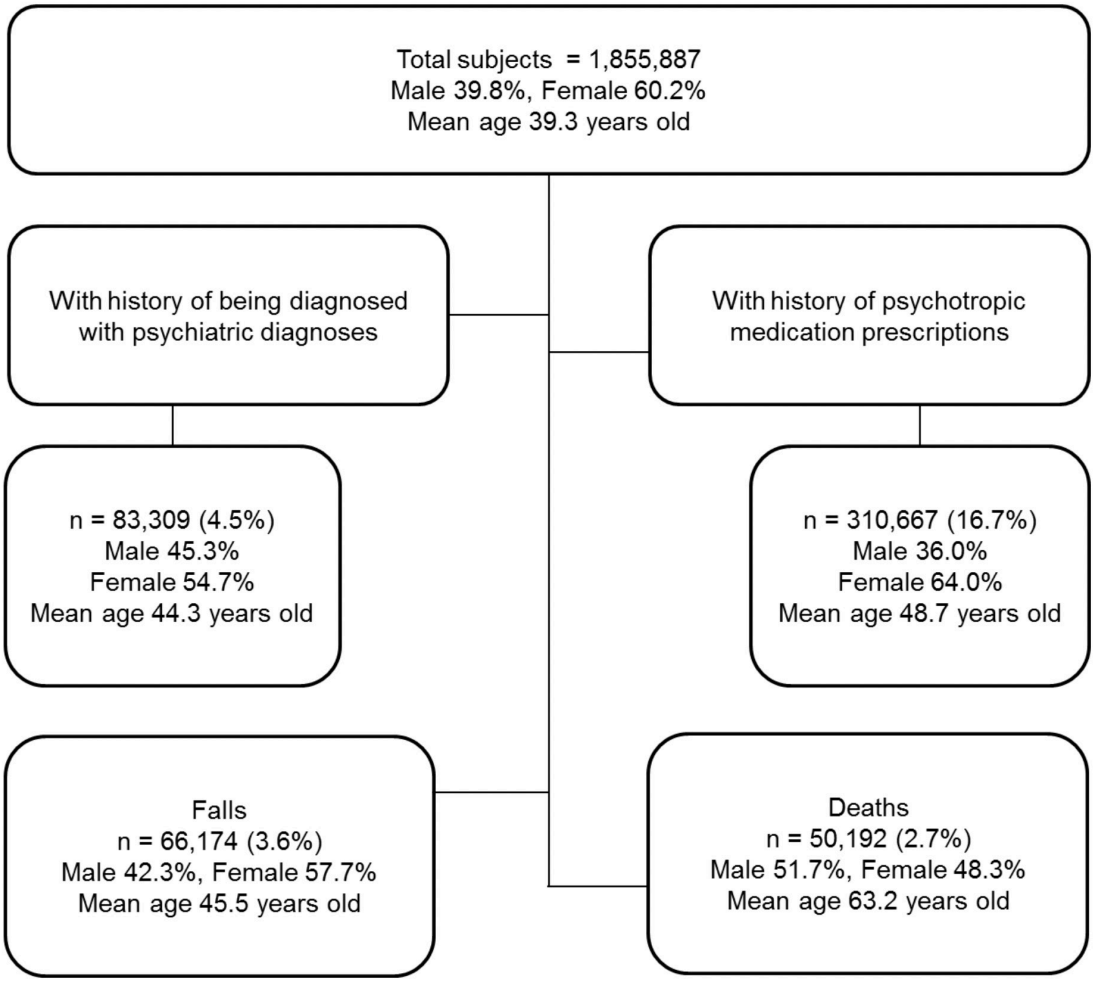

Fig 1. Diagram of the study process.

Procedure and data

The authors retrieved and classified data into four main groups: (1) subjects with and without a history of falls (ICD 10 codes: W00-W19), (2) subjects with and without a history of psychiatric diagnoses (ICD 10 codes: F00-F99), (3) subjects with and without a history of receiving any psychotropic medication before falls, including antidepressants, mood stabilizers, antipsychotics, hypnotics-anxiolytics, and cognitive enhancing agents groups, and 4) subjects with and without hospital death registration (Fig 1). We studied the association by comparing the data in each group.

Statistical analyses

Statistical analyses were performed with the Statistical Package for Social Sciences (SPSS; version 18.0). We compared dependent variables, subjects with/without a history of falls, and independent variables, such as age, sex, psychiatric diagnosis, and psychotropic medications, by using chi-square tests. Multiple logistic regression analysis, adjusted for age, was performed to assess the associations of falls with psychiatric diagnoses and psychotropic medications. Kaplan–Meier (K-M) survival curves were calculated to determine survival years after falls for subjects with a history of psychiatric diagnoses and subjects with a history of taking psychotropic medication. Significances of the log-rank tests were interpreted at a two-sided alpha value of 0.05. Multivariate comparisons were performed with the adjusted Cox proportional hazards (PH) model. Significances of the hazard ratios (HR) estimates were based on a two-sided alpha value of 0.05, and confidence intervals at 95% were obtained for the estimations. Unadjusted and adjusted-for-age Cox PH models were tested for differences in survival years after falls in subjects with a psychiatric diagnosis and taking psychotropic medication.

RESULTS

Study population

The number and gender of the population in the study are shown in Fig. 1. There was a total of 1,855,887 subjects in the hospital database from 2006 to 2015. The mean age was 39.21±21.419 years. Their age ranged from 0-117 years. 39.8% were male. There were 66,174 falls, and 50,192 deaths recorded.

Association between falls and psychiatric diagnoses and psychotropic medications

Regarding subjects with a history of psychiatric diagnoses, there were 9,326 cases (11.2%) with a history of falls, whereas this figure was only 3.2% in subjects with no psychiatric diagnosis. Falls were age-related and more common in males. Subjects with a psychiatric diagnosis had a 3.28 (adjusted OR, 95%CI 3.20-3.37) greater chance of falls. The chances of falls, after adjusting for age, sex, marital status, and employment status, were the greatest in patients with organic mental disorders (F00-F09) and mental and behavioral disorders due to psychoactive substance use (F10-F19) (Table 1).

Regarding subjects with a history of previous psychotropic medication prescriptions, there were 14,850 cases (4.9%) with a history of falls, whereas this figure was only 2.6% in subjects without a history of receiving psychotropic medication prescriptions. Subjects with psychotropic medication prescriptions had a 1.76 (adjusted OR, 95%CI 1.73-1.80) times greater chance of falls. The strongest association between psychotropic medications and falls, after adjusting for age, sex, marital status, and employment status, was found in patients taking hypnotics-anxiolytics, mood stabilizers, cognitive enhancing agents, antidepressants, and antipsychotics, respectively (Table 1).

Survival in subjects with a history of falls and a history of psychiatric diagnoses and psychotropic medication use

There was a total of 66,174 recorded cases of falls, and a total of 50,192 deaths recorded in the 10-year hospital database, of which 6,537 deaths (9.9%) were patients with a history of falls.

There were 2,082 (22.3%) deaths recorded of subjects with a history of falls and having a psychiatric diagnosis, whereas 7.8% of deaths recorded were in subjects with a history of falls but who had no psychiatric diagnosis. Psychiatric diagnoses were predictive of decreased survival in subjects with a history of falls (HR 1.15; 95%CI 1.10-1.22). However, when adjusted for age, sex, marital status, and employment status, psychiatric diagnoses were not predictive of decreased survival (adjusted HR 0.84; 95%CI 0.79-0.89). The only decrease in survival chances was found in subjects with mental and behavioral disorders due to psychoactive substance use (adjusted HR 1.43; 95%CI 1.26-1.63) (Table 1).

There were 2,300 (15.5%) deaths recorded in subjects with a history of falls after receiving psychotropic medications, whereas 8.3% of deaths were recorded in subjects with a history of falls but who had no previous history of psychotropic medication prescriptions. Psychotropic medication prescriptions were predictive factors for decreased survival in subjects with a history of falls (adjusted HR 1.27; 95%CI 1.20-1.34). The largest decrease in survival was found in subjects with antipsychotics (adjusted HR 1.49; 95%CI 1.35-1.65), cognitive enhancing agents

TABLE 1. Logistic regression assessing the risk and Cox proportional hazards analysis of falls.

Variables	Total N	Fall N (%)	Risk of falls		Death after falls N (%)	Risk of Death	
			Unadjusted OR (95%CI)	Adjusted OR[b] (95%CI)		Unadjusted HR (95%CI)	Adjusted HR[b] (95%CI)
Total	1,855,887	66,174 (3.6)			6,537 (9.9)		
Male	739,344	27,987 (3.8)	1.11 (1.09-1.13)[a]	1.13 (1.11-1.15)[a]	3,063 (10.9)	1.50 (1.43-1.57)[a]	2.01 (1.95-2.19)[a]
Age 60-79 years	307,491	16,592 (5.4)	1.91 (1.87-1.94)[a]	2.03 (1.99-2.08)[a]	3,009 (18.1)	3.53 (3.31-3.76)[a]	2.94 (2.71-3.19)[a]
Age ≥80 years	44,129	5,858 (13.3)	5.11 (4.97-5.26)[a]	4.95 (4.77-5.14)[a]	2,106 (36.0)	6.35 (5.94-6.79)[a]	4.87 (4.44-5.34)[a]
Employment status							
Employed	941,806	30,805 (3.3)	1	1	2,101 (6.8)	1	1
Non-employed	402,876	21,755 (5.4)	1.69 (1.66-1.72)[a]	1.43 (1.41-1.46)[a]	3,381 (15.5)	1.91 (1.81-2.01)[a]	1.06 (0.99-1.13)
Marital status							
Never married	799,037	28,157 (3.5)	1	1	987 (3.5)	1	1
Married	832,049	27,290 (3.3)	0.93 (0.91-0.94)[a]	0.58 (0.57-0.60)[a]	3,588 (13.1)	2.61 (2.44-2.80)[a]	1.44 (1.32-1.57)[a]
Divorced/Widowed	153,031	7,979 (5.2)	1.51 (1.47-1.54)[a]	0.73 (0.71-0.76)[a]	1,779 (22.3)	4.03 (3.73-4.35)[a]	2.03 (1.83-2.24)[a]
Psychiatric diagnoses							
F00-F09: Organic, including symptomatic, mental disorders	19,706	4,403 (22.3)	8.27 (7.98-8.56)[a]	5.17 (4.96-5.38)[a]	1,593 (36.2)	1.86 (1.75-1.96)[a]	0.92 (0.86-0.98)[a]
F10-F19: Mental and behavioral disorders due to psychoactive substance use	9,196	1,247 (13.6)	4.31 (4.05-4.57)[a]	3.98 (3.72-4.26)[a]	283 (22.7)	1.29 (1.14-1.45)[a]	1.43 (1.26-1.63)[a]
F20-F29: Schizophrenia, schizotypal, and delusional disorders	6,357	630 (9.9)	2.99 (2.76-3.25)[a]	2.40 (2.19-2.64)[a]	102 (16.2)	0.76 (0.62-0.92)[a]	0.81 (0.65-1.01)
F30-F39: Mood [affective] disorders	22,009	2,692 (12.2)	3.89 (3.73-4.05)[a]	3.20 (3.06-3.36)[a]	441 (16.4)	0.72 (0.65-0.79)[a]	0.64 (0.58-0.71)[a]
F40-F48: Neurotic, stress-related, and	24,452	2,161 (8.8)	2.68 (2.56-2.80)[a]	2.52 (2.40-2.65)[a]	190 (8.8)	0.40 (0.35-0.46)[a]	0.48 (0.41-0.56)[a]

[a] Statistically significant at $p < 0.05$, [b] Adjusted for age, sex, marital status, and employment status

Abbreviations: OR = Odds Ratio; HR = Hazard Ratio; CI = Confidence Interval

TABLE 1. Logistic regression assessing the risk and Cox proportional hazards analysis of falls. (continued)

Variables	Total N	Fall N (%)	Risk of falls		Death after falls N (%)	Risk of Death	
			Unadjusted OR (95%CI)	Adjusted OR[b] (95%CI)		Unadjusted HR (95%CI)	Adjusted HR[b] (95%CI)
F50-F59: Behavioral syndromes associated with physiological disturbances and physical factors	4,499	605 (13.4)	4.23 (3.88-4.61)[a]	3.54 (3.22-3.89)[a]	88 (14.5)	0.63 (0.51-0.78)[a]	0.52 (0.42-0.66)[a]
F60-F69: Disorders of adult personality and behavior	2,466	255 (10.3)	3.13 (2.75-3.56)[a]	3.06 (2.63-3.55)[a]	32 (12.5)	0.54 (0.38-0.77)[a]	0.77 (0.53-1.12)
F70-F79: Mental retardation	3,602	280 (7.8)	2.29 (2.02-2.58)[a]	2.68 (2.33-3.08)[a]	21 (7.5)	0.32 (0.21-0.49)[a]	1.12 (0.72-1.74)
F80-F89: Disorders of psychological development	9,571	550 (5.7)	1.65 (1.52-1.80)[a]	2.32 (2.10-2.56)[a]	14 (2.5)	0.12 (0.07-0.21)[a]	0.41 (0.23-0.71)[a]
F90-F98: Behavioral and emotional disorders with onset usually occurring in childhood and adolescence	8,356	541 (6.5)	1.88 (1.72-2.05)[a]	2.53 (2.28-2.81)[a]	10 (1.8)	0.08 (0.04-0.14)[a]	0.40 (0.21-0.77)[a]
All psychiatric diagnoses	83,309	9,326 (11.2)	3.80 (3.72-3.89)[a]	3.28 (3.20-3.37)[a]	2,082 (22.3)	1.15 (1.10-1.22)[a]	0.84 (0.79-0.89)[a]
Psychotropic medications							
Antidepressants	127,249	5,662 (4.4)	1.51 (1.47-1.56)[a]	1.36 (1.31-1.40)[a]	753 (13.3)	1.24 (1.15-1.34)[a]	1.12 (1.03-1.21)[a]
Mood stabilizers	14,036	819 (5.8)	1.83 (1.71-1.97)[a]	1.60 (1.48-1.73)[a]	134 (16.4)	1.19 (1.01-1.42)[a]	1.09 (0.91-1.31)
Antipsychotics	42,751	2,111 (4.9)	1.62 (1.55-1.70)[a]	1.30 (1.23-1.36)[a]	461 (21.8)	1.83 (1.66-2.01)[a]	1.49 (1.35-1.65)[a]
Central nervous system stimulants	5,322	135 (2.5)	0.73 (0.62-0.87)[a]	0.97 (0.79-1.19)	3 (2.2)	0.17 (0.06-0.54)[a]	0.64 (0.20-1.97)
Cognitive enhancing agents	7,048	516 (7.3)	2.56 (2.34-2.80)[a]	1.45 (1.32-1.61)[a]	180 (34.9)	2.55 (2.19-2.95)[a]	1.43 (1.22-1.67)[a]
Drugs used in substance dependence	26,319	1,029 (3.9)	1.19 (1.12-1.27)[a]	1.06 (0.99-1.14)	98 (9.5)	1.05 (0.86-1.28)	0.99 (0.80-1.23)
Hypnotics and anxiolytics	225,234	11,280 (5.0)	1.93 (1.89-1.97)[a]	1.71 (1.67-1.76)[a]	1,774 (15.7)	1.52 (1.44-1.61)[a]	1.32 (1.25-1.40)[a]
All psychotropic medications	310,667	14,850 (4.8)	1.92 (1.89-1.96)[a]	1.76 (1.73-1.80)[a]	2,300 (15.5)	1.48 (1.41-1.56)[a]	1.27 (1.20-1.34)[a]

[a] Statistically significant at $p < 0.05$, [b] Adjusted for age, sex, marital status, and employment status

Abbreviations: OR = Odds Ratio; HR = Hazard Ratio; CI = Confidence Interval

(adjusted HR 1.36; 95%CI 1.17-1.58), and hypnotics-anxiolytics prescriptions (adjusted HR 1.24; 95%CI 1.17-1.31) (Table 1).

Survival analysis revealed an average mean survival of 6.84 (SE = 0.03; 95%CI 6.77–6.90) years after falls. The average survival years after falls was age related, whereby the survival was 8.53 (SE = 0.04; 95%CI 8.45–8.61) years in subjects aged under 60 years old, 5.92 (SE = 0.05; 95%CI 5.82–6.02) years in subjects aged 60–79 years old, and 3.88 (SE = 0.06; 95%CI 3.75–4.00) years in subjects aged 80 years old or more. Survival years were significantly shorter in subjects with a history of falls and having psychiatric diagnoses (mean survival = 6.55; SE = 0.06; $p < 0.0001$), and in subjects with a history of falls and having psychotropic medication prescriptions (mean survival = 6.15; SE = 0.07; $p =< 0.0001$) (Fig 2).

DISCUSSION

The prevalence of falls was higher in subjects with psychiatric diagnoses, 11.2%, with a 3.28-times greater chance of falls compared to subjects without a psychiatric diagnosis. The highest psychiatric diagnoses associated with falls were organic mental disorders (F00-09) (adjusted OR 5.17), and mental and behavioral disorders due to psychoactive substance use (F10-19) (adjusted OR 3.98). Subjects with a history of psychotropic medication prescriptions had a 1.76 greater chance of falls. The most common psychotropic medication associated with falls was hypnotics-anxiolytics (adjusted OR 1.71). After adjusting for age, sex, marital status, and employment status, the only psychiatric diagnosis associated with death after falls was mental and behavioral disorders due to psychoactive substance use (F10-19) (adjusted HR 1.43). The psychotropic medications associated with an increased risk of death after falls were antipsychotics, cognitive enhancing agents, hypnotics-anxiolytics, and antidepressants. Survival analysis revealed an average mean survival of 6.84 years after falls. The average survival years after falls was age related.

Mental disorders were reported to be associated with accidental death in a Swedish national cohort study,[12] with the three highest disorders stated as alcohol use disorder, other substance use disorders, and dementia. The hazard ratios of accidental death due to falls (ICD 10 W00-19) in subjects with a history of any psychiatric disorders were associated more with the male gender, 6.2 in men versus 4.6 in women.[12] The present study showed that the male gender (adjusted HR 2.01) and subjects with a history of falls and having mental and behavioral disorders due to psychoactive substance use had an increased risk of death (adjusted HR 1.43). However, psychiatric diagnoses were not associated with an increased risk of death after adjusting for age, sex, marital status, and employment status. This difference might be explained by the differences in population studied and the definition of fall-related deaths.[12]

From the results of this study, psychotropic medication prescriptions; hypnotics-anxiolytics, mood stabilizers, cognitive enhancing agents, antidepressants, and antipsychotics were significantly associated with falls, which was in line with meta-analyses showing that psychotropic medications and falls in the elderly are significantly correlated.[15,16] Benzodiazepines, antidepressants, and antipsychotics have all been shown to be significantly associated with falls injuries and hospitalization.[14-16] In the present study, hypnotics-anxiolytics showed the

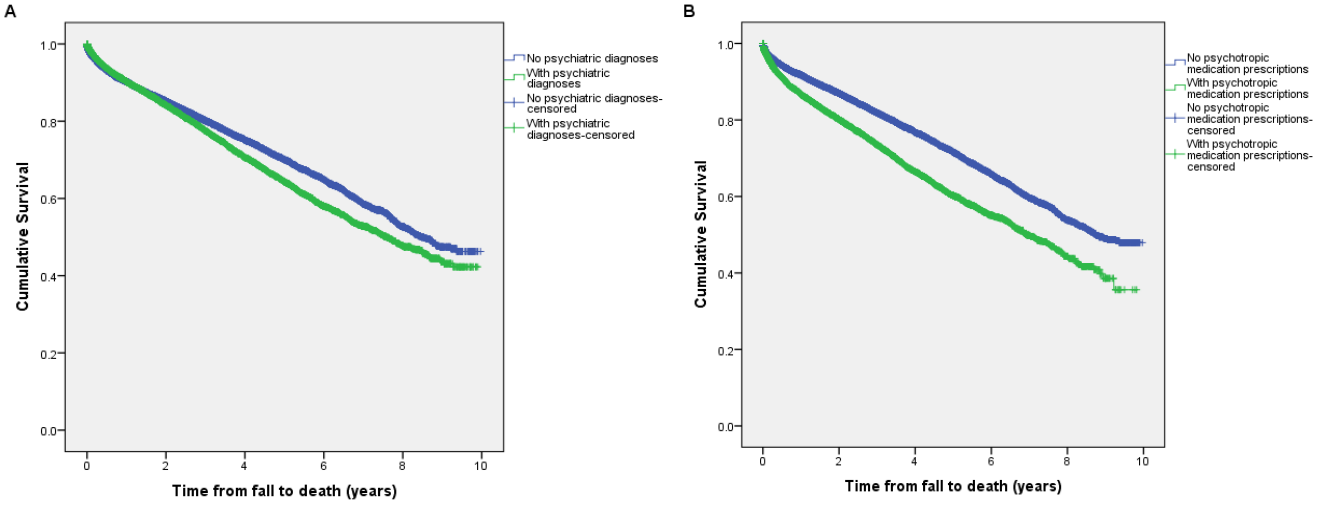

Fig 2. Time from fall to death **(A)** subjects with psychiatric diagnoses, and **(B)** subjects with history of psychotropic medication prescriptions

highest risk associated with falls, which is similar to the results from the meta-analyses.[16] Benzodiazepines are one of the most widely prescribed psychotropic medications and hypnotics-anxiolytics.[17] Benzodiazepines have been reported to increase postural sway and a loss of balance.[18] Besides the side-effects of benzodiazepines, differences in the duration of the half-life and the dosage of benzodiazepines are also related with a greater chance of falls.[19]

The association between mood stabilizers and falls is not well established. Since some anti-epileptics are classified as mood stabilizers and as most fall-related studies have been done on the elderly, their subjects were less likely to be prescribed anti-epileptics. However, in the present study, mood stabilizers were the psychotropic medications second most associated with falls. Anti-epileptics were reported to be associated with falls in emergency room visits by the elderly.[20] Further studies of falls and mood stabilizers might be needed.

In the present study, cognitive enhancing agents were the other psychotropic medications associated with falls. The detrimental effects of dementia medications may outweigh the benefits of dementia treatment in the elderly; for instance, side-effects, including syncope, dizziness, vertigo, nausea, and fatigue, were 2–5 times more common in patients who received dementia medications compared to a placebo.[21] Moreover, falls in the elderly were multifactorial. Besides psychiatric diagnoses and cognitive enhancing agent prescriptions, other causes, such as physiological changes, autonomic nervous system function, visibility, hearing, muscle strength, reaction time, a change in pharmacokinetics and pharmacodynamics,[22] multiple medical diagnoses,[23] and polypharmacy,[24] were also associated with falls.

This study showed that psychotropic medication prescriptions, antipsychotics, cognitive enhancing agents, hypnotics-anxiolytics, and antidepressants, after adjusting for age, sex, marital status, and employment status, were associated with falls and death, which was consistent with the study of mortality in a population-based cohort of older hip fracture patients.[13] Antipsychotics prescriptions had the highest association with death after falls, followed by cognitive enhancing agents, and hypnotics-anxiolytics, which was consistent with a nationwide study among older adults in Sweden.[14] A retrospective study and a meta-analysis from randomized controlled trials revealed that dementia medications might increase the risk of syncope; however, with no effects on falls, fracture, or accidental injury in dementia treatment in the elderly,[25,26] which was in contrast with the present study, which showed that after adjusting for age, cognitive enhancing agents were significantly associated with both falls and death after falls, but not the diagnosis of organic mental disorders. The dose, total number of medications, and the co-administration of medications for other physical disorders were also related with a risk of falls in the elderly,[27-29] but the data were not available in this study. In a study of falls after spinal cord injury, the mean survival was 7.4 years.[30] In the present study, subjects with a history of falls and having a psychiatric diagnosis had a shorter mean survival of 6.55 years.

Psychiatric diagnoses and psychotropic medication prescriptions were clearly associated with falls in the present study. Subjects with a history of being prescribed psychotropic medications were associated with a higher risk of mortality. Patients with psychiatric diagnoses and patients with a history of psychotropic medication prescriptions should benefit from fall-prevention measures.

The key strengths of this study were the use of a 10-year hospital database of all subjects, including outpatients, inpatients, and a death registry that was updated with the National Death Registry, and the fact all age groups were included. The limitations of this study were that the data were obtained only from one big university general hospital in Bangkok, Thailand, the retrospective nature of the study, and the fact that other clinical- and medication-related factors were not included in the study. Physical disorders, disease severity, medication adherence, use of over-the-counter drugs as well as non-psychotropic medications and total number of medications merit studying in future researches.

Our study may be confounded by other physical diagnoses and other medications besides psychotropic medications and central nervous system-acting medications. Furthermore, an ascertainment of falls diagnosis was obtained from computerized coding in the hospital database, not directly from a review of the medical records, and might possibly underrepresent the exact prevalence of falls.

In conclusion, our study demonstrates that psychiatric diagnoses and psychotropic medication prescriptions were significantly associated with 3.28-times and 1.76-times increased risks of falls, respectively. Furthermore, patients with a history of being prescribed psychotropic drugs were associated with a 1.92-times higher risk of mortality. Fall monitoring should be considered for patients with psychiatric diagnoses and for patients with a history of psychotropic medication prescriptions. In addition, physicians should consider prescribing psychotropic medication according to individuals' clinical needs and obviates unnecessary psychotropic drug use, especially in the elderly.

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Conflicts of Interest: None

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