

Polypharmacy and Falls Risk-increasing Drugs: Their Relation to Fall Recurrence

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Abstract

Background: Polypharmacy and adverse drug side effects are among the high-risk causes for falls in older adults.

Objective: To assess the association between polypharmacy and the risk of recurrent falls and different pharmacological groups of drugs with falls.

Setting: University hospital in community-dwelling older adults in Turkey.

Method: Falls risk-increasing drugs were identified as Cardiovascular drugs, Analgesics, Central Nervous System (CNS) drugs, Endocrine drugs, and others. Falls were evaluated as to whether absent or present during the past 12 months. Two or more falls were recorded as a recurrent faller.

Main outcome measure: Low hand grip strength (HGS) increased the risk of fall approximately 1.7 times (Odds Ratio (OR) 1.69 95% CI 1.11-2.58). Older age and using angiotensin-converting enzyme inhibitors (ACE-I) increased the risk of recurrent falls (OR 1.05: 95% CI 1.00-1.09 and OR 4.04: 95% CI 1.70-9.60, respectively).

Results: Patients' mean (SD) age was 71.9 (7.5) years, and 71.0% of them were female. While 87 (51.4%) participants fall once, 82 (48.5%) of participants reported recurrent falls. Two hundred and eighty-eight (55.6%) participants had four or more prescribed medications. The percentage of patients who used at least one PIM on admission, as defined by the Beers criteria, was 155 (29.9%).

Conclusion: Although the polypharmacy rate of the participants was high, there was no significant relationship between polypharmacy and falling. But low HGS, one of the components of sarcopenia, was a risk factor for fall, and older age and use of ACE-I were risk factors for recurrent fall.

Introduction

Polypharmacy is a common problem among older adults due to multi-morbidities. Drug-related problems in older adults are persistent due to changes in pharmacokinetics and pharmacodynamics of drugs (1, 2). Some of the pharmacokinetic changes are caused by a decrease in total body water and skeletal muscle and an increase in body fat with aging. Also, decreased drug clearance may be the result of a decline in renal function in older adults. An increase in the volume of distribution of lipid-soluble drugs and decreased clearance may increase the elimination of half-life and prolonged effects in older people. Polypharmacy has been associated with an increased risk of frailty, cognitive impairment, disability, falls, hospitalizations, and mortality (1, 3).

Falls frequently result from a combination of risk factors such as muscle weakness and frailty, vision and balance problems, cognitive impairment, polypharmacy, depression, and environmental hazards (3–5). Approximately 1/3 of older adults fall each year, and recurrent falls are seen in half of these the following year (4). Conditions associated with recurrent falling are the history of falling in the previous year, older

age, gender, malnutrition, dependency, difficulty sleeping, use of walkers, balance problems, fear of falls, polypharmacy, the presence of PIMs, and some types of medications classes (4, 6–11). Oral antidiabetic, antipsychotics, antidepressants, benzodiazepines, beta-blockers, pain relief medications, analgesics, antiparkinsonian, acid-related and neuroleptic drugs are found to be related to recurrent falling (4, 6, 8, 12–15). The relationship between drugs and the risk of falling has been established in several review articles. In contrast, cross-sectional studies have recently shown that polypharmacy itself is not a risk factor for falling unless a fall risk-increasing drug is part of the drug regimen (2, 16). Currently, the association between polypharmacy, type of drugs, and falls is still not clear. Thus, the present study aims to assess the association between falls, recurrent falls, a fall risk-increasing drug, polypharmacy, and inappropriate medication use in community-dwelling older adults in Turkey, thereby contributing to this controversial issue with data from our country.

Methods

The cross-sectional study was carried out at geriatric outpatient clinics between January 2020 and February 2021 with participants ≥ 60 years old. The exclusion criterion was being diagnosed with dementia. Patients' information regarding age, sex, education duration, accompanying systemic diseases, and the number of drugs used was recorded. Drugs were defined by patients' self-reports and additionally controlled from the medulla system (in Turkey). We defined polypharmacy as the regular use of four or more drugs, which is the standard definition of polypharmacy (17). Eyedrops, inhalers, and topical medications were not recorded as part of the total number of drugs. All participants provided written informed consent, and the Erciyes University Local Ethics Committee approved the study.

Falls risk-increasing drugs were identified from previous systematic reviews and meta-analysis as Cardiovascular drugs, analgesics, and Central Nervous System (CNS) drugs, Endocrine drugs, other drugs. Falls were evaluated as to whether absent or present during the past 12 months. In the present study, a fall was defined as an unexpected event in which a person came to rest on the ground or at a lower level during the past 12 months. Persons who stated that they fell according to this definition were considered fallers. Two or more falls were recorded as a recurrent faller. Functional capacity was assessed by the activities of daily living (ADL) (bathing or showering, dressing, carrying out personal toileting, moving from bed to chair, bowel or urine continence, and eating) (18) and the instrumental activities of daily living (IADL) (preparing food, telephone, doing laundry, shopping, housekeeping, using transportation, handling finances, handling medications) (19). Frailty was assessed according to the FRAIL scale (fatigue, resistance, ambulation, illnesses, and weight loss) (20). Muscle strength was assessed by handgrip strength (HGS) using a dynamometer (Takei TKK 5401 Digital Handgrip Dynamometer, Niigata-City, Japan). Low muscle strength was defined by HGS < 30 kg for males and HGS < 20 kg for females (21). The Tinetti assessment tool was used to assess the risk of falls in older adults (25–28 = low fall risk: 19–24 = medium fall risk: < 19 = high fall risk) (22). Lying and standing tensions were measured and recorded under the outpatient clinic's control of all participants. Orthostatic hypotension was defined by a drop in blood pressure of at least 20 mmHg for systolic blood pressure (SBP) and at least 10 mm Hg for diastolic blood pressure (DBP) within three minutes of standing up (23). The 2019 Updated American

Geriatrics Society Beers Criteria (1) was used to screen for Potentially Inappropriate Medication Use (PIMs).

Statistical Analysis

Histogram, q-q plots are examined, and the Shapiro-Wilk test is applied to assess the data normality. The Levene test is used to test variance homogeneity. The Pearson chi-square test or Fisher's exact test is applied for categorical variables to compare the differences between groups. The Mann-Whitney U tests are applied for continuous variables. Binary logistic regression analysis models are built to investigate the effect of variables in estimating the number of drugs of faller and recurrent faller in geriatric patients. Age and sex-adjusted, multiple models are fitted separately. Significant variables at $p < 0.25$ are included in multiple models, and backward elimination is performed to identify independent risk factors. Univariate and multiple binary logistic regression analyses were conducted in the faller and non-faller groups. The dependent variables were faller and non-faller, while the arguments for the crude model are sex, age, number of comorbidities, polypharmacy, number of PIMs, antihypertensive drug usage, ACE-I, ARB, KATZ-ADL, IADL, FRAIL, and low handgrip strength. The covariates were age and gender. The model was adjusted according to these variables, and the modified model was established and analyzed again. Univariate and multiple binary logistic regression was also carried out in the recurrent fallers and non-recurrent fallers groups. The dependent variables were recurrent fallers and non-recurrent fallers. The arguments for the Crude model are sex, age, number of comorbidities, polypharmacy, number of PIMs, antihypertensive drug usage, ACE-I, ARB, KATZ-ADL, IADL, FRAIL, and low handgrip strength. The covariates were age and gender. The model was adjusted according to these variables, and the adjusted model was established and analyzed again.

Wald statistic is used as a model selection criterion. Hosmer Lemeshow tests are used for the goodness of fit test. Odds ratios are calculated with 95% confidence intervals. The calculated p values are adjusted using the Benjamini-Hochberg procedure to control for multiple testing. All analyses are performed using TURCOSA (Turcosa Analytics Ltd. Co., www.turcosa.com.tr) statistical software; p values of less than 5% are considered statistically significant.

Results

We included 518 community-dwelling older adults whose mean age and standard deviation (SD) was 71.9 (7.5) years, of which 71.0% were females, and 29.0% were males. The mean comorbidity number of patients was 2.81 ± 1.57 (0–9). Three hundred and sixty-eight patients (70%) had diabetes mellitus (DM), and 233 (67.8 %) of patients had hypertension (HT). The drugs most used by participants were diuretics 40.7%, angiotensin receptor blockers (ARB) 29.3%, biguanides 28.8%, proton pump inhibitors (PPI) 27.4%, acetylsalicylic acid (ASA) 26.8%, beta-blockers 23.2%, insulin 22.4%, calcium canal blockers (CCB) 21.8% and angiotensin-converting enzyme inhibitors (ACE-I) 20.7%. Two hundred and eighty-eight (55.6%) patients had four or more prescribed medications. The percentage of patients who used at least one PIMs, as defined by the Beers criteria, on admission was 151 (29.1%); 106 (70.1%) were female. The most

prescribed PIMs at admission were PPI, 51 (9.8%); NSAIDs, 45 (8.7%), and antidepressants, 19 (3.7%). Participant characteristics based on polypharmacy are summarized in Table 1.

Table 1
Baseline characteristic of participants based on polypharmacy

Variables	< 4 Drugs <i>n</i> = 230	≥ 4 Drugs <i>n</i> = 288	<i>p</i>
Age, years	70.00(65.75-75.00)	72.00(67.00-78.00)	0.027
Sex, Female	162(44.00)	206(56.00)	0.819
Years of education	5.00(0-5.00)	1.00(0-5.00)	0.392
Number of drugs	2.00(1.00-2.25)	3.00(2.00-4.00)	< 0.001
PIMs n(%) Beers criteria	57(24.80)	94(32.60)	0.051
PIMs			
PPI	24(42.10)	27(28.70)	0.094
NSAIDs	16(28.10)	29(30.90)	0.717
Antidepressant	7(12.30)	12(12.80)	0.930
ADLs	1(0.40)	16(5.60)	0.001
IADLs	32(15.60)	67(25.80)	0.008
Comorbidities			
Hypertension	115(50.00)	239(81.90)	< 0.001
Diabetes Mellitus	59(25.70)	174(60.40)	< 0.001
Stroke	8(3.50)	23(8.00)	0.027
Cardiac problems	18(7.80)	66(22.90)	< 0.001
History of falls			
Non-faller	153(66.50)	196(68.10)	0.235
One-faller	45(19.60)	42(14.60)	
Recurrent fallers	32(13.90)	50(61.00)	
FRAIL score	1.00(1.00-2.00)	2.00(1.00-3.00)	< 0.001
FRAIL			
Non- frail	189(82.20)	183(63.50)	
Frail	41(28.10)	105(36.50)	

Variables	< 4 Drugs <i>n</i> = 230	≥ 4 Drugs <i>n</i> = 288	<i>p</i>
Physical Performance			
TUG	9.20(7.00-12.07)	10.00(7.00–13.00)	0.103
Low grip strength	99(46.70)	152(59.60)	0.005
Blood Pressure			
SBP	130.00(115.0-140.00)	80.00(70.00–90.00)	0.047
DBP	80.00(70.00–90.00)	80.00(70.00-82.50)	0.709
OH	36(20.60)	46(23.20)	0.535
Tinetti Fall Risk			
Low fall risk	176(80.70) ^a	173(64.60) ^b	< 0.001
Medium fall risk	24(11.00) ^a	50(18.70) ^b	
High fall risk	18(8.30) ^a	45(16.80) ^b	

Notes: ADL Activity of Daily Living, DBP Diastolic Blood Pressure, IADL Instrumental Activity of Daily Living, NSAID Non-Steroidal Anti-Inflammatory Drug, OH Orthostatic Hypotension PIM Potentially Inappropriate Medication, PPI Proton Pump Inhibitor, SBP Systolic Blood Pressure, TUG Timed Up & Go Test. Low grip strength was <20 kg for women and <30 kg for men. Tinetti 25-28 = low fall risk 19-24 = medium fall risk < 19 = high fall risk Values are expressed as *n*(%) or median(1st-3rd quartiles). Adjusted *p* values are calculated using Benjamini-Hochberg procedure and significant adjusted *p* values are shown in bold.

One hundred and sixty-nine of the 518 participants fell; while 87 (51.4%) participants fell once, 82 (48.5%) reported recurrent falls. There were no significant differences between sex, and one faller (*p* = 0.152), and recurrent faller (*p* = 0.397). In this study, no meaningful relationship was found between polypharmacy and one faller (*p* = 0.711) and recurrent fallers (*p* = 0.098). There was also no relationship between the presence of PIMs and one faller (*p* = 0.072) and recurrent fallers (*p* = 0.963). Table 2 shows the relationship between the drug groups and fallers and recurrent fallers. And there was no significant difference between drug groups vs. fallers and drug groups vs. non-fallers. However, we see that recurrent falls were significantly in those using ACE-I, ARB, and pregabalin (*p* = 0.002, 0.038, and 0.024, respectively) (Table 2).

Table 2

Comparison of Drugs of between Fallers vs. Non-fallers and Recurrent fallers vs. Non recurrent fallers

Variables	Faller <i>n=169</i>	Non-fallers <i>n=349</i>	<i>p</i>	Recurrent fallers <i>n=87</i>	Non- recurrent fallers <i>n=82</i>	<i>p</i>
<i>Endocrine Drugs</i>						
Thyroid Drugs	23(13.60)	62(17.80)	0.231	8(9.80)	15(17.20)	0.156
<i>Antidiabetic drugs</i>						
Insulin	35(20.70)	81(23.20)	0.522	20(24.40)	15(17.20)	0.252
Biguanides	46(30.90)	103(29.50)	0.589	24(29.30)	22(25.30)	0.561
Sulfonylureas	3(1.80)	8(2.30)	0.462	2(2.40)	1(1.10)	0.478
DPP4I	25(14.80)	50(14.30)	0.888	16(19.50)	9(10.30)	0.093
Other antidiabetics	1(0.60)	7(2.00)	0.221	0(0.0)	1(1.10)	0.515
<i>Analgesics</i>						
NSAIDS	19(11.20)	39(11.20)	0.982	12(14.60)	7(8.0)	0.174
<i>CNS Medicines</i>						
Antidepressants						
SSRI	10(5.90)	13(3.70)		8(9.80)	2(2.30)	
SNRI	18(10.70)	38(10.90)	0.525	6(7.30)	12(13.80)	0.060
Antiparkinsonians	13(7.70)	16(4.40)	0.149	6(7.30)	7(8.00)	0.859
Benzodiazepines	2(1.20)	3(0.90)	0.526	2(2.40)	0(0.0)	0.234
Antipsychotics	6(3.60)	15(4.30)	0.686	3(3.70)	3(3.40)	0.941
<i>Cardiovascular drugs</i>						
α -blockers	8(5.30)	15(4.30)	0.821	3(3.70)	5(5.70)	0.523
β -blockers	37(21.90)	83(23.80)	0.633	18(22.00)	19(21.80)	0.986
ACE-inhibitors	35(20.70)	72(20.60)	0.983	25(30.50)	10(11.50)	0.002
ARB	43(25.40)	109(31.20)	0.175	15(18.30)	28(32.20)	0.038
Calcium channel blockers	34(20.10)	79(22.60)	0.515	14(17.10)	20(23.00)	0.338

Diuretics	62(36.70)	149(42.70)	0.192	29(35.40)	33(37.90)	0.729
ASA	48(28.40)	91(26.10)	0.575	29(35.40)	19(21.80)	0.061
<i>Drugs other than fall risk-increasing drugs</i>						
H2RA	0(0.0)	2(0.60)	0.324	-	-	-
PPI	45(26.60)	97(27.80)	0.780	26(31.70)	19(21.80)	0.147
Dyslipidemic drugs	16(9.50)	43(12.30)	0.338	8(9.80)	8(9.80)	0.901
Steroids	2(1.20)	15(4.30)	0.047	2.40)	0(0.0)	0.234
Pregabalin	8(4.70)	16(4.60)	0.940	7(8.50)	1(1.10)	0.024
Gabapentin	7(4.10)	17(4.90)	0.711	5(6.10)	2(2.30)	0.198
Piracetam	12(7.10)	13(3.70)	0.093	9(11.00)	3(3.40)	0.074

Notes: ACE Angiotension Converting Enzyme Inhibitor, ARB Angiotension Receptor Blocker, ASA Acetyl Salicylic Acid, CNS Central Nervous System, DPP4I Dipeptidyl Peptidase 4 Inhibitor, H2RA Histamine 2 Receptor Blocker, NSAID Non-Steroidal Anti-Inflammatory Drug, PIM Potentially Inappropriate Medication, PPI Proton Pump Inhibitor, SNRI Selective Noradrenalin Reuptake Inhibitor SSRI Selective Serotonin Reuptake Inhibitor

Descriptive statistics is n (%). Adjusted *p* values are calculated using Benjamini-Hochberg procedure and significant adjusted *p* values are shown in bold.

The Hosmer-Lemeshow test applied to each final model resulted in $X^2=4.80$ $p=0.779$ for recurrent fallers, $X^2=4.59$, $p=0.802$ for fallers outcomes. These results revealed the appropriateness of the built multiple binary logistic regression model to predict the clinical outcomes in older adults. As a result of numerous binary logistic regression analyses (Table 3), having low HGS increases the risk of fall approximately 1.7 times (OR 1.69: 95% CI 1.11–2.58, $p=0.022$). When the same analysis method was applied to people with recurrent falls, we found that older age and using ACE-I increased the risk of recurrent falls 1.05 and 4 times, respectively (OR 1.05: 95 % CI 1.00-1.09 and OR 4.04: 95% CI 1.70–9.60, $p=0.031$ and 0.006, respectively) (Table 4).

Table 3
Univariate and multiple binary logistic regression analysis in estimating Faller in older adults

	Crude Model		Adjusted Model		Multiple Model	
	OR(95%CI)	p	OR(95%CI)	p	OR(95%CI)	p
Sex	1.35(0.89–2.05)	0.152	-	-	1.59(0.98–2.56)	0.058
Age	1.01(0.98–1.04)	0.312	-	-	-	-
Number of comorbidities	1.07(0.95–1.20)	0.236	1.06(0.95–1.20)	0.292	-	-
Number of medications	0.99(0.93–1.06)	0.853	0.99(0.92–1.05)	0.720	-	-
Polypharmacy	0.93(0.64–1.35)	0.711	0.91(0.62–1.31)	0.603	-	-
Number of PIMs	0.96(0.50–1.83)	0.893	1.07(0.55–2.07)	0.842	-	-
Antihypertensive drugs usage	0.71(0.48–1.05)	0.088	0.64(0.43–0.96)	0.032	0.66(0.42–1.03)	0.070
ACE-I	1.00(0.64–1.58)	0.983	1.00(0.63–1.58)	0.992	-	-
ARB	0.75(0.50–1.14)	0.176	0.70(0.46–1.07)	0.097	-	-
KATZ-ADL	2.40(0.91–6.33)	0.077	2.16(0.80–5.82)	0.129	-	-
IADL	1.51(0.95–2.40)	0.082	1.43(0.86–2.38)	0.165	-	-
FRAIL	1.49(0.99–2.21)	0.052	1.38(0.91–2.09)	0.124	-	-
Low handgrip strength	1.52(1.03–2.25)	0.036	1.43(0.95–2.16)	0.088	1.69(1.11–2.58)	0.015

Notes: : ACE Angiotension Converting Enzyme Inhibitor, ADL Activity of Daily Living, ARB Angiotension Receptor Blocker, IADL Instrumental Activity of Daily Living, PIM Potentially Inappropriate Medication,

OR: Odds ratio, CI: Confidence interval. Adjusted models are controlled for age and sex. Adjusted *p* values are calculated using Benjamini-Hochberg procedure and significant adjusted *p* values are shown in bold.

Table 4

Univariate and multiple binary logistic regression analysis in estimating Recurrent Faller in older adults

	Crude Model		Adjusted Model		Multiple Model	
	OR(95%CI)	p	OR(95%CI)	p	OR(95%CI)	p
Sex	1.35(0.67–2.74)	0.398	-	-	-	-
Age	1.04(0.99–1.08)	0.074	-	-	1.05(1.00–1.09)	0.031
Number of comorbidities	1.00(0.84–1.20)	0.941	1.00(0.84–1.20)	0.942	-	-
Number of drugs	1.08(0.97–1.21)	0.160	1.08(0.96–1.20)	0.192	-	-
Polypharmacy	1.67(0.91–3.08)	0.099	1.60(0.86–2.97)	0.135	-	-
Number of PIMs	1.22(0.44–3.37)	0.904	0.95(0.50–1.82)	0.876	-	-
Antihypertensive drugs usage	1.17(0.63–2.19)	0.618	1.11(0.58–2.12)	0.756	-	-
ACE-I	3.38(1.50–7.59)	0.003	3.38(1.49–7.69)	0.004	4.04(1.70–9.60)	0.002
ARB	0.47(0.23–0.97)	0.040	0.44(0.21–0.94)	0.034	-	-
KATZ-ADL	0.51(0.12–2.21)	0.356	0.36(0.08–1.60)	0.179	-	-
IADL	1.18(0.56–2.48)	0.656	0.88(0.38–2.01)	0.762	-	-
FRAIL	1.37(0.55–1.96)	0.911	0.86(0.44–1.68)	0.668	-	-
Low handgrip strength	1.88(0.97–3.62)	0.060	1.60(0.80–3.18)	0.182	-	-

Notes: ACE Angiotension Converting Enzyme Inhibitor, ADL Activity of Daily Living, ARB Angiotension Receptor Blocker, IADL Instrumental Activity of Daily Living, PIM Potentially Inappropriate Medication

OR: Odds ratio, CI: Confidence interval. Adjusted models are controlled for age and sex. Adjusted *p* values are calculated using Benjamini-Hochberg procedure and significant adjusted *p* values are shown in bold.

Discussion

This is the first study to our knowledge to investigate the associations between falls, recurrent falls, and a fall risk-increasing drug, polypharmacy, and inappropriate medication use in community-dwelling older adults in Turkey. There is a limited number of studies in the literature evaluating the relationship between recurrent falls and polypharmacy. The relationship between certain drug groups and falls and recurrent falls could not be clearly shown in this study, as in other studies. In this study, 55.6% of older adults had polypharmacy, and 29.1% of the study participants had used at least one PIMs. Thirty-two percent of older adults had fallen at least once in the past year, and 48.5% of falling participants reported recurrent falls. In our research, having low HGS increases the risk of falling, and older age and ACE-I usage increases the risk of recurrent falling. The fall rate in this study (32%) is lower than in several other studies of older adults, which reported fall rates of 13.1 to 41.8% and recurrent fall rates of 13.1 to 86.9% (4, 6, 24). These studies were carried out with either unhealthy (e.g., people with chronic stroke) or different populations (e.g., home health patients). However, no relation was found between polypharmacy and falling or recurrent falling.”

In the literature, the prevalence of polypharmacy ranges from 25–90% (1,3,5,24). In our study, the polypharmacy prevalence was 55.6%. Different types of drugs have been reported as the most used in previous studies (5, 24). In this study, the most widely used drugs were diuretics, ARB, biguanides, PPI, and ASA. This is due to the differences in the drugs preferred across populations and the lack of standardization in drug selection worldwide.

Studies have shown that polypharmacy is an independent risk factor for falls. Drugs are significant risk factors for falls, and stopping drugs that increase the risk of falling is an effective intervention to prevent falls (5, 16, 25). In 13 of the 19 studies evaluated in a meta-analysis, no relation was found between polypharmacy and falling (2). As seen in other meta-analyses (26, 27), polypharmacy was not a risk factor for falls in our study. Although the relationship between polypharmacy and falls is controversial, many studies have shown the relationship between recurrent falls and polypharmacy. However, in our study, no association was found between polypharmacy and recurrent falls. When we look at the reasons for this difference, we found that the rate of people reporting recurrent falls in other studies is less than our study (12.2%, 28%, 19.7%, and 22% vs. 48.5%) (4, 6, 8, 12). Therefore, as the sample size has increased, the relationship seen in others may have disappeared.

Some studies have found that the inappropriate use of drugs that cause falling was more critical in increasing the risk of falling than the number of drugs used by older adult patients (3, 28–30). In some studies, this relationship between fall and PIM usage was not found (24, 31). In research, there was no difference in terms of falls between patients using PIMs, which increased the risk of falling and those who did not (31) In a study involving 99 people, 11 types of drugs (ibuprofen, gabapentin, sertraline, alprazolam, ranitidine, zolpidem) were determined as PIMs. At the same time, there was no relationship between PIMs use and falling and recurrent falling, and there was no relationship between recurrent falls and either polypharmacy or PIM (24). In the present study, although polypharmacy was high, the PIM rate was found in only 29.2% of the patients. No significant correlation was found between the presence of PIMs and drug types on the Beers criteria and falling and recurrent falling.

Drug classes that have been associated with an increased risk of falls include the following: antihypertensive agents, sedatives and hypnotics, neuroleptics and antipsychotics, antidepressants, benzodiazepines, and nonsteroidal anti-inflammatory drugs (NSAIDs). In the studies conducted, a direct relationship between some drug groups and falling was observed. A two-way relationship was found between fall risk increase drugs (FRID) and polypharmacy in one study. While the prevalence of FRIDs was higher in patients with polypharmacy, polypharmacy was also more common in patients with FRIDs (25). Using FRIDs was an increased risk of falls (32). When we looked at the specific drug groups, NSAIDs, benzodiazepine, antidepressants, hypnotics, opioids, and antihypertensive drugs were associated with falls in some research (2, 26, 33). However, nine of 13 studies showed no association between NSAID use and falls (34). In a meta-analysis, opioid and antiepileptic usage were significantly associated with an increased risk of falling. Still, NSAIDs, proton pump inhibitors, anti-dementia drugs, antiplatelets, antiparkinsonian drugs, analgesics were not associated with falling (16). In another study, no significant relationship was observed between 23 drug types and falls (24). Antipsychotic, antidepressant, analgesic, antiparkinsonian, acid-related, nasal preparation, and ophthalmological drugs were all associated with recurrent falls (17). Formiga et al. found that individuals with recurrent falls have more polypharmacy and use of neuroleptics (12). In a cohort study (13), only oral antidiabetic usage was related to recurrent falls. We evaluated the relationship between oral antidiabetic drugs and recurrent falling, and we did not find any association between them. As shown in a study, the use of psychoactive drugs defined as PIMs based on the Beers criteria increases the risk of falling by up to 20% (35). Anderson et al. found a relationship between using only antidepressants and recurrent falls among antipsychotic, antianxiety, antidepressant, or diuretic medications (9). In a study involving community-dwelling older adults, the relationship between recurrent falls and SSRI use, moderate dosage, and short duration of use was shown (36). As in our study, Chiu et al. did not establish a relationship between anticoagulant use and recurrent falls (37). Also, in a meta-analysis, the use of psychotropic drugs increased the risk of falling in some studies, while in others, it was found not to increase the risk of falling (2). To our surprise, we found no association between the benzodiazepine, antipsychotics, antidepressants (tricyclic antidepressants, serotonin reuptake inhibitors, serotonin-noradrenalin reuptake inhibitors, and NSAIDs) with recurrent falls. The reason for this may be the restriction on the use of hypnotic drugs and on prescribing imposed on individual physicians in Turkey by the Ministry of Health. Also, the participants may have forgotten to notify them that they can take NSAIDs without a prescription; the non-prescription drugs are not seen in the Medulla system, so these drugs were not included.

In our research, ACE-I usage was an increased risk of recurrent falls. It is known that antihypertensive drugs can cause falls through several mechanisms. They increase the risk of falling by causing sudden blood pressure drops, orthostatic hypotension, and electrolyte imbalance (38, 39).

In this study, when the relationship between recurrent falls and advanced age was examined, we demonstrated that older age increases recurrent falls, as seen in other studies (28, 32, 40). To date, many studies have shown that there is a relationship between falls and walking speed (5, 39). Patients with decreased walking speed have an increased risk of falling, but we did not investigate their relationship in the present study. Few studies examine the relationship between muscle strength and falling. In some of

these studies, people with recurrent falls had low HGS values (6, 40). Sarcopenia is known to increase the risk of falling. People with low HGS are probable sarcopenic (21). Our study showed a strong relationship between low HGS and recurrent falls, which is one of the sarcopenia criteria affecting muscle strength in falling.

In our study, there were some limitations. One of the limitations was that the presence of drug-drug interaction had not been studied. While some drugs may not increase the risk of falling alone, they increase the risk of falling significantly due to their accumulated effects when used with drugs from another group. Over-the-counter drugs, nasal drugs, ophthalmological drugs, and the use of herbal medicines are not included in the study. Since only outpatient participants were included, the study population may be healthier than the older adult population in the community. Furthermore, the study was designed as a cross-sectional study; it may have been limited in showing the relationship between fall risk factors and recurrent falling.

Conclusion

The findings in this study did not confirm results from previous studies demonstrating correlations with certain drug classes and fall risks among older adults. Drugs are a well-known risk factor for falls. However, it is crucial to consider the reason for taking medication before deciding to stop or withdraw a drug to prevent the fall because the condition where the medication is used to treat itself can be a risk factor for the fall. Therefore, each drug should be examined individually, and the benefits and risks of stopping or continuing to use it should be carefully weighed. As a result, the relationship between certain drug groups and falls and recurrent falls could not be clearly shown in this study, as in other studies. However, low HGS, one of the components of sarcopenia, is a risk factor for falling. The importance of screening and detecting sarcopenia in the geriatric patient population has once again been demonstrated.

Impact statements

1. Use of ACE-I may be a risk factor for recurrent fall
2. Low hand grip strength (HGS), one of the components of sarcopenia, is a risk factor for fall
3. Each drug should be examined individually, and the benefits and risks of stopping or continuing to use it should be carefully weighed

Declarations

Funding :

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Conflicts of interest :

The authors declare no conflict of interest.

Availability of data and material :

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Code availability :

Not applicable

Ethics approval :

Ethics Committee of the institution within which the work was undertaken and it conforms to the provisions of the Declaration of Helsinki (2019/136; 20.02.2019).

Consent to participate :

All participants signed the informed consent form.

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