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Potentially inappropriate medications and time to full functional recovery after hip fracture

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Abstract

Background—Older adults after hip fracture are at increased risk of being prescribed potentially inappropriate medications (PIM), and may be particularly vulnerable to their adverse effects.

Objective—To examine the association of PIM use with time to full functional recovery within one year of hip fracture repair.

Design—Secondary analysis of a prospective longitudinal study.

Setting—Eight St. Louis, Missouri hospitals.

Participants—Older adults (n = 477) aged 60 years or older who had surgical repair of a hip fracture free of delirium, dementia, or depression at baseline.

Measurements—Drugs at baseline were categorized using the American Geriatrics Society 2012 Beers criteria. The outcome was the Functional Recovery Scale (FRS) total score measured at four time points during a 12-month period of observation. Cox proportional hazards models

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Compliance with Ethical Standards

Conflicts of Interest
Andrea Iaboni, Kerri Rawson, and Craig Burkett have no conflicts to report.

Ethical Approval
Procedures were approved by the institutional review boards at Washington University School of Medicine and the eight participating hospitals.

examined time to 95% recovery of function ('full recovery'), adjusting for demographics, cognition, depression, medical comorbidity, pre-fracture functioning, and pain as covariates.

Results—PIM use was common following hip fracture, with 51% of participants prescribed at least one PIM and 17.4% prescribed two or more PIM. PIM use was significantly associated with longer time to achieve full recovery with a hazard ratio (HR) of 0.69 (95% CI: 0.52–0.92; p = 0.012) and this association was stronger for two or more PIM compared to one PIM (HR = 0.60; 95% CI 0.40–0.90; p = 0.014).

Conclusion—PIM use was associated with longer time to full functional recovery in older adults who underwent surgery for a hip fracture, particularly in those using two or more PIM at baseline.

1. Introduction

A hip fracture is a watershed moment for older adults with the potential for significant impact on future disability, loss of independence and risk of mortality [1, 2]. Poor short-term functional recovery is associated with a poor long-term prognosis [3]. At least one-third of patients who suffer a hip fracture do not regain pre-fracture function; those who do recover take an average of six months to do so [4]. The failure to functionally recover threatens the independence of older adults [5]. Achievement of full functional recovery after hip fracture has important implications for the quality of life of older adults [6].

The use of potentially inappropriate medication (PIM) may be a modifiable risk factor for poor recovery after hip fracture. Following hip fracture, older adults are particularly vulnerable to the adverse effects of PIM, with risks of delirium, recurrent falls, repeat hip fracture, and mortality [7–10]. They may also exhibit psychiatric symptoms and distress, and are thus at increased risk of being newly prescribed PIM post-fracture [11]. While patients with hip fracture are both a high-risk population for being prescribed PIM and more likely to suffer adverse outcomes with the use of these drugs, no study has yet examined the impact of PIM use on the achievement of functional recovery after hip fracture.

In this secondary analysis of a prospective longitudinal hip fracture study, we examined the association of PIM with time to full functional recovery after hip fracture. The study excluded patients with delirium, dementia, or major depression at baseline: all of these excluded conditions are strongly associated with poor outcomes and are also associated with the use of PIM. As a result, the study sample represents a population with a good probability of achieving recovery. We hypothesized that the use of PIM would be associated a longer time to achieve full recovery in function after hip fracture.

2. Methods

2.1 Setting and sample

Participants were older adults after hip fracture recruited from eight hospitals in St. Louis, MO between 2008–2012, with full details of recruitment and assessment as previously described [12, 13]. Procedures were approved by the institutional review boards at Washington University School of Medicine in St. Louis, MO, and at the eight participating area hospitals. Participants provided written informed consent prior to undergoing study

procedures. All procedures were in compliance with the ethics principles for human experimentation stated in the Declaration of Helsinki.

Inclusion criteria were age 60 years or older and a primary diagnosis of hip fracture with surgical repair. Exclusion criteria were non-ambulatory status prior to the fracture, cognitive impairment at the time of the fracture consistent with a diagnosis of dementia (assessed by chart review and brief bedside assessment), delirium (by observation, chart review and completion of delirium rating scale), major depressive episode at the time of fracture (based on baseline Structured Clinical Interview for Diagnosis and Statistical Manual of Medical Disorders-IV[14]), metastatic cancer, interferon treatment, severe sensory impairment, non-English speaking, and inability to consent or cooperate with study protocol. For this study, we excluded seven individuals who had missing information about medications at baseline; this resulted in 477 participants for statistical analyses.

Analyses in this study are based on variables collected at baseline (within 2–14 days after surgical hip fracture repair) and at weeks 4, 12, 26, and 52 following baseline.

2.2 Measures

Medication use at baseline was recorded from the patient's chart. PIM was classified according to the American Geriatrics Society 2012 Beers Criteria [15], which were created through literature review and expert consensus. In the current study, PIM was defined using the Beers Criteria's: i) 'disease-independent recommendations' [15] and ii) specific recommendations for older adults with a history of falls or fractures.

Functional recovery was measured with the Functional Recovery Scale score [FRS;16]. Patients were asked to rate how much help they needed with basic and instrumental activities of daily living and mobility on a scale of 0 (cannot do at all) to 4 (no help needed). The total FRS is a score out of 100 (optimal function). At the baseline visit, the patient was asked to rate their immediate pre-fracture function; post-fracture function was measured at weeks 4, 12, 26, and 52. For the purpose of this study, full recovery was defined as achieving 95% of pre-fracture function. This threshold is consistent with previous literature [17], accommodates both the risk of inflation of pre-fracture function due to a retrospective assessment, and an expected decline in function that would normally be observed over a one-year time frame in older adults [16].

Other variables that may influence functional recovery were included as covariates. Severity of depressive symptoms was measured with the Montgomery Asberg Depression Rating Scale at weeks 4, 12, 26, and 52 (MADRS). At the baseline visit, pre-fracture severity of depressive symptoms was rated retrospectively for the week prior to fracture using the MADRS. The Duke Social Support Index (DSSI) instrumental support sub-scale at baseline assessed the amount of help received from a support network with higher scores representing more support. The Cumulative Illness Rating Scale for Geriatrics (CIRS-G) measured cumulative medical burden at the time of the fracture, including conditions that arose during the hospitalization. Cognitive function was assessed at baseline by the Short Blessed Test (SBT), with higher scores indicating more cognitive impairment. Pain at all time points was measured using a numerical rating scale from 0 (no pain) to 10 (worst pain).

2.3 Data analysis

Time-to-event curves were constructed using Kaplan-Meier methods. A Cox proportional hazards model examined time to full recovery during the 12-month period of observation. As a sensitivity analysis, we repeated the survival analysis dividing the cohort by the number of PIM (0, 1, or >1) to which they were exposed. We selected a broad range of variables a priori for inclusion in the model based on variables relevant to exposure to PIM use or functional outcomes after hip fracture. The following variables were included as fixed effect covariates: age, sex, marital status, race, education, pre-fracture FRS, pre-fracture MADRS, baseline SBT score, baseline CIRS-G score, baseline pain, smoking status, drinking status, social support and total number of baseline medications (excluding PIM). Time was subject to interval censoring. Pain and depression were included as time-varying covariates. We used a backwards elimination technique, with variables not contributing to the prediction of time to recovery being sequentially removed from the model. Statistical analyses were completed using R version 3.2.3 (R Foundation for Statistical Computing, Vienna, Austria).

3. Results

3.1 Description of Baseline PIM Use

Fifty one percent of the participant group was prescribed at least one PIM and 17.4% was prescribed two or more PIM at baseline. The most commonly used PIM were sedative/hypnotics (26.4% of participants), antidepressants (19.1%), and medications with anticholinergic properties (15.3%). Table 1 lists the baseline demographic and clinical characteristics of PIM users and non-users.

3.2 Association of Baseline PIM Use with Time to Full Functional Recovery

Overall, 48.6% (95% CI: 44.1–53.2%) of all participants achieved full functional recovery, defined as achieving at least 95% of pre-fracture function. As shown in the Kaplan-Meir time to event curve (Figure 1a), 43.9% (95% CI: 37.6–50.3%) of the PIM user group achieved full functional recovery, compared to 53.7% (95% CI: 47.0–60.2%) of non-PIM users, for a crude hazard ratio of 0.69 (95% CI: 0.53–0.91; p = 0.008).

Using Cox proportional hazards modeling, we investigated the effect of PIM use on time to full functional recovery while controlling for age, sex, marital status, race, education, pre-fracture FRS, pre-fracture MADRS, baseline SBT score, baseline CIRS-G score, baseline pain, smoking status, drinking status, social support and total number of baseline medications. After a backwards removal of variables not contributing to the model, age, race, cognition, medical comorbidities, baseline pain and pre-fracture FRS remained along with PIM group membership (Table 2). Use of PIM was associated with significantly longer time to full recovery with an adjusted hazard ratio of 0.69 (95% CI: 0.52–0.92; p = 0.012). In other words, PIM users were 31% (95% CI: 8% to 48%) less likely than non-PIM users to achieve full recovery at any given time within 12 months of hip fracture. When the group was divided by the number of PIM at baseline, two or more PIM (Hazard ratio (HR) = 0.60; 95% CI 0.40–0.90; p = 0.014), but not one PIM (HR = 0.77; 95% CI: 0.55–1.06; p = 0.11), was associated with a statistically significantly longer time to recovery compared to no PIM.

In other words, subjects who used two or more PIM were 40% (95% CI: 10% to 60%) less likely to achieve full recovery than those receiving no PIM.

4. Discussion

In this study, we present two important findings: 1) the high prevalence of PIM use after hip fracture and 2) the association between PIM use and time to full functional recovery after hip fracture. The frequency (51%) of PIM use in this sample of patients with hip fracture corresponds with previously reported PIM rates in the United States in older hospitalized patients (58.4%;[19]) and older community populations (42.6%; [20]). Our cohort had more sedative-hypnotic use, but less antidepressant use than a recent cohort of community-dwelling Medicare beneficiaries experiencing a fragility fracture [21].

We found an association between PIM use and increased time to functional recovery after a hip fracture, as hypothesized. This finding was most pronounced in persons taking two or more PIM, and was independent of other variables known to impact on functional recovery. Although PIM use was associated with less chance of achieving full functional recovery by the end of the 12-month observation period, almost half of the study group nevertheless achieved full recovery, reflecting the overall recovery potential of a post-hip fracture group once those with dementia and delirium are excluded.

This is the first study to consider the effect of PIM prescribing on long-term functional outcomes after hip fracture. One study found relationship between anticholinergic use for short-term functional outcomes on an orthogeriatric rehab unit, although the effect was quite small [22]. Prior studies have examined the relationship between medication use and hip fracture mortality. For example, anticholinergic risk score predicts three-month mortality after hip fracture [9]. Another retrospective cohort study found that inappropriate prescribing increased three-year risk of mortality post-fracture by 28%, as measured by the screening tool of older people's prescriptions (STOPP) and screening tool to alert to right treatment (START), [10]. A recent study identified that fall-related medications and polypharmacy were both associated with mortality after hip fracture [23]. Each of these studies examined an older and much more cognitively impaired cohort than is included in this study.

A unique strength of this study is that the hip fracture sample excluded those individuals at highest risk of poor outcomes (those with dementia, delirium or depression], removing important confounders in the interaction between PIM use and functional recovery. Confounding is a significant risk in retrospective or observational studies of PIM use. PIM use is a marker of medical complexity and psychological distress, and is correlated with polypharmacy, older age, and greater medical burden [24], all of which are associated with worse functional outcomes in older adults. We know that depressive symptoms, cognitive function, and pain have been independently linked to poorer functional outcomes after hip fracture [12, 25–27], but there are few studies of PIM use and functional outcomes that have controlled for these variables [28, 29] as we have done here. Another strength of this study is that the outcome assessments and clinical covariates were collected prospectively and through validated assessment tools, allowing inclusion of a broad number of demographic and clinical variables.

In this study, we demonstrate that, irrespective of dementia, delirium and depression, and independent of other well-known contributors to poor hip fracture outcomes such as depressive symptoms, cognition and pain, PIM use is associated with a longer time to achieve recovery. Our findings suggest that there may be an opportunity to improve long-term recovery after hip fracture through use of prescribing interventions that reduce PIM use. Unfortunately, to date there is little evidence that interventions to reduce PIM prescribing improve functional outcomes [30]. The challenge of effecting change in the prescribing of inappropriate medication was highlighted by a recent study that found that the prevalence of falls-promoting medications does not change post-fracture, with the small number of medication discontinuations balanced by the initiation of falls-promoting medication [21].

A limitation to the interpretation of this study is that PIM use was measured only at baseline, i.e. at the end of the patient's hospitalization for hip fracture. While we don't know whether patients continued to be prescribed these medications in the 12 months post-hip fracture, previous studies have found that hospitalization tends to increase the prevalence of medications classed as PIM rather than decrease them [11, 21, 31] and PIM are rarely stopped after a fracture [21]. Studies designed to systematically reduce the use of PIM during hospitalization have shown that intensive intervention is required to effect even a small change in prevalence of PIM use [32]. Thus it is unlikely there would have been a significant reduction in PIM use during the 12-month post-hospitalization period.

5. Conclusion

PIM use was associated with a lower probability of achieving full functional recovery in a 12-month period after hip fracture, especially in those using two or more PIM at baseline. This finding could have implications for decision-making around post-hip fracture prescribing, particularly with regards to prescribing of multiple PIM, and the need to identify therapies that support rather than hinder recovery.

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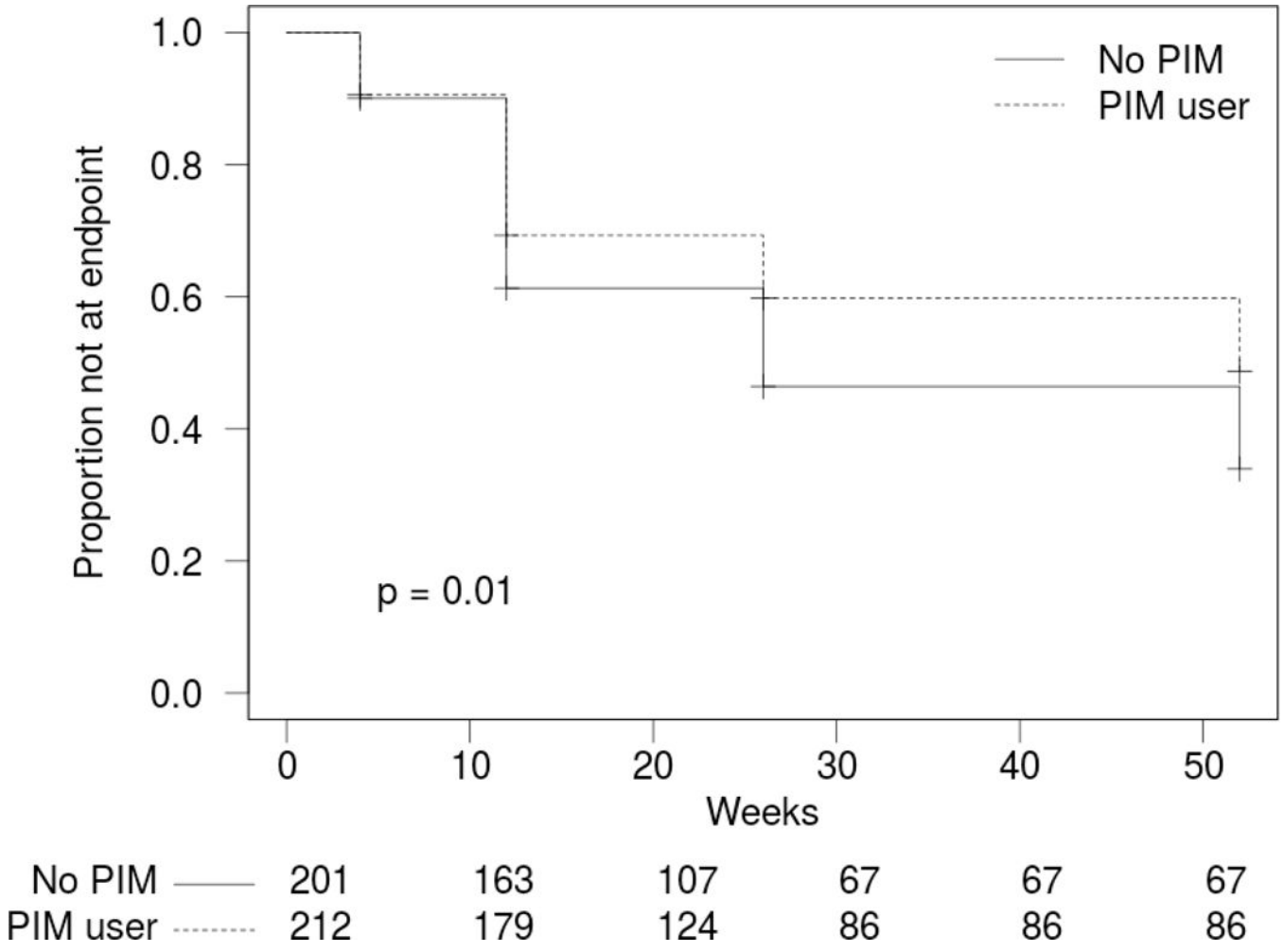
Key points

1. The prescribing of potentially inappropriate medication (PIM) is common in the period after a hip fracture.
2. PIM use is independently associated with longer time to full functional recovery after a hip fracture
3. The association between PIM use and longer functional recovery after hip fracture is most pronounced in persons prescribed two or more PIM.



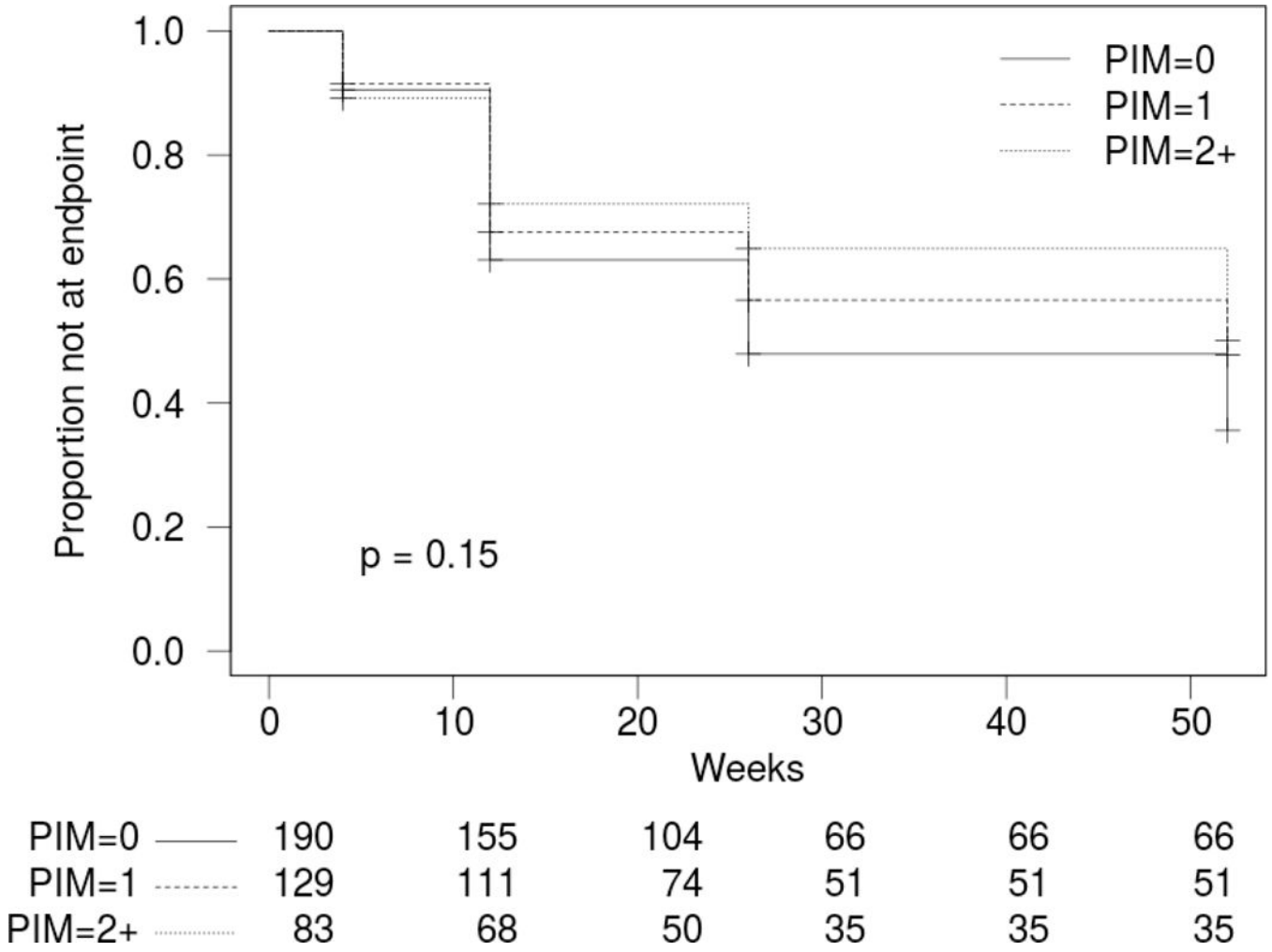


Figure 1. Kaplan-Meir survival curves demonstrating time to 95% hip fracture recovery a) In PIM users vs non-PIM users and b) By number of PIM

PIM: Potentially Inappropriate Medication

Table 1

Baseline characteristics of PIM users compared to PIM non-users.

	PIM user	Non-user	p-Value
	n=233	n=244	
Female	160 (68.7)	200 (82.0)	**0.001**[a]
Age (y)	78.5 ± 8.4	78.4 ± 9.1	0.92
Race:			
White/Caucasian	235 (96.3)	212 (91.0)	**0.022**[a]
Other	9 (3.7)	21 (9.0)	
Education:			
Elementary school	16 (6.6)	14 (6.0)	0.092[a]
High school	120 (49.2)	93 (39.9)	
Bachelors degree	75 (30.7)	80 (34.3)	
Graduate degree	14 (5.7)	25 (10.7)	
Marital status:			
Married	86 (35.2)	94 (40.3)	0.067[a]
Never married	11 (4.5)	21 (9.0)	
Separated/Divorced	26 (10.7)	26 (11.1)	
Widowed	121 (49.6)	92 (39.5)	
Smoking status:			
Never	106 (43.4)	86 (36.9)	0.325[a]
Past	109 (44.7)	118 (50.6)	
Current	28 (11.5)	29 (12.4)	
>7 alcoholic drinks weekly	81 (33.2)	91 (39.0)	0.215[a]
Total number of medications	6.1 ± 3.4	5.0 ± 3.2	**<0.001**
CIRS-G	13.6 ± 3.8	11.7 ± 3.3	**<0.001**
FRS (pre-fracture)	94.5 ± 7.8	97.1 ± 5.9	**<0.001**
Pain score	3.6 ± 2.9	2.9 ± 2.7	**0.0055**
SBT	4.8 ± 3.4	4.3 ± 3.2	0.092
MADRS	3.9 ± 4.8	2.6 ± 3.6	**0.0013**
DSSI	9.9 ± 2.0	9.9 ± 2.1	0.66

PIM: Potentially Inappropriate Medications; CIRS-G: Cumulative Illness Rating Scale for Geriatrics; FRS: Functional Recovery Score; SBT: Short Blessed Test; MADRS: Montgomery Asberg Depression Rating Scale; DSSI: Duke Social Support Index (Instrumental)

Values are mean ± SD or n (%). T-test unless otherwise indicated.

[a]Fischer's exact test

Table 2

Cox proportional hazards model of time to full recovery[a] after hip fracture.

	coef	exp(coef)	se(coef)	z	Pr(>|z|)
Baseline PIM user	−0.371	0.690	0.147	−2.52	0.012
Age	−0.047	0.954	0.008	−5.67	0.000
Race (Other)	−0.755	0.470	0.310	−2.43	0.015
CIRS-G	−0.056	0.946	0.022	−2.59	0.010
Baseline pain	−0.092	0.913	0.028	−3.32	0.001
Pre-fracture FRS	−0.045	0.956	0.009	−4.81	0.000

PIM: Potentially Inappropriate Medication; CIRS-G: Cumulative Illness Rating Scale for Geriatrics; FRS: Functional Recovery Scale.

[a]Full recovery is defined as recovering at least 95% of pre-fracture FRS score