

# Polypharmacy and Falls-risk-increasing Drugs in Community-dwelling Older Adults

© Sibel Akın<sup>1</sup>, © Nurdan Şentürk Durmuş<sup>1</sup>, © Tuba Soysal<sup>1</sup>, © Firuzan Fırat Özer<sup>1</sup>, © Bilge Müge Gökçekuyu<sup>1</sup>, © Gözde Ertürk Zararsız<sup>2</sup>

<sup>1</sup>Erciyes University Faculty of Medicine, Department of Internal Medicine, Division of Geriatrics, Kayseri, Turkey

<sup>2</sup>phD, Erciyes University Faculty of Medicine, Department of Biostatistics, Kayseri, Turkey

## Abstract

**Objective:** To evaluate the relationship between polypharmacy and the risk of recurrent falls and to assess the fall risk with different pharmacological groups of drugs.

**Materials and Methods:** In this cross-sectional study, falls risk-increasing drugs were defined as cardiovascular drugs, analgesics, central nervous system drugs, endocrine drugs, and others. Falls were evaluated according to their presence during the past 12 months. Two or more falls were recorded as recurrent fallers.

**Results:** Five hundred and eighteen participants had a mean age of 71.9 years (7.5) and 71.0% were female. While 87 (51.4%) participants fell once, 82 (48.5%) participants reported recurrent falls. Two hundred and eighty-eight (55.6%) participants had polypharmacy. The percentage of patients who used at least one potentially inappropriate medication on admission, as defined by the Beers criteria, was 155 (29.9%). The determinants of the risk of recurrent falls were older age and use of angiotensin-converting enzyme inhibitors (ACE-I) [odds ratio (OR) 1.05: 95% confidence interval (CI) 1.00-1.09 and OR 4.04: 95% CI 1.70-9.60, respectively]. Low handgrip strength (HGS) increased the risk of falls approximately 1.7 times (OR 1.69 95% CI 1.11-2.58).

**Conclusion:** Although the polypharmacy rate of the participants was high, there was no significant relationship between polypharmacy and falling. However, we found low HGS, a component of sarcopenia, as a risk factor for falls, and use of ACE-I and older were risk factors for recurrent falls.

**Keywords:** Falls risk-increasing drugs, handgrip, older adults, polypharmacy, recurrent falls

## Introduction

Polypharmacy is widespread in older adults because of comorbidities. One of the most important reasons why polypharmacy is seen in older adults is that; aging increases the incidence of chronic diseases (1). Changes in the pharmacokinetics and pharmacodynamics of drugs in older age lead older adults to be more susceptible to drug-induced adverse events (2,3). Decrease in total skeletal muscle and body water and increase in body fat with aging are associated with more frequent pharmacokinetic changes. In addition, decreased renal function in older adults affects drug clearance (2,3). An

increase in the volume of distribution of lipid-soluble drugs and decreased clearance may increase the half-life of the drug and prolong its effect in older people. Polypharmacy is associated with an increased risk of poor outcomes such as frailty, disability, cognitive impairment, falls, hospitalizations, and mortality (2,4).

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 (4-6). Approximately 1/3 of older adults fall each year, and recurrent falls are seen in half of these the following year (5). Conditions associated with recurrent falling include a history of falling in the previous year, older age, sex,

**Address for Correspondence:** Sibel Akın, Erciyes University Faculty of Medicine, Department of Internal Medicine, Division of Geriatrics, Kayseri, Turkey

**Phone:** +90 352 207 66 66 **E-mail:** sibelyanmaz@gmail.com **ORCID:** orcid.org/0000-0002-6139-7254

**Received:** 22.09.2023 **Accepted:** 14.12.2023

**Cite this article as:** Akın S, Şentürk Durmuş N, Soysal T, Fırat Özer F, Gökçekuyu BM, Ertürk Zararsız G. Polypharmacy and Falls-risk-increasing Drugs in Community-dwelling Older Adults. Eur J Geriatr Gerontol 2024;6(1):65-72



Copyright© 2024 The Author. Published by Galenos Publishing House on behalf of Turkish Academic Geriatrics Society.

This is an open access article under the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 (CC BY-NC-ND) International License.

malnutrition, dependency, sleeping problems, use of walkers, balance problems, fear of falls, polypharmacy, the presence of potentially inappropriate medications (PIM), and some types of drug classes (5,7,8). Data from several studies suggest that oral antidiabetics, antipsychotics, antidepressants, benzodiazepines, beta-blockers, pain relief drugs, analgesics, antiparkinsonian, antiacids, and neuroleptic drugs are related to recurrent falling (5,9-13). More recently, contradictory findings have emerged that polypharmacy itself is not a risk factor for falling unless a fall-risk-increasing drug (FRID) is part of the drug regimen (3,14). Much uncertainty still exists regarding the relationship between polypharmacy, types of drugs, and falls. Thus, the present study aims to assess the associations among falls, recurrent falls, FRIDs, polypharmacy, and PIM in community-dwelling older adults in Turkey, thereby contributing to this controversial issue with data from Turkey.

## Materials and Methods

This cross-sectional study was conducted in a tertiary geriatric outpatient clinic between January 2020 and February 2021 with participants >60 years. The exclusion criterion was being diagnosed with dementia. Patient information regarding age, sex, comorbidities, and the number of drugs used was recorded. Patients' self-reports were used for drug recording and were additionally controlled from the national medulla system (in Turkey). Polypharmacy was defined as the regular use of four or more drugs (1). Eyedrops, inhalers, and topical drugs were not recorded as a part of the total number of drugs. All participants provided written informed consent, and the Erciyes University Local Ethics Committee approved the study (decision number: 2019/136, date: 20.02.2019).

FRIDs were identified from previous systematic reviews and meta-analyses as cardiovascular drugs, analgesics, central nervous system drugs, endocrine drugs, and other drugs. Falls were evaluated according to their presence during the past 12 months. A fall was defined as an unexpected event in which a person came to rest on the ground or at a lower level. Persons who stated that they fell according to this definition were considered fallers. Two or more falls were recorded as recurrent fallers. Functional capacity was evaluated by the activities of daily living (ADL) (bathing or showering, dressing, moving from bed to chair, carrying out personal toileting, urine or bowel continence, and eating) (15) and the instrumental ADL (IADL) (preparing food, telephone, doing laundry, shopping, housekeeping, using transportation, handling finances, handling drugs) (16). Frailty was defined on the basis of the fatigue, resistance, ambulation, illnesses, and weight loss scale (17). Muscle strength was assessed by handgrip strength (HGS) using a dynamometer (Takei TTK 5401 Digital Handgrip Dynamometer, Niigata City, Japan). Low muscle strength was defined by HGS <30 kg and HGS <20 kg, for males and females, respectively (18).

The Tinetti (19) assessment tool was used to determine the risk of falls in older adults (<19= high fall risk, 19-24= medium fall risk, and 25-28= low fall risk). Lying and standing tensions were measured and recorded under the outpatient clinic's control of all participants. A drop in blood pressure of at least 20 mmHg for systolic blood pressure and at least 10 mmHg for diastolic blood pressure within 3 min of standing up was accepted as the presence of orthostatic hypotension (20). The 2019 Updated American Geriatrics Society Beers Criteria (2) was used to screen for PIM.

## Statistics

The histogram and q-q plots were examined. The normality of the data was tested using the Shapiro-Wilk test. The Levene test was used to test the homogeneity of variance. Pearson's chi-squared or Fisher's exact test was used to compare differences between groups for categorical variables. The Mann-Whitney U test was used to compare continuous variables. To investigate the effect of variables in estimating the number of drugs used for fallers and recurrent fallers in geriatric patients, binary logistic regression analysis models were constructed. Age- and sex-adjusted multiple logistic regression models were adjusted. Univariate and multiple binary logistic regression analyses were performed in the faller/non-faller and recurrent faller/non-recurrent faller groups.

The Wald statistic was used as a criterion for selecting models. Goodness-of-fit tests were performed using the Hosmer-Lemeshow test. Odds ratios were calculated with 95% confidence intervals. To control for multiple testing, the calculated p-values were adjusted using the Benjamini-Hochberg procedure. All analyses were performed using TURCOSA (Turcosa Analytics Ltd. Co., [www.turcosa.com.tr](http://www.turcosa.com.tr)); p-values below 0.050 were considered statistically significant.

## Results

Of the 518 participants with a mean age of  $71.9 \pm 7.5$  years, 71.0% were female. The mean number of comorbidities was  $2.81 \pm 1.57$  (0-9). Seventy percent (386) patients had diabetes mellitus and 67.8% (233) had hypertension. The most commonly used drugs were, in descending order, diuretics (40.7%), angiotensin receptor blockers (ARBs) (29.3%), biguanides (28.8%), proton pump inhibitors (PPIs) (27.4%), acetyl salicylic acid (ASA) (26.8%), beta-blockers (23.2%), insulin (22.4%), calcium channel blockers (21.8%), and angiotensin-converting enzyme inhibitors (ACE-I) (20.7%). Approximately half of the patients (288) had polypharmacy. The percentage of patients using at least one PIM on admission according to the Beers criteria was 29.1% (151). The most commonly prescribed PIMs on admission were PPIs, 9.8% (51); non-steroidal anti-inflammatory drugs (NSAIDs), 8.7% (45); and antidepressants, 3.7% (19). Differences between participants are highlighted in Table 1.

<b>Table 1. Baseline characteristic of participants based on polypharmacy</b>			
<b>Variables</b>	<b>&lt;4 drugs n=230</b>	<b>≥4 drugs n=288</b>	<b>p</b>
Age, years	70.0 (65.8-75.0)	72.0 (67.0-78.0)	<b>0.027</b>
Sex, female	162 (44.0)	206 (56.0)	0.819
Years of education	5.0 (0-5.0)	1.0 (0-5.0)	0.392
Number of drugs	2.0 (1.0-2.3)	3.00 (2.0-4.0)	<b>&lt;0.001</b>
PIMs n (%) Beers criteria	57 (24.8)	94 (32.6)	0.051
PIMs			
PPI	24 (42.1)	27 (28.7)	0.094
NSAIDs	16 (28.1)	29 (30.9)	0.717
Antidepressant	7 (12.3)	12 (12.8)	0.930
ADLs	1 (0.4)	16 (5.6)	<b>0.001</b>
IADLs	32 (15.6)	67 (25.8)	<b>0.008</b>
Comorbidities			
Hypertension	115 (50.0)	239 (81.9)	<b>&lt;0.001</b>
Diabetes mellitus	59 (25.7)	174 (60.4)	<b>&lt;0.001</b>
Stroke	8 (3.5)	23 (8.0)	<b>0.027</b>
Cardiac problems	18 (7.8)	66 (22.9)	<b>&lt;0.001</b>
History of falls			
Non-faller	153 (66.5)	196 (68.1)	
One-faller	45 (19.6)	42 (14.6)	
Recurrent fallers	32 (13.9)	50 (61.0)	0.235
FRAIL score	1.0 (1.0-2.0)	2.0 (1.0-3.0)	<b>&lt;0.001</b>
FRAIL			
Non-FRAIL	189 (82.2)	183 (63.5)	<b>&lt;0.001</b>
FRAIL	41 (28.1)	105 (36.5)	
Physical performance			
TUG	9.2 (7.0-12.1)	10.0 (7.0-13.0)	0.103
Low handgrip strength	99 (46.7)	152 (59.6)	<b>0.005</b>
Blood pressure			
SBP	130.0 (115.0-140.0)	80.0 (70.0-90.0)	0.047
DBP	80.0 (70.0-90.0)	80.0 (70.0-82.5)	0.709
OH	36 (20.6)	46 (23.2)	0.535
Tinetti fall risk			
Low fall risk	176 (80.7)	173 (64.6)	
Medium fall risk	24 (11.0)	50 (18.7)	
High fall risk	18 (8.3)	45 (16.8)	<b>&lt;0.001</b>

Low handgrip 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 (1<sup>st</sup>-3<sup>rd</sup> quartiles). Adjusted p-values are calculated using Benjamini-Hochberg procedure and significant adjusted p-values are shown in bold. ADL: Activities of daily living, DBP: Diastolic blood pressure, IADL: Instrumental activities 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, FRAIL: Fatigue, resistance, ambulation, illnesses, and weight loss

Falling was reported by 32.6% (169/518) of the participants, 51.4% (87) of the participants fell once, and 48.5% (82) reported recurrent falls. No significant differences were found between sex and single faller ( $p=0.152$ ), and recurrent faller ( $p=0.397$ ). The chi-square test did not show any significant differences between polypharmacy and one fall ( $p=0.711$ ) and recurrent falls ( $p=0.098$ ). No statistically significant difference could be observed between PIM and single-faller ( $p=0.072$ ) and recurrent fallers ( $p=0.963$ ). The relationship between the drug groups and fallers and recurrent fallers is shown in Table 2. There was no evidence that drug groups have an influence on falling. The results shown in Table 2 indicate that recurrent falls were

significantly higher in those using ACE-I, ARB, and pregabalin ( $p=0.002$ , 0.038 and 0.024 respectively).

The Hosmer-Lemeshow test applied to each final model showed  $\chi^2=4.80$ ,  $p=0.779$  for recurrent fallers,  $\chi^2=4.59$ ,  $p=0.802$  for fallers. These results demonstrate the appropriateness of the multiple binary logistic regression model constructed for the prediction of clinical outcomes in older adults. From the data presented in Table 3, having a low HGS increased the risk of falling by approximately 1.7-fold (OR 1.69: 95% CI 1.11-2.58,  $p=0.022$ ). Further analysis showed that older age and use of ACE-I were linked to the risk of recurrent falls (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).

Variables	Faller n=169	Non-fallers n=349	p	Recurrent fallers n=87	Non-recurrent fallers n=82	p
<b>Endocrine drugs</b>						
Thyroid drugs	23 (13.6)	62 (17.8)	0.231	8 (9.8)	15 (17.2)	0.156
<b>Antidiabetic drugs</b>						
Insulin	35 (20.7)	81 (23.2)	0.522	20 (24.4)	15 (17.2)	0.252
Biguanides	46 (30.9)	103 (29.5)	0.589	24 (29.3)	22 (25.3)	0.561
Sulfonylureas	3 (1.8)	8 (2.3)	0.462	2 (2.4)	1 (1.1)	0.478
DPP4I	25 (14.8)	50 (14.3)	0.888	16 (19.5)	9 (10.3)	0.093
Other antidiabetics	1 (0.6)	7 (2.0)	0.221	0 (0.0)	1 (1.1)	0.515
<b>Analgesics</b>						
NSAIDS	19 (11.2)	39 (11.2)	0.982	12 (14.6)	7 (8.0)	0.174
<b>CNS medicines</b>						
<b>Antidepressants</b>						
SSRI	10 (5.9)	13 (3.7)		8 (9.8)	2 (2.3)	
SNRI	18 (10.7)	38 (11.0)	0.525	6 (7.3)	12 (13.8)	0.060
<b>Antiparkinsonians</b>	13 (7.7)	16 (4.4)	0.149	6 (7.3)	7 (8.0)	0.859
<b>Benzodiazepines</b>	2 (1.2)	3 (0.9)	0.526	2 (2.4)	0 (0.0)	0.234
<b>Antipsychotics</b>	6 (3.6)	15 (4.3)	0.686	3 (3.7)	3 (3.4)	0.941
<b>Cardiovascular drugs</b>						
α-blockers	8 (95.3)	15 (4.3)	0.821	3 (3.7)	5 (5.7)	0.523
β-blockers	37 (21.9)	83 (23.8)	0.633	18 (22.0)	19 (21.8)	0.986
ACE-inhibitors	35 (20.7)	72 (20.6)	0.983	25 (30.5)	10 (11.5)	<b>0.002</b>
ARB	43 (25.4)	109 (31.2)	0.175	15 (18.3)	28 (32.2)	<b>0.038</b>
Calcium channel blockers	34 (20.1)	79 (22.6)	0.515	14 (17.1)	20 (23.0)	0.338
Diuretics	62 (36.7)	149 (42.7)	0.192	29 (35.4)	33 (37.9)	0.729
ASA	48 (28.4)	91 (26.1)	0.575	29 (35.4)	19 (21.8)	<b>0.061</b>
<b>Drugs other than fall risk-increasing drugs</b>						
H2RA	0 (0.0)	2 (0.6)	0.324	-	-	-
PPI	45 (26.6)	97 (27.8)	0.780	26 (31.7)	19 (21.8)	0.147
Dyslipidemic drugs	16 (9.5)	43 (12.3)	0.338	8 (9.8)	8 (9.8)	0.901
Steroids	2 (1.2)	15 (4.3)	<b>0.047</b>	4 (2.4)	0 (0.0)	0.234
Pregabalin	8 (4.7)	16 (4.6)	0.940	7 (8.5)	1 (1.1)	<b>0.024</b>
Gabapentin	7 (4.1)	17 (4.9)	0.711	5 (6.1)	2 (2.3)	0.198
Piracetam	12 (7.1)	13 (3.7)	0.093	9 (11.0)	3 (3.4)	0.074

Descriptive statistics is n (%). Adjusted p-values are calculated using Benjamini-Hochberg procedure and significant adjusted p-values are shown in bold. ACE: Angiotension converting enzyme, 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, PPI: Proton pump inhibitor, SSRI: Selective serotonin reuptake inhibitor, SNRI: Selective noradrenalin reuptake inhibitor

## Discussion

To our knowledge, this is the first study to evaluate the associations between falls, recurrent falls, FRID, polypharmacy, and PIM use in community-dwelling older adults. Studies investigating the association between recurrent falls and polypharmacy are limited. In the present study, 55.6% of older adults had polypharmacy and 29.1% of participants had taken at least one PIM. Thirty-two percent of older adults had fallen at least once in the previous year, and approximately half reported recurrent falls. The most important result was that having low HGS increased the risk of falling, and older age and using ACE-I increased the risk of recurrent falls.

The fall rate in this study (32%) was lower than that in several other studies in older adults, which reported fall rates of 13.1-41.8% and recurrent fall rates of 13.1-86.9% (5,21). These

studies included either unhealthy populations (e.g., people with chronic stroke) or different populations (e.g., home care patients). However, polypharmacy was not correlated with falling or recurrent falling.

Consistent with the literature, this research found that the polypharmacy prevalence was 55.6 (2,4,6,21). Different types of drugs have been reported as the most commonly used in previous studies (6,21). In this study, the most commonly used drugs were diuretics, ARBs, biguanides, PPIs, and ASA. Differences in preferred drugs between populations and the lack of standardization in drug selection worldwide may explain this.

Studies have shown that polypharmacy is an independent risk factor for falls. Drugs are significant risk factors for falls, and discontinuing drugs that increase the risk of falling is an

**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)	<b>0.032</b>	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)	<b>0.036</b>	1.43 (0.95-2.16)	0.088	1.69 (1.11-2.58)	<b>0.015</b>

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. ACE: Angiotension converting enzyme, PIM: Potentially inappropriate medication, ARB: Angiotension receptor blocker, ADL: Activities of daily living, IADL: Instrumental activities of daily living, FRAIL: Fatigue, resistance, ambulation, illnesses, and weight loss, OR: Odds ratio, CI: Confidence interval

**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)	<b>0.031</b>
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)	<b>0.003</b>	3.38 (1.49-7.69)	<b>0.004</b>	4.04 (1.70-9.60)	<b>0.002</b>
ARB	0.47 (0.23-0.97)	<b>0.040</b>	0.44 (0.21-0.94)	<b>0.034</b>	-	-
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	-	-

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. ACE: Angiotension converting enzyme, PIM: Potentially inappropriate medication, ARB: Angiotension receptor blocker, ADL: Activities of daily living, IADL: Instrumental activities of daily living, FRAIL: Fatigue, resistance, ambulation, illnesses, and weight loss, OR: Odds ratio, CI: Confidence interval

effective intervention to prevent falls (6,14,22). In 13 of the 19 meta-analysed studies, polypharmacy was not associated with falling (3). As shown in other meta-analyses (23), polypharmacy did not appear to be a risk factor for falls in our study. Although the relationship between polypharmacy and falls is debated, the relationship between recurrent falls and polypharmacy has been shown in many studies. In our study, the rate of recurrent falls was higher than that reported in few other studies (48.5% vs. 12.2% and 28%) (12.2% and 28% vs. 48.5%) (5,7). This study was unable to demonstrate that polypharmacy and recurrent falls were related.

Some studies have found that PIM use leading to falls was more important in increasing the risk of falls than the number of drugs used by older adult patients (24,25). Some studies have found no association between falls and PIM use (21,25). One study found no difference in falls between patients who used PIM, which increases the risk of falls, and those who did not (25). Eleven types of drugs (ibuprofen, gabapentin, sertraline, zolpidem) were identified as PIM in a study of 99 participants. However, no association was reported between PIM and falls or recurrent falls. No association was observed between recurrent falls and polypharmacy (21). Atak et al. (4) reported that 28.8%

of participants used PIM, which increased the risk of falling according to the Beers criteria. The risks associated with PIM were associated with the number of drugs used and the number of comorbidities, but no analysis of FRIDs was performed in this study (4). In the present study, only 29.1% of patients were found to have a PIM, despite the high rate of polypharmacy. Between the presence of PIM and the types of drugs according to the Beers criteria and falls and recurrent falls, no significant correlation was found.

Drug classes that have been associated with an increased risk of falls include the following: antihypertensive agents, sedatives and hypnotics, neuroleptics and antipsychotics, antidepressants, benzodiazepine, and NSAIDs. In the studies conducted, a direct relationship between some drug groups and falls was observed. A two-way relationship was found between FRID and polypharmacy in one study (22). Although the prevalence of FRIDs was higher in patients with polypharmacy, polypharmacy was also more common in patients with FRIDs (22). Using FRIDs increases the risk of falls (26).

When we looked at the specific drug groups, NSAIDs, benzodiazepines, antidepressants, hypnotics, opioids, and antihypertensive drugs were associated with falls in some studies (3,27). However, nine of 13 studies showed no association between NSAID use and falls (28). In a meta-analysis, opioid and antiepileptic usage were significantly associated with an increased risk of falling. However, NSAIDs, PPIs, anti-dementia drugs, antiparkinsonian drugs, and analgesics were not associated with falling (14). Lawson et al. (21) reported that no significant relationship was observed between 23 drug types and falls.

Antipsychotic, antidepressant, analgesic, antiparkinsonian, nasal, and ophthalmic drugs have been associated with recurrent falls (8). Formiga et al. (9) found that people with recurrent falls were more likely to have polypharmacy and to use neuroleptic drugs. One study showed that the use of psychoactive drugs, defined as PIM according to the Beers criteria, increased the risk of falling by up to 20% (29). Anderson and Lane (7) found an association between the use of antidepressants and recurrent falls among drugs including antipsychotics, anti-anxiety agents, antidepressants, and diuretics. A study of community-dwelling older adults showed an association between recurrent falls and selective serotonin reuptake inhibitor use, moderate dose, and short duration (30). A meta-analysis also found that the use of psychotropic drugs increased the risk of falling in some studies, and not others (3). To our surprise, we did not find an association between the use of benzodiazepines, antipsychotics, antidepressants, and NSAIDs and recurrent falls. The reason for this may be the restriction on the use of hypnotic drugs and on the prescribing of these drugs imposed on individual doctors in Turkey by the Ministry of Health. It may also be that

participants were unaware that they could take NSAIDs without a prescription; non-prescription drugs are not part of the medulla system; therefore, these drugs were not included. We found that only ACE-I use was associated with an increased risk of recurrent falls. Antihypertensive drugs cause falls through several mechanisms. They increase the risk of falls due to sudden falls in blood pressure, orthostatic hypotension, and electrolyte disturbances (31).

Our study showed a strong relationship between low HGS and recurrent falls, which is a sarcopenia criteria affecting muscle strength in falling. In line with other studies (26,32), we showed in this study that older age was associated with an increase in recurrent falls. Older people are known to be more prone to falls, recurrent falls, and fall injuries (9). To date, many studies have shown an association between falling and walking speed (6,32). The relationship between muscle strength and falling has only been investigated in a few studies. In some of these trials, individuals who fell repeatedly had low HGS levels, as in our study (32). It is a well-known fact that sarcopenia increases the risk of falling and that people with a low HGS are likely to be sarcopenic (18).

### Study Limitations

In our study, there were some limitations. A limitation of this study was the lack of an investigation of drug interactions. Although some drugs may not increase the risk of a fall on their own, they may significantly increase the risk of a fall because of their cumulative effects when used together with drugs from another group. It is unfortunate that the study did not include the use of over-the-counter medicines, nasal medicines, ophthalmic medicines, and herbal medicines. By including only outpatients, the study population may be healthier than the community older adult population. In addition, the study was designed as a cross-sectional study, which may have limited its ability to show a causal relationship between the risk factors for fall and recurrent falls.

### Conclusion

The results of this study did not confirm the findings of previous studies linking certain classes of drugs to the risk of falling in older adults. Drugs are a known risk factor for falls. However, it is important to consider the reason for taking a drug before deciding to stop or withdraw a drug for fall prevention because the condition that the drug is being used to treat may itself be a risk factor for falls. Therefore, each drug should be considered individually, and the benefits and risks of stopping or continuing the drug should be carefully weighed. This study may not have been able to prove the association between certain groups of drugs and falls and recurrent falls, as other studies have done. However, low HGS, a component of sarcopenia, is a risk factor

for falls. This once again highlights the importance of screening and detecting sarcopenia in the geriatric population.

### Ethics

**Ethics Committee Approval:** This study was approved by the Erciyes University Ethics Committee (decision number: 2019/136, date: 20.02.2019).

**Informed Consent:** Informed consent was obtained from all participants.

### Authorship Contributions

Surgical and Medical Practices: S.A., Concept: S.A., N.Ş.D., T.S., F.F.Ö., B.M.G., G.E.Z., Design: S.A., N.Ş.D., Data Collection or Processing: S.A., N.Ş.D., T.S., F.F.Ö., B.M.G., G.E.Z., Analysis or Interpretation: S.A., N.Ş.D., G.E.Z., Literature Search: S.A., N.Ş.D., T.S., F.F.Ö., B.M.G., Writing: S.A., N.Ş.D., G.E.Z.

**Conflict of Interest:** No conflict of interest was declared by the authors.

**Financial Disclosure:** The authors declared that this study received no financial support.

### References

- Masnoon N, Shakib S, Kalisch-Ellett L, Caughey GE. What is polypharmacy? A systematic review of definitions. *BMC Geriatr* 2017;17:230.
- 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.
- Park H, Satoh H, Miki A, Urushihara H, Sawada Y. Medications associated with falls in older people: systematic review of publications from a recent 5-year period. *Eur J Clin Pharmacol* 2015;71:1429-1440.
- Atak BM, Aktas G, Duman TT, Kurtkulagi O, Bilgin S, Kahveci G, Demirkol ME. Inappropriate medication use in older adults according to Beers Criteria in a Tertiary Referral Hospital, in Bolu, Turkey. *Russian Open Medical Journal* 2021;10:211.
- Alenazi AM, Alshehri MM, Alothman S, Rucker J, Dunning K, D'Silva LJ, Kluding PM. Functional Reach, Depression Scores, and Number of Medications Are Associated With Number of Falls in People With Chronic Stroke. *PM R* 2018;10:806-816.
- Dhalwani NN, Fahami R, Sathanapally H, Seidu S, Davies MJ, Khunti K. Association between polypharmacy and falls in older adults: a longitudinal study from England. *BMJ Open* 2017;7:e016358-e.
- Anderson LK, Lane K. Characteristics of falls and recurrent falls in residents of an aging in place community: A case-control study. *Appl Nurs Res* 2020;51:151190.
- Askari M, Eslami S, Scheffer AC, Medlock S, de Rooij SE, van der Velde N, Abu-Hanna A. Different risk-increasing drugs in recurrent versus single fallers: are recurrent fallers a distinct population? *Drugs Aging* 2013;30:845-851.
- Formiga F, Navarro M, Duaso E, Chivite D, Ruiz D, Perez-Castejon JM, Lopez-Soto A, Pujol R. Factors associated with hip fracture-related falls among patients with a history of recurrent falling. *Bone* 2008;43:941-944.
- Lee JS, Kwok T, Leung PC, Woo J. Medical illnesses are more important than medications as risk factors of falls in older community dwellers? A cross-sectional study. *Age Ageing* 2006;35:246-251.
- Seppala LJ, Petrovic M, Ryg J, Bahat G, Topinkova E, Szczerbińska K, van der Cammen TJM, Hartikainen S, Ilhan B, Landi F, Morrissey Y, Mair A, Gutiérrez-Valencia M, Emmelot-Vonk MH, Mora MÁC, Denkinger M, Crome P, Jackson SHD, Correa-Pérez A, Knol W, Soulis G, Gudmundsson A, Ziere G, Wehling M, O'Mahony D, Cherubini A, van der Velde N. STOPPFall (Screening Tool of Older Persons Prescriptions in older adults with high fall risk): a Delphi study by the EuGMS Task and Finish Group on Fall-Risk-Increasing Drugs. *Age Ageing* 2021;50:1189-1199.
- Bahat G, Ilhan B, Erdogan T, Oren MM, Karan MA, Burkhardt H, Denkinger M, Garfinkel D, Cruz-Jentoft AJ, Morrissey Y, Onder G, Pazan F, Tommelein E, Topinkova E, van der Velde N, Petrovic M. International Validation of the Turkish Inappropriate Medication Use in the Elderly (TIME) Criteria Set: A Delphi Panel Study. *Drugs Aging* 2021;38:513-521.
- Bahat G, Ilhan B, Erdogan T, Halil M, Savas S, Ulger Z, Akyuz F, Bilge AK, Cakir S, Demirkan K, Erelel M, Guler K, Hanagasi H, Izgi B, Kadioglu A, Karan A, Kulaksizoglu IB, Mert A, Ozturk S, Satman I, Sever MS, Tukek T, Uresin Y, Yalcin O, Yesilot N, Oren MM, Karan MA. Turkish inappropriate medication use in the elderly (TIME) criteria to improve prescribing in older adults: TIME-to-STOP/TIME-to-START. *Eur Geriatr Med* 2020;11:491-498.
- Seppala LJ, van de Glind EMM, Daams JG, Ploegmakers KJ, de Vries M, Wermelink AMAT, van der Velde N; EUGMS Task and Finish Group on Fall-Risk-Increasing Drugs. Fall-Risk-Increasing Drugs: A Systematic Review and Meta-analysis. III. Others. *J Am Med Dir Assoc* 2018;19:372.e1-e8.
- Katz S, Downs TD, Cash HR, Grotz RC. Progress in development of the index of ADL. *The Gerontologist* 1970;10:20-30.
- Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. *The Gerontologist* 1969;9:179-186.
- Morley JE, Malmstrom TK, Miller DK. A simple frailty questionnaire (FRAIL) predicts outcomes in middle aged African Americans. *J Nutr Health Aging* 2012;16:601-608.
- Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, Cooper C, Landi F, Rolland Y, Sayer AA, Schneider SM, Sieber CC, Topinkova E, Vandewoude M, Visser M, Zamboni M; Writing Group for the European Working Group on Sarcopenia in Older People 2 (EWGSOP2), and the Extended Group for EWGSOP2. Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing* 2019;48:16-31.
- Tinetti ME. Performance-oriented assessment of mobility problems in elderly patients. *J Am Geriatr Soc* 1986;34:119-126.
- Consensus statement on the definition of orthostatic hypotension, pure autonomic failure, and multiple system atrophy. The Consensus Committee of the American Autonomic Society and the American Academy of Neurology. *Neurology* 1996;46:1470.
- Lawson K, Vinluan CM, Oganessian A, Gonzalez EC, Loya A, Strate JJ. A retrospective analysis of prescription medications as it correlates to falls for older adults. *Pharm Pract (Granada)* 2018;16:1283.
- Correa-Pérez A, Delgado-Silveira E, Martín-Aragón S, Rojo-Sanchis AM, Cruz-Jentoft AJ. Fall-risk increasing drugs and prevalence of polypharmacy in older patients discharged from an Orthogeriatric Unit after a hip fracture. *Aging Clin Exp Res* 2019;31:969-975.
- Richardson K, Bennett K, Kenny RA. Polypharmacy including falls risk-increasing medications and subsequent falls in community-dwelling middle-aged and older adults. *Age Ageing* 2015;44:90-96.
- Beer C, Hyde Z, Almeida OP, Norman P, Hankey GJ, Yeap BB, Flicker L. Quality use of medicines and health outcomes among a cohort of community dwelling older men: an observational study. *Br J Clin Pharmacol* 2011;71:592-599.
- Bor A, Matuz M, Csatornai M, Szalai G, Bálint A, Benkő R, Soós G, Doró P. Medication use and risk of falls among nursing home residents: a retrospective cohort study. *Int J Clin Pharm* 2017;39:408-415.

26. Musich S, Wang SS, Ruiz J, Hawkins K, Wicker E. Falls-Related Drug Use and Risk of Falls Among Older Adults: A Study in a US Medicare Population. *Drugs Aging* 2017;34:555-565.
27. Rynnänen OP, Kivelä SL, Honkanen R, Laippala P, Saano V. Medications and chronic diseases as risk factors for falling injuries in the elderly. *Scand J Soc Med* 1993;21:264-271.
28. Hegeman J, van den Bemt B, Duysens J, van Limbeek J. NSAIDs and the risk of accidental falls in the elderly: a systematic review. *Drug Saf* 2009;32:489-498.
29. Agashivala N, Wu WK. Agashivala N, Wu WK. Effects of potentially inappropriate psychoactive medications on falls in US nursing home residents: analysis of the 2004 National Nursing Home Survey database. *Drugs Aging* 2009;26:853-860.
30. Marcum ZA, Perera S, Thorpe JM, Switzer GE, Castle NG, Strotmeyer ES, Simonsick EM, Ayonayon HN, Phillips CL, Rubin S, Zucker-Levin AR, Bauer DC, Shorr RI, Kang Y, Gray SL, Hanlon JT; Health ABC Study. Antidepressant Use and Recurrent Falls in Community-Dwelling Older Adults: Findings From the Health ABC Study. *Ann Pharmacother* 2016;50:525-533.
31. 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.
32. Zia A, Kamaruzzaman SB, Tan MP. The consumption of two or more fall risk-increasing drugs rather than polypharmacy is associated with falls. *Geriatr Gerontol Int* 2017;17:463-470.