

Original Article

The prevalence of polypharmacy and fall-risk-increasing drugs after hospital discharge for hip fracture: A retrospective study

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Abstract

Objectives: To evaluate the incidence of polypharmacy and the use of fall-risk-increasing drugs (FRIDs) in patients >65 years of age. **Methods:** 478 patients >65 years old, discharged from an Orthopaedic Department because of hip-fracture surgery, capable of walking before surgery, were included. The baseline characteristics of the patients and the total numbers of drugs and FRIDs were recorded from the electronic hospital registration system. Polypharmacy was defined as the average daily use of five or more drugs. The gender differences in drug prescriptions were calculated. **Results:** All the patients took medications except for eight (1.7%); 46% of the patients were taking <5 medications, while 386 (80.8%) were taking ≤ 3 FRIDs. The female patients were taking more drugs (5 ± 2.7) and FRIDs (2.4 ± 1.3) than the male ones (4.5 ± 3 and 1.9 ± 1.3) (both $p < 0.01$). The average numbers of drugs and FRIDs prescribed at discharge were 4.9 ± 2.8 and 2.3 ± 1.3 , respectively. The Barthel Index was higher for patients taking <5 drugs, while the length of hospital stay was greater for patients taking ≥ 5 medications. Increased age was associated with taking ≥ 5 medications ($p < 0.05$). **Conclusions:** Polypharmacy and FRID use are prevalent among patients over 65 years old who have been hospitalized and surgically treated because of hip fractures.

Keywords: Elderly, Fall-risk-increasing drugs, Falls, Polypharmacy

Introduction

Increases in average human lifespans are observable in most industrialized countries, which may have orthopedic consequences because there is a greater incidence of falls and injuries related to falls in older adults^{1,2}. Fractures of the hip are one of the most serious injuries in elderly patients. Pain, disability, an increased need for support in basic daily activities and increased morbidity and mortality are the most frequent effects of hip fractures³. Increased age, female gender, comorbidities, functional decline, musculoskeletal problems, a history of previous falls and polypharmacy (usually defined as the concurrent use of more than four or five drugs) are potential risk factors for falls⁴⁻⁶.

Recently, an association of polypharmacy and FRIDs with a potentially increased risk of falls in the elderly has been documented^{7,8}. Polypharmacy, as an independent risk factor for falls in older people, can be more clearly related

to the use of antidepressants or benzodiazepines⁹. Drugs that were listed by Van der Velde in 2007 are related to an increased risk of falls and are called FRIDs¹⁰. The list was based on several previous studies showing that patients who were hospitalized due to falls were taking more FRIDs than those who did not experience falls^{11,12}. Additionally,

The authors have no conflict of interest.

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Edited by: George Lyritis

Accepted 28 September 2021

hip-fracture patients may require multiple drugs and a multidisciplinary approach.

The primary purpose of the present study was to estimate the incidence of polypharmacy and FRID use (by pharmacological group and total number) at hospital discharge in patients >65 years of age who were hospitalized and surgically treated because of a hip fracture in an Orthopaedic Unit. The secondary purpose was to explore gender differences in the total numbers of medications and FRIDs prescribed at discharge, as well as differences between patients grouped by FRIDs (>3) and polypharmacy (≥ 5).

Methods

Study design and population

This observational retrospective study describes the baseline characteristics of a study population using health data that were collected in a systematic fashion. The data were collected in order to quantify the correlation between polypharmacy, FRID use and traumatic falls after discharge in patients >65 years old who were hospitalized and surgically treated because of hip fractures. This hospital-based study was conducted in the Orthopaedic Department of a community hospital in Greece and included a 2-year follow-up period starting from hospital discharge (January 2018) to the end of the follow-up period (2 years later). The exclusion criteria were: i) patients who were not permitted by the surgeon to load the broken leg for operative treatment, ii) patients without medication information at hospital discharge and iii) patients receiving palliative care at the end of their lives.

Variables of the Study

The following data were collected: i) anthropometric characteristics (age and gender), ii) clinical and functional variables (the type of fracture and length of hospital stay), activities of daily living (Barthel index), iii) living status (widowed, with spouse, or in a nursing home), iv) the number of drugs being taken at hospital discharge (polypharmacy ≥ 5) and v) the number and classification of FRIDs. According to the Scottish Polypharmacy Guide¹³, FRIDs were classified into two groups: those considered to be correlated with low and moderate risks of falls (antihypertensives, beta-blocking agents, calcium channel blockers (CCB), diuretics, opioids, angiotensin-converting-enzyme inhibitors) and those considered to be correlated with a high risk of falls (antidepressants, benzodiazepines, and antipsychotic and dopaminergic agents). In our study, FRIDs were defined in accordance with previous published work^{5,10,12} on fall-risk-related medications: i) psychotropic medications (antidepressants, levodopa, benzodiazepines and opioids) and ii) cardiovascular medications (CCB, angiotensin-converting-enzyme (ACE)-inhibitors, beta-adrenoceptor blockers and diuretics).

The definitions of polypharmacy widely vary with regard to the actual number of medications. Although there is no

uniform definition, we defined it, in accordance with the literature, as the use of five or more medications^{3,9,13,14}. Likewise, two categories were established based on the number of regular FRIDs: ≤ 3 and more than three. Previous studies have shown that, in older cancer patients and patients with hip fractures, there is a positive association between falls and the use of three or more FRIDs^{13,15}. The total number of drugs prescribed at discharge included not only medications for comorbidities and chronic diseases but also drugs usually prescribed for post-operative care (such as opioids, supplements and heparins).

Data collection

The baseline characteristics of the study population were recorded from the electronic registration system of the hospital. The total numbers of drugs and FRIDs prescribed at discharge were obtained from the hospital discharge letters.

Statistical analysis

SPSS (Version 24.0) was used to analyze the collected data. Continuous variables (age, the Barthel index, the number of medications and the number of FRIDs) are expressed as the means and standard deviations (SD), while categorical variables (gender, the type of fracture, the living status and the type of drugs) are expressed as counts and percentages. The Kolmogorov–Smirnov test was utilized for normality analysis. The Mann–Whitney U test was used to compare the quantity-continuous variables for our independent samples that were not normally distributed, divided into two subpopulations. Pearson's chi-square (cross-tabulation) test was utilized for the comparison of the categorical variables. A multivariable analysis was conducted to determine what baseline findings for patients could contribute to the prevalence of polypharmacy or a high prevalence of FRID use. A receiver operator characteristic (ROC) curve was used to determine a threshold for the number of medications or FRIDs, to help to stratify the risk of falls among the subgroups (gender, the type of fracture, the length of hospital stay, the living status and the Barthel index). The level of significance was set at $p < 0.05$.

Results

Baseline findings

A total of 534 patients, who were discharged between January 2018 and December 2019, were screened, and 56 patients were excluded. The most common reasons for exclusion were a disability in walking before the hip fracture (21 patients), not being allowed by the surgeon to load the broken leg at hospital discharge (25 patients) and palliative care (10 patients). A total of 478 patients met all the eligibility criteria. The baseline characteristics are shown in Table 1.

The comparative baseline findings between the male ($n=125$) and female patients ($n=353$) showed no significant

Variable	All (n = 478)	Male (n = 125)	Female (n = 353)	p value
Age	81.6 ± 9.7	80.2 ± 11.9	81.6 ± 8.7	0.88
Age group, years, n (%)				0.21
< 70	59	20 (33.9)	39 (66.1)	
70 – 79	108	23 (21.3)	85 (78.7)	
≥ 80	311	82 (26.4)	229 (73.6)	
Type of fracture, n (%)				0.82
Subcapital	211 (44.1)	55 (44.0)	156 (44.2)	
Peritrochanteric	231 (48.3)	59 (47.2)	172 (48.7)	
Subtrochanteric	36 (7.6)	11 (8.8)	25 (7.1)	
Length of hospital stay, days	9.9 ± 5.4	9.3 ± 4.2	10.2 ± 5.7	0.29
Living status, n (%)				0.98
Home (widowed)	109 (22.8)	28 (22.4)	81 (22.9)	
Home (spouse)	318 (66.5)	84 (67.2)	234 (66.3)	
Nursing home	51 (10.7)	13 (10.4)	38 (10.8)	
Barthel index	80.0 ± 5.3	81.3 ± 5.9	79.6 ± 5.0	0.01
Number of FRIDs, n	2.3 ± 1.3	1.9 ± 1.3	2.4 ± 1.3	< 0.01
FRIDs				< 0.05
0	20 (4.2)	7 (5.6)	13 (3.7)	
≤ 3	366 (76.6)	103 (82.4)	263 (74.5)	
> 3	92 (19.2)	15 (12.0)	77 (21.8)	
Number of medications, n	4.9 ± 2.8	4.5 ± 3.0	5.0 ± 2.7	0.06
Medications				0.01
0	8 (1.7)	6 (4.8)	2 (0.6)	
< 5	220 (46.0)	61 (48.8)	159 (45.0)	
≥ 5	250 (52.3)	58 (46.4)	192 (54.4)	
Drugs, n (%)				
b-Blockers	206 (43.1)	45 (36.0)	161 (45.6)	0.06
CCA	180 (37.7)	41 (32.8)	139 (39.4)	0.19
Diuretics	179 (37.5)	39 (31.2)	140 (39.7)	0.09
Antidepressants	174 (36.4)	34 (27.2)	140 (39.7)	< 0.05
ACE inhibitors	160 (33.5)	41 (32.8)	119 (33.7)	0.85
Benzodiazepines	141 (29.5)	24 (19.2)	117 (33.1)	< 0.05
Statins	128 (26.8)	30 (24.0)	98 (27.8)	0.41
Supplements	100 (20.9)	21 (16.8)	79 (22.4)	0.18
Oral antidiabetics	93 (19.5)	22 (17.6)	71 (20.1)	0.54
Gastroprotectants	67 (14.0)	19 (15.2)	48 (13.6)	0.65
Thyroid hormones	63 (13.2)	10 (8.0)	53 (15.0)	< 0.05
Levodopa	31 (6.5)	6 (4.8)	25 (7.1)	0.37
Corticosteroids	28 (5.9)	4 (3.2)	24 (6.8)	0.14
Insulin	24 (5.0)	10 (8.0)	14 (4.0)	0.07
Opioids	7 (1.5)	1 (0.8)	6 (1.7)	0.47

n = number; FRIDs = fall-risk increasing drugs; b-Blockers = beta-Blockers; CCA = calcium channel antagonists; ACE inhibitors = Angiotensin-converting enzyme inhibitors

Table 1. Characteristics of the study population.

Variable	FRIDs, ≤ 3 (n = 386)	FRIDs, > 3 (n = 92)	p value	Medications, < 5 (n = 220)	Medications, ≥ 5 (n = 250)	p value
Age, years	80.9 ± 10.2	82.7 ± 6.9	0.50	80.5 ± 10.9	82.4 ± 7.8	0.26
Age group, years, n (%)			0.09			<0.05
<70	46 (11.9)	4 (4.4)		30 (13.6)	15 (6.0)	
70–79	88 (22.8)	21 (22.8)		47 (21.4)	60 (24.0)	
≥80	252 (65.3)	67 (72.8)		143 (65.0)	175 (70.0)	
Gender, n (%)			<0.05			0.26
Male	110 (28.5)	15 (16.3)		61 (27.7)	58 (23.2)	
Female	276 (71.5)	77 (83.7)		159 (72.3)	192 (76.8)	
Type of fracture, n (%)			0.54			0.91
Subcapital	174 (45.1)	37 (40.2)		98 (44.5)	107 (42.8)	
Peritrochanteric	185 (47.9)	46 (50.0)		106 (48.2)	123 (49.2)	
Subtrochanteric	27 (7.0)	9 (9.8)		16 (7.3)	20 (8.0)	
Length of hospital stay, days	9.8 ± 5.6	10.8 ± 4.1	<0.01	9.3 ± 5.7	10.6 ± 5.0	<0.01
Living status, n (%)			0.19			0.51
Home (widowed)	84 (21.8)	25 (27.2)		46 (20.9)	63 (25.2)	
Home (spouse)	264 (68.4)	54 (58.7)		151 (68.6)	160 (64.0)	
Nursing home	38 (9.8)	13 (14.1)		23 (10.5)	27 (10.8)	
Barthel index	81.2 ± 4.9	75.3 ± 4.4	<0.01	82.6 ± 4.2	77.4 ± 4.7	<0.01

n = number; FRIDs = fall-risk increasing drugs.

Table 2. Baseline differences between patients grouped by FRIDs and grouped by polypharmacy.

differences except for the Barthel index ($p=0.01$), number of drugs ($p=0.01$) and FRIDs ($p<0.01$). The Barthel index was higher (indicating a greater ability to function independently following hospital discharge) in male patients than female ($p=0.01$). The numbers of drugs and FRIDs at hospital discharge were higher in female patients (5.02 and 2.4, respectively) than males (4.5 and 1.95, respectively) ($p=0.01$ and $p<0.01$, respectively). Additionally, the use of antidepressants, benzodiazepines and thyroid hormones at hospital discharge was higher in female patients (39.7%, 33.1% and 15%, respectively) than males (27.2%, 19.2% and 8%, respectively) ($p<0.05$).

Frequency of polypharmacy and use of FRIDs

The average number of drugs prescribed upon hospital discharge was 4.9 ± 2.8 . All the patients except eight (1.7%) were taking at least one medication; 46% of them were prescribed fewer than five medications and 52.3% were prescribed five or more medications at hospital discharge (polypharmacy). A total of 458 of the patients (95.8%) were taking at least one FRID. The average number of FRIDs per patient at hospital discharge was 2.28 ± 1.3 . A total of 92 patients (19.2%) were

prescribed more than three FRIDs.

The most prevalent FRIDs were beta-blockers; 43.1% of the patients were prescribed at least one of these drugs. These were followed by calcium channel blockers (37.7%), diuretics (37.5%), antidepressants (36.4%), ACE inhibitors (33.5%), benzodiazepines (29.5%), supplements (20.9%), dopaminergic agents (6.5%) and opioids (1.5%) (Table 1). According to the Scottish risk stratification, 13.26% of the patients were using low-to-moderate-risk FRIDs, 14.5% were using high-risk FRIDs and 57.2% were using both groups of FRIDs at hospital discharge.

No significant differences were found upon comparing the baseline characteristics between patients on three or fewer FRIDs and those on more than three FRIDs, except for gender, the length of hospital stay and the Barthel index ($p<0.05$, $p<0.01$ and $p<0.01$, respectively). Females were more likely to be taking more than three FRIDs than males. The hospital stays were longer for patients taking more than three FRIDs, and the Barthel index was higher for patients with three or fewer FRIDs. Increased age, the type of fracture and the living status were not correlated with the number of FRIDs (Table 2).

The comparison of the baseline characteristics between

patients on fewer than five medications and those on five or more medications showed that there were no significant differences between the two groups except for the Barthel index and length of hospital stay ($p < 0.01$). Additionally, the Barthel index was higher for patients on fewer than five medications, while the length of hospital stay was greater for patients on five or more medications. Increased age was associated with being on five or more medications ($p < 0.05$) (Table 2).

Discussion

The main finding of the present study was that polypharmacy and FRID use were common in patients aged over 65 years old who were discharged after being surgically treated due to hip fractures, with a mean of 4.9 ± 2.8 medications and a median of 2.3 ± 1.3 FRIDs.

A recent systematic review was designed to answer the question of the association between polypharmacy and either falls or fall-related outcomes (e.g., dizziness and hip fractures)¹⁴. Although the studies in this review varied widely in their approaches, their results were mixed, with some of them demonstrating an association between polypharmacy and fractures¹⁴⁻¹⁷, while other studies found that the fall risk and hip fractures were associated with polypharmacy only when at least one established fall-risk-increasing drug was part of the daily regimen^{6,14}. The increased risk of falls could be explained by the mechanism of the drug's action, e.g., diuretics can cause dizziness as a consequence of orthostatic hypotension⁶. Benzodiazepine derivatives significantly affect the central nervous system and can result in serious consequences, including a risk of falls and higher rates of fractures^{6,10,11}. Our study found that 37.5% and 29.5% of the patients who were hospitalized and surgically treated because of hip fractures were taking diuretics and benzodiazepines, respectively.

Recent studies have examined polypharmacy and the number of FRIDs at hospital discharge in the elderly^{3,5,13}. One study, which included patients over 80 years old hospitalized for hip-fracture repair, found that the average numbers of drugs and FRIDs prescribed at hospital discharge were 11.6 ± 3.0 and 2.9 ± 1.6 , respectively¹³. In addition, in a single-center study, which analyzed the data for 272 consecutive hip-fracture patients who underwent hip replacement, they observed an increase in the number of medications from 6.2 ± 3.9 (on admission) to 7.8 ± 3.6 (at discharge), and they also showed that the number of medications upon discharge was predictive of readmission¹⁸. In a Swedish study, 6 months after hospital discharge, the incidence of polypharmacy (≥ 5 drugs) and extreme polypharmacy (≥ 10 drugs) was 88.1% and 53.7%, respectively, while the FRID use frequency was 97.7%¹⁹. On the contrary, our study found a mean number of 4.9 ± 2.8 medications upon discharge, and this may indicate a possible lower risk for readmission, as well as possibly being associated with better functional outcomes in the post-operative rehabilitation period.

Data regarding the calculated numbers of FRIDs in patients admitted due to hip fractures show different results. In a study by Ekstam and Elmstahl³, they determined the frequency of exposure to four or more FRIDs (25.4%) in patients aged 60 years or older who were diagnosed with hip fractures. Another study, which was conducted in a Geriatric Department and included patients over 65 years old who underwent surgery for a hip fracture, found that the mean number of FRIDs per patient at hospital discharge was 2.9 ± 2.1 and 3.1 ± 2.2 in the intervention (medication reviews) and control group, respectively⁵. Additionally, they did not find significant differences between the groups with regard to FRIDs at admission and 12 months after discharge⁵. A Swedish population-based cohort study, which included 2043 patients with hip fractures aged 60 years and older, showed that, before hip fracture, two-thirds of the participants were prescribed FRIDs and that the number increased significantly to 97.7% at 6 months afterward¹⁹. In line with these results, an observational and prospective study, which was performed in a tertiary-level hospital in Spain, indicated a 92.5% prevalence of FRID use one month after hospital discharge due to bone fractures (hip, ankle or pelvis)²⁰. In accordance with these findings, our study showed that 458 patients (95.8%) were taking at least one FRID at discharge.

Other studies have measured the prevalence of FRID use by pharmacological groups. In a study with patients older than 80 years who were discharged after hip fractures, the most prevalent FRIDs were agents acting on the renin-angiotensin system (43.9%) and anxiolytics (39.9%)¹³. In one study with patients aged 65 years and older, who were surgically operated due to hip fractures, the most frequent FRIDs were opioids (88%) and anxiolytics (50%)⁵. A recent study from Spain showed a 45.6% incidence of antidepressant use, 44.8% incidence of the use of agents acting on the renin-angiotensin system, and 42.9% incidence of diuretic use²⁰. In our study, we found that the most common FRIDs were beta-adrenergic blocking agents (43.1%), calcium channel antagonists (37.7%), diuretics (37.5%) and angiotensin-converting-enzyme inhibitors (33.5%). These differences may be explained by the fact that either the baseline findings of the study population or the standard clinical practices were different.

In our study, gender, the lengths of hospital stays and the Barthel Index showed significant differences according to the incidence of being on three FRIDs. The Barthel index was higher in patients taking three or fewer FRIDs and fewer than five drugs than in those who used more medications. Additionally, we found an overall female predominance for taking many FRIDs. This female predominance might reflect the higher burden of comorbidities in the female population, which could also adversely affect the rehabilitation outcomes. In addition, we found a higher Barthel index in the male population. A possible explanation may be the fact that, in the present study, the male population was generally

younger and, therefore, took fewer medications than the female population surgically treated for hip fractures; younger, healthier and more independent people tend to take fewer medications²¹. Polypharmacy is a very common practice in many clinical settings, such as nursing homes. Living in a nursing home was correlated with the incidence of high-risk polypharmacy¹³.

There are some limitations to our study. The collection of the data could have been affected by the quality of the recorded information in the electronic registration system of the hospital. It was not clear if medication use preceded falling. In chronic diseases, the prescription of drugs is continuous. Therefore, the majority of the medications were already in use before the falls. Most of the relevant comorbidities were not taken into account in our work. For example, we were not able to determine the influence of cognitive impairment, visual or hearing disturbances, or chronic renal failure (GFR <45 ml/min). Finally, drug interactions may have played a role in causing falls, but the methodology of our study was not appropriate for addressing that issue. Finally, the patients were discharged in a post-acute situation, and they needed short-term drugs to prevent post-operative complications: heparins to prevent thrombosis, iron supplements for anemia, laxatives to counter constipation, and analgesics for pain. The mean number of these short-term medications was not calculated in our study.

In conclusion, this retrospective study showed that polypharmacy and FRID use are prevalent among patients aged over 65 years old who are hospitalized and surgically treated because of hip fractures. Risk-reducing interventions in elderly hip-fracture patients, such as hip protectors, vitamin D with calcium supplementation, supervised exercise and appropriate exposure to sunlight²²⁻²⁴, in whom polypharmacy is inevitable for controlling underlying comorbidities are necessary. A recent systematic review found that there was a lack of robust, high-quality evidence to support or refute the deprescribing of FRIDs alone as an effective fall-prevention strategy²⁵. Although a number of studies have already assessed these interventions, prospective, randomized and controlled trials with longer follow-up are necessary to confirm a potential impact on falls in this high-risk population.

Ethics approval

The study protocol was approved by the Ethics Committee of the "G. Papageorgiou" General Hospital of Thessaloniki in Greece (341-21/4/2021).

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