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Generalized and localized osteoarthritis and risk of fall among older adults: the role of chronic diseases and medications using real world data from a single center

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Abstract. – OBJECTIVE: This study examined the prevalence of falls among older adults with generalized and localized osteoarthritis (OA) and identified the association between falls and both chronic diseases and medications.

PATIENTS AND METHODS: A retrospective design using the Healthcare Enterprise Repository for Ontological Narration (HERON) database was used. A cohort of 760 patients aged ≥65 years with at least two diagnosis codes for either localized or generalized OA were included. The extracted data included demographics (age, sex, and race), body mass index (BMI), fall history, comorbid health conditions (i.e., type 2 diabetes, hypertension, dyslipidemia, neuropathy, cardiovascular diseases, depression, anxiety, and sleep disorders), and medications [i.e., pain medication (opioids, non-opioids), antidiabetics (insulin or hypoglycemic), antihypertensives, antilipemic, and antidepressants].

RESULTS: The prevalence rates of falls and recurrent falls were 27.77% and 9.88%, respectively. Individuals with generalized OA had a higher prevalence of falls (33.8%) than those with localized OA (24.2%). Multivariable logistic regression analysis showed that individuals with OA who had hypertension [odds ratio (OR): 1.86, 95% CI, (1.20, 2.89), p=0.006] and used antidepressants [OR: 1.72, 95% CI, (1.04, 2.84), p=0.035] were more likely to have a fall. Individuals with OA who had hypertension [OR: 2.69, 95% CI, (1.30, 5.60), p=0.008], neuropathy [OR: 4.95, 95% CI, (2.95, 11.68), p<0.001], and insulin [OR: 2.85, 95% CI, (1.12, 7.22), p=0.035] were more likely to have a recurrent fall (two or more falls).

CONCLUSIONS: Falls are common in individuals with generalized OA. Comorbid health conditions including hypertension and neuropathy, need to be considered in the screening of the risk of fall. Fall risk needs to be considered when discussing medication prescriptions, especially antidepressants and insulin.

Key Words:
Arthritis, Diabetics, Depressive, Falling, Prescriptions, Frequent falls.

Introduction

Falls are considered the leading cause of morbidity and mortality among older adults[1,2]. The prevalence of falls increases with age, ranging from 15-33%[1,2]. Falls may lead to significant injuries and deaths[3], and are a common serious problem among older adults with chronic conditions such as osteoarthritis (OA)[4]. The risk of falls is higher in people with OA than in those without OA[5,6]. A previous systematic[7] review showed an association between knee OA and falls. This study found associated risk factors, including knee OA symptoms, muscle weakness, and the presence of chronic conditions[7].

Limited evidence has linked chronic conditions and medications to the risk of falls in people with and without knee OA[8-10]. Potential chronic diseases that are associated with falls in older adults with knee OA include fractures, diabetes, and visual impairment[7,9]. Past work has linked pain medications, such as opioids and analgesics, and recurrent falls in people with knee OA[8]. Other chronic diseases such as hypertension and neuropathy may affect vascular and sensory func-

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tions, respectively. No study has examined chronic conditions and their medications with risk of falls and recurrent falls (two or more falls).

Some limitations in previous studies[7-10] on the risk of falls included focusing on specific joints, such as knee OA, and ignoring the interactions between chronic diseases and their medications. Studies[11,12] of generalized OA (affecting three or more joints) and localized OA (affecting one or two joints) are limited. The prevalence of generalized OA is estimated to be 50% in the OA population[12]. Our previous work[13] identified a relationship between chronic diseases, such as diabetes, hypertension, dyslipidemia, and other diseases and generalized OA. Thus, having links between chronic diseases and OA in multiple joints (generalized OA) may increase the risk of falls in this population. Recurrent falls (two or more falls) have not been extensively studied in previous reports[7]. However, multiple falls are more clinically relevant than a single fall due to their relationship with physical and cognitive deficits, as well as mobility decline and subsequent falls[14].

Objectives

The aims of this study were 1) to examine the prevalence of falls between individuals with generalized OA compared to the prevalence of falls in those with localized OA, 2) to identify chronic diseases associated with falls and recurrent falls among individuals with OA, and 3) to identify medications associated with falls and recurrent falls in this population.

Patients and Methods

Study Design

This study was a retrospective analysis using de-identified electronic medical record data for patients who visited a tertiary medical center or its affiliated clinics (Epic Corporation) using the Healthcare Enterprise Repository for Ontological Narration (HERON) database[16]. HERON included other sources of data, including other administrative, research, and public sources, such as the clinics' billing system related to health care systems for Internet Data Exchange (GE IDX), the University Health System Consortium, tumor registries, and the death index from the Social Security Administration. The database contains demographic data (i.e., age, sex, and race), service use, clinical data (i.e., diagnostic codes, flowsheet data, laboratory data, and patient vitals), and pharmacy data. The HERON database does not require ethical approval because all existing data were de-identified. However, the Data Request Oversight Committee approved this dataset for research purposes. This type of retrospective analysis does not require informed consent because it is considered exempt from the consent forms.

Study Cohort

All participants in this dataset were included if they had at least two diagnosis codes for either localized or generalized OA and were examined between January 2011 and December 2017. Participants were selected using the i2b2 query and analysis tool, designed and developed at several centers related to Informatics for Integrating Biology & the Bedside for the HERON database[15,16]. Diagnosis codes must be separated by at least one day using either the International Classification of Disease 9th revision (ICD-9) or International Classification of Disease 10th revision (ICD-10). To establish the index date for localized and generalized OA, the first OA diagnosis code was set as the index date. Participants who were 45 years old and older were included in the study. Further selection for the current study dataset included participants who were ≥65 years. For all participants, a self-reported history of falls within the previous 12 months must have been present on the flowsheet. To ensure links between OA and risk of fall, fall data were obtained within one year of the index date (first OA diagnosis or after). Figure 1 shows the flowchart of participants selection. Participants were excluded if they had at least one specific ICD-9 or ICD-10 code for type 1 diabetes, neoplasm, gout, systemic lupus, arthritis with infection, fibromyalgia, secondary OA, rheumatoid arthritis, trigeminal nerve disorders, or carpal tunnel syndrome.

Demographics

The demographic data included age, sex, and race. Age was recorded in years, sex was recorded as male or female, and race was categorized as Caucasian, African American, or other.

Fall History

Fall history was defined as no fall, one fall, two falls or more. For the current analysis, we categorized the participants into non-fallers (no fall) and fallers (at least one fall). For further analysis and to minimize the chance of one fall, we categorized the participants into recurrent fallers (two or more falls) and non-recurrent fallers (one or no fall).

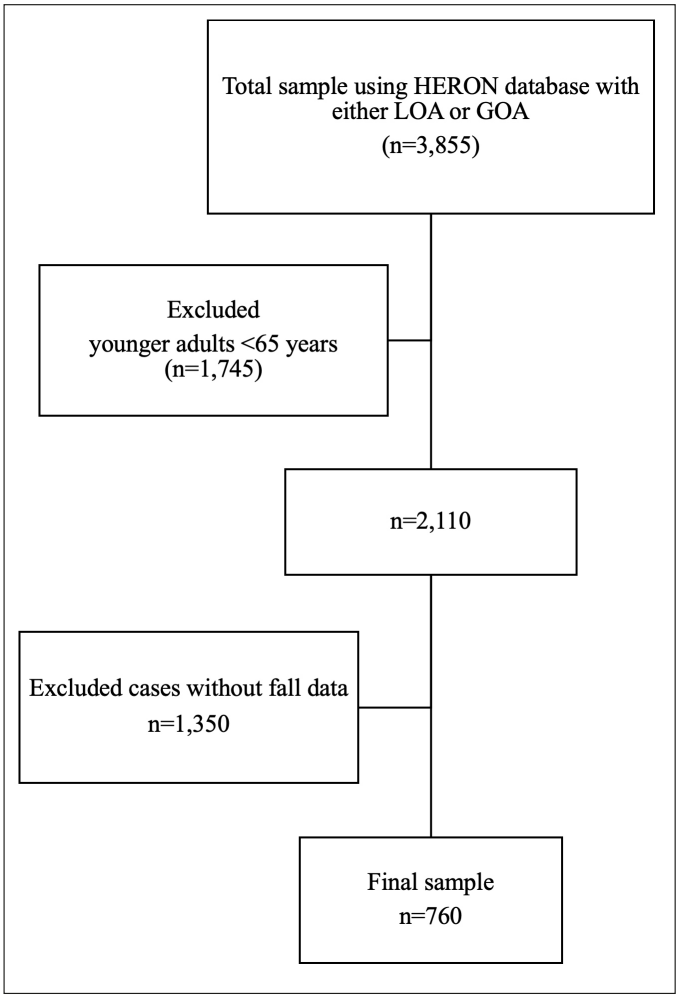

Figure 1. Flowchart of participant selection. GOA, generalized osteoarthritis; LOA, localized osteoarthritis.

Chronic Diseases

All data regarding chronic diseases were included using ICD-9 or ICD-10 based on at least two diagnosis codes separated by at least one day. Chronic diseases included type 2 diabetes, hypertension, dyslipidemia, neuropathy, cardiovascular diseases, depression, anxiety, and sleep disorders. Due to missing values in the index data for body mass index (BMI), it was obtained from within two years before or after the index data (first OA diagnosis).

Medications

Regarding pharmacy data, we included data within 90 days of the OA index date. Medication data had specified categories for each type, and each category included the name of the medication. The medications included pain medications (opioids, non-opioids), antidiabetics (insulin or hypoglycemic), antihypertensives, antilipemic, and antidepressants. We further categorized pharmacy data using medications (YES) or not (NO).

Statistical Analysis

Descriptive data are presented using frequencies and percentages for categorical data and means with standard deviations for continuous data. To compare fallers (at least one fall or more) and non-fallers (no fall), we used the Chi-square and Fisher's exact tests for categorical data and the independent *t*-test for continuous data.

To compare the prevalence of falls (fallers *vs.* non-fallers) between participants with generalized OA and localized OA, we used Chi-square with standardized residuals (R) as calculated by the following formula: This approach has been used by Haberman to test deviation from the expected values separately for each cell. Residuals greater than 1.9 or less than -1.9 were considered significantly different and were selected as cut-offs[16, 17].

To examine the association between chronic diseases [i.e., OA category (localized or generalized OA), diabetes, hypertension, dyslipidemia, neuropathy, cardiovascular disease (CVD), sleep disorders, depression, and anxiety] and the risk of falls (fallers *vs.* non-fallers), multivariable logistic regression was used. The reference category was set as non-fallers (no falls). Results are presented as calculated odds ratios (ORs) with 95% confidence intervals (95% CIs). The analysis was adjusted for age, sex, race, OA category, BMI, and other chronic diseases including diabetes, hypertension, dyslipidemia, neuropathy, CVD, sleep disorders, depression, and anxiety.

To examine the association between medication use [i.e., pain medication (opioids, non-opioids), antidiabetics (insulin or hypoglycemic), antihypertensives, antilipemic, and antidepressants], and risk of falls *vs.* non-fallers), we used multivariable logistic regression. The reference category was set as non-fallers (no falls). Results are presented as calculated odds ratios (ORs) with 95% confidence intervals (95% CIs). The analysis was adjusted for age, sex, race, OA category, BMI, and other medications [pain medication (opioids and non-opioids), antidiabetics (insulin or hypoglycemic), antihypertensives, antilipemic, and antidepressants].

All statistical analyses were performed using SPSS software (IBM Corp., Armonk, NY, USA, version 25) for Mac computers. The *p*-value was set at 0.05.

Results

A total of 760 patients were included in this study. The prevalence of falls in this population was 27.77%. The prevalence of recurrent falls (≥2 falls) was 9.88% among older adults with OA. Table I shows a comparison between fallers and non-fallers. In brief, fallers were older and had diabetes, hypertension, dyslipidemia, neuropathy, CVDs, depression, anxiety, and sleep disorders.

The prevalence of falls was significantly different between patients with generalized and localized OA (Table II). The prevalence of falls was 33.8% among patients with generalized OA (n=96) and 24.2% among those with localized OA (n=115). This difference was significant, as the standardized residuals were 1.9, which was at the cut-off of 1.9.

The results of the multivariable logistic regression analysis examining the association between chronic conditions and falls are shown in Table III. Hypertension was the only significant chronic condition associated with falls in older adults with OA after controlling for covariates [OR: 1.86, 95% CI, (1.20, 2.89), p=0.006]. This indicates that individuals with OA and hypertension were 86% more likely to fall.

The results of the multivariable logistic regression analysis of medications associated with falls are shown in Table IV. Antidepressants were the only medication significantly associated with falls in older adults with OA after controlling for covariates. [OR: 1.72, 95% CI, (1.04, 2.84), p=0.035]. This indicates that individuals with OA who used antidepressants were 72% more likely to experience falls.

The results of the multivariable logistic regression examining the associated chronic conditions with recurrent falls (two or more falls compared to no or one fall) are shown in Table V. Hypertension [OR: 2.69, 95% CI, (1.30, 5.60), p=0.008] and neuropathy [OR: 4.95, 95% CI, (2.95, 11.68), p<0.001] were the only significant chronic conditions associated with recurrent falls among older adults with OA after controlling for covariates.

The results of the multivariable logistic regression analysis examining the medications associated with recurrent falls are shown in Table VI. Insulin was the only medication significantly associated with recurrent falls in older adults with OA after controlling for covariates [OR: 2.85, 95% CI, (1.12, 7.22), p=0.035]. This indicates that individuals with OA who used insulin were 85% more likely to experience recurrent falls.

Discussion

This study examined the prevalence of falls between individuals with generalized OA compared to the prevalence of falls in those with localized OA. The current study also aimed to identify chronic diseases and medications associated with falls and recurrent falls in individuals with OA. Falls were more prevalent among individuals with generalized OA than among those with localized OA, and this prevalence was significant. Hypertension and neuropathy are the only chronic diseases associated with recurrent falls. The use of antidepressants and insulin was significantly associated with falls and recurrent falls in patients with OA. Therefore, individuals with OA may benefit from programs specifically designed to reduce and prevent falls.

Table I. Demographics and clinical variables.

	Non-Fallers N=549	Fallers N=211	*p*-value
Age, Years (Mean±SD)	73.52±6.49	75.18±7.34	**0.004**
Sex, Female, N (%)	344 (62.7)	146 (69.2)	0.09
Race, N (%)			0.45
White	437 (79.6)	163 (77.3)	
Black	58 (10.6)	29 (13.7)	
Others	54 (9.8)	19 (9.0)	
Body Mass Index (Mean±SE)	30.05±6.39	30.22±6.78	0.76
OA Category, GOA, N (%)	188 (34.2)	96 (45.5)	**0.004**
Diabetes, N (%)	100 (18.2)	66 (31.3)	**<0.001**
Hypertension, N (%)	276 (50.3)	149 (70.6)	**<0.001**
Dyslipidemia, N (%)	239 (43.5)	128 (60.7)	**<0.001**
Neuropathy, N (%)	22 (4.0)	24 (11.4)	**<0.001**
CVD, N (%)	91 (16.6)	60 (28.4)	**<0.001**
Depression, N (%)	59 (10.7)	37 (17.5)	**0.012**
Anxiety, N (%)	53 (9.7)	32 (15.2)	**0.031**
Sleep Disorders, N (%)	55 (10.0)	37 (17.5)	**0.004**
Medications			
Opioid, N (%)	202 (36.8)	63 (29.9)	0.072
Non-Opioid, N (%)	169 (30.8)	62 (29.4)	0.71
Insulin, N (%)	30 (5.5)	15 (7.1)	0.39
Hypoglycemic, N (%)	47 (8.6)	17 (8.1)	0.82
Antihypertensive, N (%)	62 (11.3)	26 (12.3)	0.69
Antilipemic, N (%)	169 (30.8)	50 (23.7)	0.053
Antidepressants, N (%)	82 (14.9)	43 (20.4)	0.070

SD: Standard Deviation, OA: Osteoarthritis, GOA: generalized osteoarthritis, CVD: Cardiovascular disease, SE: Standard Error.

The results of this study suggest that hypertension, neuropathy, and depression are all associated with recurrent falls. Several prospective cohort studies[17-19] have reported that the risk of falling increases in patients with cohort studies. In a cross-over design study of (n=90,127) participants, Shimbo et al[19] revealed that the increase in falls is transient after medication and not linked to serious injuries. There are several explanations for the increased risk of falling among hypertensive people[20,21]. Orthostatic hypotension (OH) is a common clinical problem associated with hypertension. Postural hypotension in either systolic or diastolic blood pressure, or both, is inversely related to falls[22]. Moreover, postural blood pressure variations in older adults are larger than those with a regulated systolic blood pressure in those with high blood pressure[23]. For those with moderate-to-high levels of antihypertensive medication exposure, the decrease in systolic blood pressure

Table II. The prevalence of falls in people with generalized and localized OA.

	Generalized OA N=284	Localized OA N=476
Fallers, n (%)	96 (33.8)	115 (24.2)
Standardized residuals	1.9	-1.5
Non-fallers, n (%)	188 (66.2)	361 (75.8)
Standardized residuals	-1.2	0.9

OA: Osteoarthritis.

Table III. Multivariable logistic regression for the association between chronic diseases with falls, n=661.

	Adjusted OR (95% CI)	*p*-value
Age	1.02 (0.98, 1.05)	0.22
Sex	1.25 (0.84, 1.86)	0.27
Race	1.20 (0.64, 2.24)	0.56
OA category, GOA	0.97 (0.64, 1.47)	0.88
Body Mass Index	0.99 (0.97, 1.03)	0.95
Diabetes	1.39 (0.87, 2.23)	0.17
Hypertension	1.86 (1.20, 2.89)	**0.006**
Dyslipidemia	1.16 (0.75, 1.80)	0.49
Neuropathy	2.03 (0.96, 4.24)	0.061
CVD	1.15 (0.70, 1.89)	0.56
Sleep disorders	1.31 (0.72, 2.38)	0.36
Depression	1.22 (0.71, 2.10)	0.48
Anxiety	1.31 (0.73, 2.36)	0.37

OA: Osteoarthritis, GOA: generalized osteoarthritis, CVD: Cardiovascular disease Adjusted OR: adjusted for age, gender, race, OA category, body mass index, and other chronic diseases including diabetes, hypertension, dyslipidemia, neuropathy, CVD, sleep disorders, depression, and anxiety.

is likely to be more significant. Postural hypotension, a common adverse effect of diuretics, is linked to an increased risk of falling[18,24]. Beta blockers have been shown to reduce the chance of falling[25].

Our findings are consistent with a growing body of literature suggesting that neuropathy increases the risk of falling[26,27]. Peripheral neuropathy has been associated with decreased muscular strength, balance, and coordination, leading to poor gait control[28]. Consequently, people with neuropathy are more likely to have injuries attributable to falls[29-31]. Moreover, it has been shown that people with neuropathy have a heightened fear of falling[32], which may cause them to avoid tasks within their capabilities, resulting in less mobility and an increased risk of falling.

In the current study, there was an increased risk of falls associated with antidepressant and insulin use, but not with opioid use. These findings are consistent with those of previous studies[33-36]. Adverse events such as dizziness and drowsiness have been reported among patients who used terazosin, as it blocks alpha-1 adrenergic and histaminergic receptors[33]. Furthermore, a large cohort study[34] of 74,444 older adults that examined the effects of antidepressant use on the risk of fall-re-

Table IV. Multivariable logistic regression for the association between medication use with falls n=661.

	Adjusted OR (95% CI)	*p*-value
Age	1.03 (0.99, 1.06)	0.06
Sex	0.89 (0.60, 1.31)	0.56
Race	1.32 (0.76, 2.29)	0.33
OA category, GOA	1.46 (0.98, 2.17)	0.06
Body Mass Index	1.00 (0.97, 1.03)	0.65
Opioid	0.74 (0.46, 1.18)	0.19
Non-opioid	1.21 (0.76, 1.92)	0.42
Antidepressants	1.72 (1.04, 2.84)	**0.035**
Antilipemic	0.73 (0.45, 1.17)	0.18
Antihypertensive	1.18 (0.68, 2.05)	0.56
Insulin	1.45 (0.70, 3.01)	0.32
Hypoglycemic	0.96 (0.50, 1.86)	0.90

OA: Osteoarthritis, GOA: generalized osteoarthritis. Adjusted OR: adjusted for age, gender, race, OA category, body mass index, and other medications including opioids, non-opioids, antidepressants, antilipemic, antihypertensives, insulin, and hypoglycemic.

Table V. Multivariable logistic regression for the association between chronic diseases with recurrent falls n=661.

	Adjusted OR (95% CI)	*p*-value
Age	1.04 (0.99, 1.09)	0.058
Sex	0.95 (0.51, 1.78)	0.88
Race	1.47 (0.65, 3.39)	0.36
OA category, GOA	0.93 (0.50, 1.72)	0.82
Body Mass Index	1.01 (0.97, 1.06)	0.57
Diabetes	1.43 (0.72, 2.84)	0.30
Hypertension	2.69 (1.30, 5.60)	**0.008**
Dyslipidemia	0.76 (0.40, 1.48)	0.42
Neuropathy	4.95 (2.95, 11.68)	**<0.001**
CVD	0.84 (0.40, 1.77)	0.65
Sleep disorders	0.76 (0.30, 1.95)	0.57
Depression	3.10 (1.53, 6.27)	**0.002**
Anxiety	1.27 (0.54, 2.99)	0.58

OA: Osteoarthritis, GOA: generalized osteoarthritis. Adjusted OR: adjusted for age, gender, race, OA category, body mass index, and other medications including opioids, non-opioids, antidepressants, antilipemic, antihypertensives, insulin, and hypoglycemic.

lated injuries found that the risk of fall-related injuries in users of serotonin-norepinephrine reuptake inhibitors (SNRIs) and other antidepressants increased by 54% and 47%, respectively. In a systematic review and meta-analysis[35] of 248 studies, Seppala et al[35] explored the effect of psychotropic medication on the risk of falls in older adults. They found that there was an increased risk of falls among antidepressant users, and that a higher dosage of psychotropics appeared to result in a higher fall risk. A possible reason for the association of falls and antidepressant use may be their sedative properties. Antidepressants have psychotropic effects, can impair alertness and neuromuscular function, and cause sedation, insomnia and confusion[36]. Another potential mechanism that may contribute to the increased risk of falls associated with antidepressant use is orthostatic hypotension[34]. Some antidepressants (e.g., imipramine) are reportedly associated with a higher incidence of orthostatic hypotension, which can contribute to a higher risk of falls[34].

Moreover, participants on insulin therapy demonstrated a significant recurrence of falls, which is consistent with previous studies[37-39]. A study has investigated the prevalence of falls in

Table VI. Multivariable logistic regression for the association between medication use with recurrent falls n=661.

	Adjusted OR (95% CI)	*p*-value
Age	1.044 (1.003, 1.09)	0.037
Sex	0.98 (0.55, 1.77)	0.96
Race	1.36 (0.62, 3.01)	0.44
OA category, GOA	1.41 (0.78, 2.53)	0.26
Body Mass Index	1.02 (0.98, 1.06)	0.36
Opioid	0.60 (0.29, 1.24)	0.17
Non-opioid	0.98 (0.48, 2.02)	0.42
Antidepressants	1.97 (0.96, 4.06)	0.065
Antilipemic	1.28 (0.62, 2.64)	0.49
Antihypertensive	0.97 (0.42, 2.21)	0.93
Insulin	2.85 (1.12, 7.22)	**0.028**
Hypoglycemic	0.85 (0.32, 2.21)	0.74

OA: Osteoarthritis, GOA: generalized osteoarthritis. Adjusted OR: adjusted for age, gender, race, OA category, body mass index, and other medications including opioids, non-opioids, antidepressants, antilipemic, antihypertensives, insulin, and hypoglycemic.

older patients with diabetes and compared the prevalence of falls among patients on insulin therapy with that among those on oral hypoglycemic drugs[37]. Their results showed that there was a significant relationship between falls and insulin therapy, and that 20.7% of insulin users experienced falls in the previous 12 months. The underlying mechanism behind the association between insulin use and falls may be hypoglycemia. In a large cohort study[38] of 21,613 patients with type 2 diabetes, those who reported having an episode of hypoglycemia had a high incidence of fall-related events, with an adjusted OR of 1.77 (95% CI 1.48-2.12). Another possible explanation for this association is that the rapid correction of hyperglycemia caused by insulin therapy might induce rapid metabolic disequilibrium and neuronal hypoxia, resulting in acute nerve damage that affects sensory functions and increases the risk of falls[39].

In contrast to the findings reported in the literature, our results showed that opioid use was not associated with falls. This finding might be due to the relatively small sample size (n=63 fallers who used opioids)[3,8,40]. Our study included medications such as opioids administered within 90 days of the index date (OA diagnosis). This approach might limit the actual impact of opioids on the risk of falls in this population. Future research should examine the association between opioids and the risk of falls in individuals with OA using a prospective design with a larger sample.

Therefore, physicians should consider the patient's functional level and risk factors for falls during the drug selection decision-making process. Screening and measurement of hypoglycemic symptoms must be performed to minimize the risk of hypoglycemia and falls. Moreover, an appropriate selection of antidepressants needs to be considered when prescribing medication for those at risk of falls. For example, the American Geriatrics Society in their last update (2019) for potentially inappropriate medication use in older adults added SNRIs to the list of drugs to avoid in patients with a history of falls or fracture[41]. Future work should examine the polypharmacy and their types with falls and recurrent falls since it has a link in a previous report[10].

Limitations

This study has some limitations that need to be considered. First, the retrospective design might have affected the results, although every possible effort has been made to minimize recall bias, such as linking fall to within one year of the index date of OA diagnosis. Second, the use of diagnostic codes, which may include diagnostic errors. Nevertheless, we used at least two codes separated by at least one day to minimize errors. Pharmacy data may have affected the findings of this study. However, we used 90 days within the index date of OA to limit its impact. The strength of this study is the use of real-world data to examine the risk of falls in patients with generalized and localized OA. Future research should examine the association between chronic diseases and medications by using a prospective design.

Conclusions

People with generalized OA are at a higher risk of falls and recurrent falls than those with localized OA. The presence of hypertension and neuropathy increases the risk of falls in individuals with OA. Antidepressants and insulin were found to be the risk factors for falls in this cohort. Therefore, a greater focus on fall prevention is required for this population, including fall screening and customization of fall prevention strategies to target any modifiable risk factors.

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Authors' Contributions

AMA conceptualized the study and design, drafted the manuscript, and interpreted the data. ASA, MMA, BAA, NAA, LRW, and PMK contributed to the design and conception of the study and interpretation of data. All authors contributed substantially to the review of the manuscript prior to submission. All authors critically evaluated and revised the manuscript and approved the submitted version.

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Conflict of Interest

All authors declare they have no conflict of interest.

Informed Consent
No informed consent was required for the current study due to de-identified data, and the study was considered exempt from consent forms.

Ethics Approval
No ethical approval was required because all the data were de-identified. However, the Data Request Oversight Committee approved this dataset for research purposes.

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Data Availability
Data will be available from the corresponding author based on reasonable request.

References

1) Rubenstein LZ. Falls in older people: epidemiology, risk factors and strategies for prevention. Age Ageing 2006; 35: ii37-ii41.
2) Tinetti ME. Preventing falls in elderly persons. N Engl J Med 2003; 348: 42-49.
3) Soh SE, Barker AL, Morello RT, Ackerman IN. Applying the International Classification of Functioning, Disability and Health framework to determine the predictors of falls and fractures in people with osteoarthritis or at high risk of developing osteoarthritis: Data from the Osteoarthritis Initiative. BMC Musculoskeletal Disord 2020; 21: 1-8.
4) Barbour KE, Stevens JA, Helmick CG, Luo YH, Murphy LB, Hootman JM, Theis K, Anderson LA, Baker NA, Sugerman DE. Falls and fall injuries among adults with arthritis—United States, 2012. MMWR Morb Mortal Wkly Rep 2014; 63: 379-383.
5) Gillespie LD, Robertson MC, Gillespie WJ, Sherrington C, Gates S, Clemson LM, Lamb SE. Interventions for preventing falls in older people living in the community. Cochrane Database Syst Rev 2012; 9: 1-254.
6) Hoops ML, Rosenblatt NJ, Hurt CP, Crenshaw J, Grabiner MD. Does lower extremity osteoarthritis exacerbate risk factors for falls in older adults? Womens Health (Lond) 2012; 8: 685-698.
7) Manlapaz DG, Sole G, Jayakaran P, Chapple CM. Risk factors for falls in adults with knee osteoarthritis: a systematic review. PM R 2019; 11: 745-757.
8) van Schoor NM, Dennison E, Castell MV, Cooper C, Edwards MH, Maggi S, Pedersen NL, van der Pas S, Rijnhart JJ, Lips P, Deeg DJ. Clinical osteoarthritis of the hip and knee and fall risk: The role of low physical functioning and pain medication. Semin Arthritis Rheum 2020; 50: 380-386.
9) Mat S, Tan PJ, Ng CT, Fadzli F, Rozalli FI, Khoo EM, Hill KD, Tan MP. Mild joint symptoms are associated with lower risk of falls than asymptomatic individuals with radiological evidence of osteoarthritis. PloS One 2015; 10: 1-10.
10) Alenazi AM. Number of Medications and Polypharmacy are Associated with Risk of Fall in Saudi Community-Dwelling Adults. Saudi Pharm J 2023; 31: 1-6.
11) Lawrence J. Generalized osteoarthrosis in a population sample. Am J Epidemiol 1969; 90: 381-389.
12) Forestier R, Francon A, Briole V, Genty C, Chevalier X, Richette P. Prevalence of generalized osteoarthritis in a population with knee osteoarthritis. Joint Bone Spine 2011; 78: 275-278.
13) Alenazi AM, Alothman S, Alshehri MM, Rucker J, Waitman LR, Wick J, Sharma NK, Kluding PM. The prevalence of type 2 diabetes and associated risk factors with generalized osteoarthritis: a retrospective study using ICD codes for clinical data repository system. Clinical Rheumatology 2019; 38: 3539-3547.
14) Cumming RG, Kelsey JL, Nevitt MC. Methodologic issues in the study of frequent and recurrent health problems falls in the elderly. Ann Epidemiol 1990; 1: 49-56.
15) Murphy SN, Weber G, Mendis M, Gainer V, Chueh HC, Churchill S, Kohane I. Serving the enterprise and beyond with informatics for integrating biology and the bedside (i2b2). J Am Med Inform Assoc 2010; 17: 124-130.
16) Waitman LR, Warren JJ, Manos E, Connolly DW. Expressing observations from electronic medical record flowsheets in an i2b2 based clinical data repository to support research and quality improvement. AMIA Annu Symp Proc 2011; 2011: 1454-1463.
17) Butt D, Mamdani M, Austin P, Tu K, Gomes T, Glazier R. The risk of falls on initiation of antihypertensive drugs in the elderly. Osteoporosis Int 2013; 24: 2649-2657.
18) Gribbin J, Hubbard R, Gladman J, Smith C, Lewis S. Risk of falls associated with antihypertensive medication: self-controlled case series. Pharmacoepidemiol Drug Saf 2011; 20: 879-884.
19) Shimbo D, Barrett Bowling C, Levitan EB, Deng L, Sim JJ, Huang L, Reynolds K, Muntner P. Short-term risk of serious fall injuries in older adults initiating and intensifying treatment with antihypertensive medication. Circ Cardiovasc Qual Outcomes 2016; 9: 222-229.
20) Berlowitz DR, Breaux-Shropshire T, Foy CG, Gren LH, Kazis L, Lerner AJ, Newman JC, Powell JR, Riley WT, Rosman R, Wadley VG. Hypertension treatment and concern about falling: baseline data from the systolic blood pressure intervention trial. J Am Geriatr Soc 2016; 64: 2302-2306.
21) Tinetti ME, Han L, Lee DS, McAvay GJ, Peduzzi P, Gross CP, Zhou B, Lin H. Antihypertensive medications and serious fall injuries in a nation-

ally representative sample of older adults. JAMA Intern Med 2014; 174: 588-595.

22) Juraschek SP, Daya N, Appel LJ, Miller ER, Windham BG, Pompeii L, Griswold ME, Kucharska-Newton A, Selvin E. Orthostatic hypotension in middle-age and risk of falls. Am J Hypertens 2017; 30: 188-195.

23) Berry SD, Kiel DP. Treating hypertension in the elderly: should the risk of falls be part of the equation? JAMA Intern Med 2014; 174: 596-597.

24) Klein D, Nagel G, Kleiner A, Ulmer H, Rehberger B, Concin H, Rapp K. Blood pressure and falls in community-dwelling people aged 60 years and older in the VHM&PP cohort. BMC Geriatr 2013; 13: 1-7.

25) Seppala LJ, Van der Velde N, Masud T, Blain H, Petrovic M, Van der Cammen TJ, Szczerbińska K, Hartikainen S, Kenny RA, Ryg J, Eklund P. EuGMS task and finish group on fall-risk-increasing drugs (FRIDs): position on knowledge dissemination, management, and future research. Eur Geriatr Med 2019; 10: 275-283.

26) Riandini T, Wee HL, Khoo EY, Tai BC, Wang W, Koh GC, Tai ES, Tavintharan S, Chandran K, Hwang SW, Venkataraman K. Functional status mediates the association between peripheral neuropathy and health-related quality of life in individuals with diabetes. Acta Diabetol 2018; 55: 155-164.

27) Timar B, Timar R, Gaiță L, Oancea C, Levai C, Lungeanu D. The impact of diabetic neuropathy on balance and on the risk of falls in patients with type 2 diabetes mellitus: a cross-sectional study. PloS One 2016; 11: 1-11.

28) Gregg EW, Sorlie P, Paulose-Ram R, Gu Q, Eberhardt MS, Wolz M, Burt V, Curtin L, Engelgau M, Geiss L. Prevalence of lower-extremity disease in the US adult population≥ 40 years of age with and without diabetes: 1999-2000 national health and nutrition examination survey. Diabetes Care 2004; 27: 1591-1597.

29) Schwartz A. Diabetes mellitus: does it affect bone? Calcif Tissue Int 2003; 73: 515-519.

30) Riandini T, Khoo EY, Tai BC, Tavintharan S, Phua MS, Chandran K, Hwang SW, Venkataraman K. Fall risk and balance confidence in patients with diabetic peripheral neuropathy: an observational study. Front Endocrinol 2020; 11: 1-5.

31) Armstrong DG, Cohen K, Courric S, Bharara M, Marston W. Diabetic foot ulcers and vascular insufficiency: our population has changed, but our methods have not. J Diabetes Sci Technol 2011; 5: 1591-1595.

32) Kelly C, Fleischer A, Yalla S, Grewal GS, Albright R, Berns D, Crews R, Najafi B. Fear of falling is prevalent in older adults with diabetes mellitus but is unrelated to level of neuropathy. J Am Podiatr Med Assoc 2013; 103: 480-488.

33) Fagiolini A, Albert U, Ferrando L, Herman E, Muntean C, Pálová E, Cattaneo A, Comandini A, Di Dato G, Di Loreto G, Olivieri L. A randomized, double-blind study comparing the efficacy and safety of trazodone once-a-day and venlafaxine extended-release for the treatment of patients with major depressive disorder. Int Clin Psychopharmacol 2020; 35: 137-146.

34) Jung YS, Suh D, Choi HS, Park HD, Jung SY, Suh DC. Risk of fall-related injuries associated with antidepressant use in elderly patients: a nationwide matched cohort study. Int J Environ Res Public Health 2022; 19: 1-13.

35) Seppala LJ, Wermelink AM, de Vries M, Ploegmakers KJ, van de Glind EM, Daams JG, van der Velde N, Blain H, Bousquet J, Bucht G, Caballero-Mora MA. Fall-risk-increasing drugs: a systematic review and meta-analysis: II. Psychotropics. J Am Med Dir Assoc 2018; 19: 371.E311-371.E317.

36) Marcum ZA, Perera S, Thorpe JM, Switzer GE, Castle NG, Strotmeyer ES, Simonsick EM, Ayonayon HN, Phillips CL, Rubin S, Zucker-Levin AR. Antidepressant use and recurrent falls in community-dwelling older adults: findings from the Health ABC Study. Ann Pharmacother 2016; 50: 525-533.

37) Mansoor RKTS, Algawwam HGW. Falls in elderly patients with diabetes mellitus on insulin therapy and/or oral hypoglycemic drugs. Iraq Med J 2019; 3: 31-36.

38) Kachroo S, Kawabata H, Colilla S, Shi L, Zhao Y, Mukherjee J, Iloeje U, Fonseca V. Association between hypoglycemia and fall-related events in type 2 diabetes mellitus: analysis of a US commercial database. J Manag Care Spec Pharm 2015; 21: 243-253.

39) Berlie HD, Garwood CL. Diabetes medications related to an increased risk of falls and fall-related morbidity in the elderly. Ann Pharmacother 2010; 44: 712-717.

40) Ofori-Asenso R, Ackerman IN, Soh SE. Prevalence and correlates of falls in a middle-aged population with osteoarthritis: Data from the Osteoarthritis Initiative. Health Social Care Community 2021; 29: 436-444.

41) By the 2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. J Am Geriatr Soc 2019; 67: 674-694.