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Risk Factors for Falls in HIV-Infected Persons

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Abstract

Background—The incidence of and risk factors for falls in human immunodeficiency (HIV)-1-infected persons are unknown.

Methods—Fall history during the prior 12 months, medical diagnoses, and functional assessments were collected on HIV-infected persons 45 to 65 years of age receiving effective antiretroviral therapy. Fall risk was evaluated using univariate and multivariate regression analyses.

Results—Of 359 subjects, 250 persons (70%) reported no falls, 109 (30%) had 1 fall; 66 (18%) were recurrent fallers. Females, Caucasians, and smokers were more like to be recurrent fallers ($p = 0.05$). HIV-related characteristics including current and nadir CD4 T-cell count, estimated HIV duration, and Veterans Aging Cohort Study Index scores were not predictors of falls (all $p > 0.09$); didanosine recipients were more likely to be recurrent fallers ($p = 0.04$). The odds of falling increased 1.7 for each comorbidity and 1.4 for each medication ($p < 0.001$), and were higher in persons with cardiovascular disease, hypertension, dementia, neuropathy, arthritis, chronic pain, psychiatric disease, frailty or disability (all OR 1.8; $p = 0.05$). Beta-blockers, antidepressants, antipsychotics, sedatives, and opiates were independently associated with falling (all OR 2.7; $p = 0.01$). Female gender, diabetes, antidepressants, sedatives, opiates, didanosine, exhaustion, weight loss, and difficulty with balance were the most significant predictors of falls in logistic regression (all OR 2.5; $p = 0.05$).

Conclusion—Middle-aged HIV-infected adults have high fall risk. Multiple comorbidities, medications, and functional impairment were predictive of falls, but surrogate markers of HIV infection or an HIV-specific multimorbidity index were not. Fall risk should be assessed routinely as part the care of HIV-infected persons.

Keywords

HIV; aging; accidental falls

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CONFLICTS OF INTEREST:

The authors report no conflicts of interest.

INTRODUCTION

Falls are common among community dwelling adults 65 years and older, with more than one-third of older adults sustaining a fall each year^{1,2}. Falls are one of the most common causes of emergency room visits and loss of independence among aging adults, with a non-injurious fall increasing the risk of placement in a skilled nursing facility by more than three-fold³. As a geriatric syndrome, falls are the consequence of multiple interrelated factors including comorbidities (arthritis, diabetes, pain, depression among many others), physical impairments (vision, cognition, neuropathy, strength, gait), and polypharmacy (especially psychoactive medications)⁴.

Persons aging with human immunodeficiency (HIV)-1 infection are thought to manifest “accelerated aging” with an earlier than expected occurrence of many diseases of aging⁵. Similarly, persons with HIV infection have a high prevalence of several comorbidities and physical impairments associated with an elevated fall risk⁶. Approximately 75% of HIV-infected persons receive at least one prescription medication in addition to antiretroviral therapy, and prescriptions associated with high-fall risk (cardiovascular and psychoactive medications) are among the most common⁷.

Despite heightened awareness of aging complications in the HIV-infected population, the rate of falls and risk factors for falls among HIV-1-infected adults are unknown. We hypothesized that a greater number of fall risk factors would result in a higher than expected fall rate among middle-aged HIV-1-infected adults.

METHODS

Study population

All individuals who received care for HIV-1 infection within twelve months prior to February 2010 in the Infectious Diseases Group Practice clinic at the University of Colorado Hospital were evaluated for participation. Individuals meeting the following criteria were eligible: 1) 45 to 65 years of age; 2) able to consent and participate in study procedures; and 3) taking combination (two or more) antiretroviral therapy for at least six months with one undetectable plasma HIV-1 RNA (<48 copies/mL) and no plasma HIV-1 RNA >200 copies/mL in the prior six months. Eligible individuals were contacted in person, by telephone, or by letter to determine interest in study participation. Approval was obtained by from the Colorado Multiple Institutional Review Board, and informed consent was obtained from all participants. All participants completed a single study visit that included a medical record review, a standardized interview, and a physical function assessment.

Clinical Assessments

Fall was defined as unintentionally coming to rest on the ground or other lower level, not as a result of a major intrinsic event or external hazard⁸. A history of one or more falls during the past twelve months was collected. Persons falling more than one time during the prior twelve months were considered recurrent fallers and were compared to non-fallers for the analyses. Recurrent fallers represent a higher risk group than those with a single fall, with significantly higher mortality and risk of admission to long-term care compared to single-fallers or non-fallers⁹⁻¹¹.

Fried’s frailty score was assessed as previously described¹². Shrinking was defined as unintentional weight loss of 10 pounds, or decrease of 5% of body weight in the last year (self-reported and verified by records when available). Exhaustion was defined by three to four times per week of feeling “everything I do is an effort” or “sometimes I just cannot get going”. Low activity was defined as self-report of being “limited a lot” in vigorous physical

activities^{13,14}. Weakness was assessed by the average of three dominant hand grip measurements using a Lafayette dynamometer, applying previously defined gender and body mass index (BMI) cut-offs¹². Slowness was defined by 4.5-m walk time: men >173 cm and women >159 cm in height requiring >7 seconds or men >173 cm and women >159 cm requiring >6 seconds met a criterion¹². One point was given for each abnormality; a score of three or more was considered frail.

The Short Physical Performance Battery (SPPB) assessed tandem stand by ability to stand heel-to-toe for ten seconds, walking speed by the faster of two 4-m walks at usual pace, and sit-stand test time by five repetitions of sit-to-stand without use of the arms¹⁵. On each task, zero points indicated inability to complete, two or less points was considered “difficulty”, and three or four points was considered performance within the expected range. A total score of 9 or less was considered disability¹⁶. 400-m walk time was measured on a set walking course by asking the participant to walk the distance as quickly as possible¹⁷.

The presence or absence of the following comorbidities were determined by medical record review and included in a comorbidity count: seizure disorder, dementia, stroke, neuropathy, psychiatric disease, arthritis, osteopenia or osteoporosis (prior stress fracture or T-score < -1 on bone densitometry scan), diabetes, kidney disease (calculated creatinine clearance <30 mL/min by Cockcroft-Gault, SI units 0.5mL/s/m²), malignancy (excluding non-melanoma skin cancer), solid organ transplant, lung disease, hypertension, cardiovascular disease, viral hepatitis (hepatitis B or C), and chronic liver disease. Current medication usage was determined by medical record and self-report; laboratory values were the most recent values available in the medical record. Current/prior alcohol use was defined as drinking >7 drinks per week or a self-reported history of abuse; debilitating pain was defined as responding “moderately”, “quite a bit”, or “extremely” to the question “during the past four weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?”. The Veterans Aging Cohort Study (VACS) Index score for predicted mortality was calculated for each subject as previously described¹⁸.

Statistical Analysis

Data were collected and managed with Research Electronic Data Capture (REDCap) tools hosted at the University of Colorado¹⁹. Demographic characteristics were summarized with mean and standard error (SE) for continuous outcomes, and frequency with percentage for categorical variables. Relationships between comorbid conditions, medications, functional assessment and odds of recurrent falls versus no falls were described by odds ratios (OR) and 95% confidence intervals (CI), and tested with Wald Chi-square. A sensitivity analysis was performed to evaluate the effect of the potential confounders of age >50, female gender, and current CD4+ lymphocyte count <200 cells/μL on demographics, comorbidities, medications, and functional assessment components. Odds ratios for medications were additionally adjusted for underlying treatment indication. To jointly assess demographics, comorbid conditions, and individual components of functional testing on the odds of falling, a logistic model was estimated. Comorbid conditions, medications, and individual components of functional testing with univariate-screen p value <0.05 were used to evaluate odds of falling in a logistic regression model. To create a model that could be implemented at the bedside without specialized equipment, grip strength was excluded. Model selection involved removal of suspected co-linear terms where concordance index was lower than 0.6 in univariate analysis, followed by terms with p>0.05 from the full model. The predictive power of the final model was described with receiver-operator-characteristic area-under-the-curve (ROC-AUC). Analyses were performed in SAS v9.2 (SAS Institute Inc., Cary, NC).

RESULTS

A total of 359 subjects completed the study visit, of whom 85% were male, 74% self-reported Caucasian, 18% Hispanic or Latino, 65% were men having sex with men, 21% with a history of intravenous drug use, and less than one percent reporting current intravenous drug use. The mean age was 52 ± 0.3 years, the mean CD4+ lymphocyte count was 594 ± 16 cells/ μ L, and 95% had plasma HIV-1 RNA below the limits of detection.

Thirty-percent (109 subjects) reported at least one fall during the year prior to study visit. Of the fallers, 43 (39%) reported one fall and 66 (61%) were recurrent fallers. Females and tobacco users were more likely to be recurrent fallers, while persons using illicit substances (majority marijuana) were more likely to be non-fallers (Table 1). Age, ethnicity, and alcohol use were not significant predictors of falls ($p = 0.30$). In a sensitivity analysis, odds of falling predicted by demographic characteristics did not differ by more than 10% after adjusting for age, gender, and CD4 lymphocyte count with the exception of a 13% increase in the odds of falling among Caucasian persons.

HIV-Related Factors and Fall Risk

Although recurrent fallers had a longer time since HIV diagnosis compared to non-fallers, nadir CD4+ lymphocyte count, current CD4+ lymphocyte count, and persons with HIV-1 RNA below detection (Table 1, all $p = 0.54$) were not predictive of falling. VACS Index score was not a significant predictor of falls (Table 1, $p = 0.13$). In a sensitivity analysis, odds of falling predicted by HIV-related characteristics did not differ by more than 10% after adjusting for age, gender, and CD4 lymphocyte count with the exception of a 12% decrease in the odds of falling among persons with HIV-1 RNA below detection.

Comorbidity and Fall Risk

Comorbidity was associated with an increased odds of recurrent falls, with each additional comorbid condition associated with 1.7 greater odds of falls (95% CI 1.5, 2.1; $p < 0.001$). The odds of falls with each individual comorbid condition are shown in Table 2. Hemoglobin was lower among recurrent fallers (14.7 ± 0.2 g/dL) than non-fallers (15.3 ± 0.1 g/dL; $p = 0.007$). Blood pressure, heart rate, and body mass index were not significant predictors of recurrent falls (all $p > 0.4$).

Medications and Fall Risk

Polypharmacy was associated with an increased odds of falls, with each additional prescribed medication associated with an incremental increase of 1.4 in the odds of falls (CI 1.3, 1.6; $p < 0.001$). Odds of falling with the use of individual medications are shown in Table 2. To examine the relationship of medications with falls, when adjusted for the underlying comorbid condition, the respective comorbidity being treated was added to each model. Didanosine and stavudine were adjusted for the comorbidity (neuropathy) presumed to be resultant from current or prior use of the medication (Table 2). Use of beta-blockers, opiates, antidepressants, antipsychotics, sedatives, and didanosine remained significantly more common among fallers than non-fallers after adjusting for the comorbidity being treated. In further sensitivity analysis, after adjusting for age, gender, and CD4 lymphocyte count, the odds of falling did not differ by more than 10% with the exception of a 12% increase with any stavudine use.

Functional Capacity and Fall Risk

In functional assessments, both frailty and disability were associated with falls ($p < 0.001$). A one point worsening on Fried's frailty score increased the odds of falls by 3.1 (CI 2.3, 4.2; $p < 0.001$), while a one point worsening on the SPPB increased the odds by 1.4 (CI 1.3, 1.8; p

<0.001). With the exception of the short walk components, all of the frailty and SPPB components were associated with recurrent falls (Table 3). Recurrent fallers had a significantly slower pace on the 400-m walk (1.33 ± 0.04 m/sec) than non-fallers (1.52 ± 0.02 m/sec, $p < 0.001$).

Multi-component Fall Risk

In a multivariate analyses, nine predictors of fall risk remained in a logistic model (Table 4). An ROC curve to assess the ability of the model to predict fall risk had an area under the curve of 0.866 (Figure 1A). The incremental odds of falling for each additional condition was 2.2 (CI 1.7, 2.8), with four risk factors having a sensitivity of 75% and specificity of 71% in predicting recurrent falls (Figure 1B).

DISCUSSION

Although fall rates and risk factors for falls are well described in community dwelling and institutionalized elders, no prior studies have evaluated the rate or risk factors for falls among HIV-1-infected adults. We found that the fall rate in middle-aged adults (mean age 52.0 years) with HIV-1 infection is as common as in uninfected persons aged 65 years older². Falls in our cohort were associated with several previously reported risk factors such as hypertension, diabetes, impaired balance, and pain, as well as medications used in the treatment of these comorbidities^{1,4}. A trend towards longer estimated duration of HIV-infection and a significant association with current or prior didanosine may reflect a greater number of accumulated comorbidities over time with HIV treatment. Other HIV-related risk factors were not seen, and, surprisingly, an HIV-specific multimorbidity index (the VACS Index) did not predict fall risk. Ultimately, the best predictors of fall risk were those factors known to be associated with fall risk in geriatric populations.

Our inclusion criteria provide a closer look at the fall rate and risk factors among middle-aged persons adherent to antiretroviral therapy. Although our study sample is reflective of the majority of persons engaged in HIV care²⁰, our results may not be applicable to all HIV-infected populations. We expect that our fall rates may underestimate the fall rate among HIV-infected persons less compliant with antiretroviral therapy, with advanced immunodeficiency, or with greater intravenous drug abuse. Reliance on subject recall of fall history may even further underestimate the fall risk in our study population²¹.

Similar to other geriatric syndromes, such as frailty, multiple factors increase fall risk. Thus, understanding the etiology of falls requires a syndromic approach that assesses the multitude of potential factors demonstrated among recurrent fallers in our cohort, including tobacco use, comorbidities, medications, and functional status. Given that multiple factors lead to an increased fall risk, it is expected that successful interventions to reduce falls in HIV-infected persons will require a multipronged approach including medication adjustment, behavioral modifications, vitamin D supplementation, physical therapy, and exercise or balance programs^{22,23}.

Available data suggest that HIV-infected persons have low bone density, increased fracture risk, and premature frailty^{5,6,13,14,24,25}. Thus, in addition to increased risk of falls, aging HIV-infected persons are likely to be at increased risk of morbidity when falls occur. Providers caring for HIV-infected persons should routinely inquire about falls, assess fall risk factors in those at risk for falling, and when high fall risk is identified, intervene to reduce risk. Interventions such as discontinuation of psychotropic or other high risk medications, balance training, home safety evaluations, and exercise programs decrease fall risk in elderly, non-HIV-infected persons^{2,22,23}. Future research is needed to investigate the

effectiveness of interventions to reduce fall risk in middle-aged and older HIV-infected persons.

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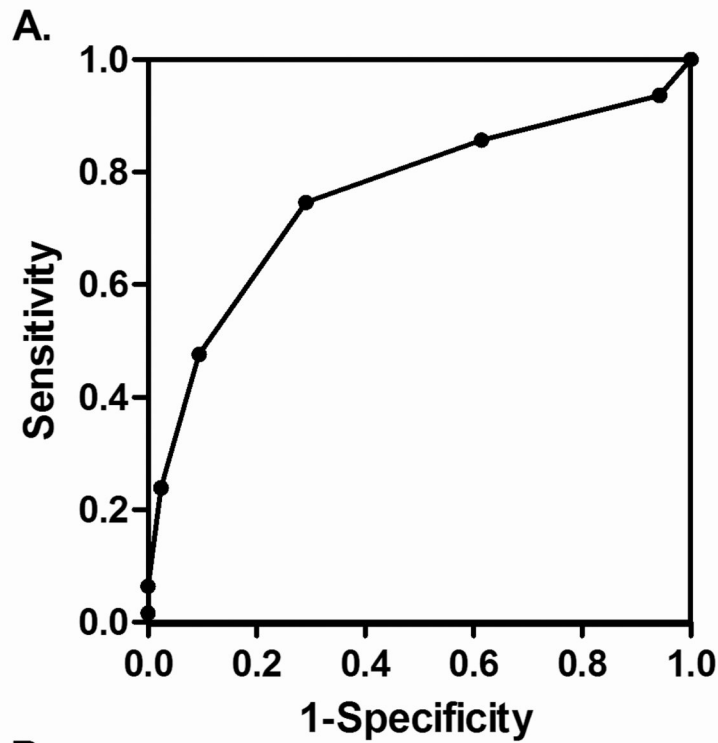
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B.

Number of Risk Factors*	Probability of Falling	Sensitivity	Specificity
1	3%	1.0	0
2	7%	0.94	0.06
3	14%	0.86	0.285
4	26%	0.75	0.71
5	44%	0.48	0.91
6	63%	0.24	0.94
7	79%	0.06	1.0
≥8	89%	0.02	1.0

Figure 1.

Risk of recurrent falls estimated by regression model. A) Fall risk shown by area under the receiver-operator-characteristic (ROC) curve, as estimated from the logistic regression model. B) Probability, sensitivity, and specificity of each additional fall risk factor. The risk factors identified through regression analyses were: difficulty with tandem stand, antidepressant use, exhaustion, diabetes, female gender, shrinking, opiate use, current/prior didanosine, and sedative use.

Table 1

Odds of recurrent falling by demographic characteristics

Demographic	Non-Fallers N= 250 (%)	Single Fallers N=43 (%)	Recurrent Fallers N= 66 (%)	Odds Ratio (95% CI)*
Age in years (mean ± SE)	52.0 ± 0.3	51.8 ± 0.7	52.1 ± 0.5	1.0 (0.96, 1.1)
Female gender	31 (12)	6 (14)	17 (26)	2.5 (1.3, 4.8)
Caucasian	177 (71)	35 (81)	53 (80)	1.7 (0.9, 3.3)
Hispanic ethnicity	45 (18)	5 (12)	15 (23)	1.3 (0.7, 2.6)
Current tobacco use	74 (30)	18 (42)	31 (47)	2.1 (1.2, 3.7)
Alcohol use > 7 drinks/week	11 (4)	3 (7)	1 (2)	0.3 (0.04, 2.7)
Current illicit drugs	80 (32)	11 (26)	12 (18)	0.5 (0.2, 0.9)
Years since HIV diagnosis (mean ± SE)	14.0 ± 0.5	16.8 ± 1.1	15.8 ± 0.9	1.0 (1.0, 1.1) [‡]
Current CD4 count (mean ± SE)	595 ± 20	586 ± 28	599 ± 38	1.0 (1.0, 1.1) [‡]
Nadir CD4 count (mean ± SE)	168 ± 10	169 ± 27	164 ± 17	1.0 (0.9, 1.1) [‡]
HIV-1 RNA below detection	238 (95)	40 (93)	64 (97)	1.6 (0.4, 7.4)
VACS Index Score (mean ± SE)	17.6 ± 0.9	17.9 ± 2.4	20.7 ± 1.8	1.0 (1.0, 1.03) [‡]

CI, confidence interval; SE, standard error; VACS, Veterans Aging Cohort Study,

* Odds ratio comparing non-fallers and recurrent fallers

Table 2

Odds of recurrent falling by comorbidity and medications

Comorbidities	Non-Fallers N=250	Single Fallers N=43	Recurrent Fallers N=66	Fall Rate (any fall)	Odds Ratio (95% confidence interval)	
					Unadjusted	Adjusted*
CVD	17 (7)	5 (12)	12 (18)	50%	3.0 (1.4, 6.8)	3.4 (1.5, 7.8)
Hypertension	95 (38)	20 (47)	33 (50)	36%	1.6 (0.95, 2.8)	1.8 (1.0, 3.1)
Diabetes	15 (6)	5 (12)	17 (27)	60%	5.6 (2.6, 12.1)	6.2 (2.8, 13.7)
Stroke	7 (3)	2 (5)	4 (6)	46%	2.2 (0.6, 7.9)	1.9 (0.5, 7.0)
Lung disease	30 (12)	9 (20)	10 (15)	39%	1.1 (0.5, 2.4)	1.1 (0.5, 2.4)
Hepatitis	59 (24)	11(26)	19 (28)	34%	1.3 (0.7, 2.4)	1.3 (0.7, 2.4)
Dementia	3 (1)	2 (5)	6 (9)	73%	10.5 (2.5, 43.7)	10.5 (2.5, 43.7)
Neuropathy	78 (31)	19 (44)	39 (59)	43%	3.3 (1.9, 5.9)	3.3 (1.9, 5.9)
Arthritis	75 (30)	17 (40)	38 (58)	42%	4.8 (2.7, 8.7)	3.0 (1.7, 5.4)
Chronic Pain	49 (20)	12 (28)	35 (53)	49%	4.8 (2.7, 8.7)	4.8 (2.7, 8.7)
Psychiatric disease	125 (50)	30 (70)	52 (79)	40%	3.6 (1.9, 6.8)	3.6 (1.9, 6.8)
Medications						
Beta-blocker	22 (9)	3 (7)	17 (26)	48%	3.6 (1.8, 7.3)	3.4 (1.5, 7.6) [†]
Calcium channel blocker	13 (5)	5 (12)	8 (12)	50%	2.5 (1.0, 6.4)	1.9 (0.7, 5.3) [†]
Diabetes therapy (any)	13 (5)	5 (12)	13 (20)	59%	4.5 (2.0, 10.2)	0.8 (0.1, 5.7) [‡]
Testosterone (men)	33 (15)	7 (19)	8 (16)	31%	1.1 (0.5, 2.6)	1.1 (0.5, 2.6)
Vitamin D	41 (16)	8 (19)	16 (24)	37%	1.4 (0.8, 2.5)	1.5 (0.8, 3.0)
Bladder/prostate	16 (6)	3 (7)	8 (19)	41%	1.6 (0.7, 3.7)	2.0 (0.8, 5.0)
Antidepressant	52 (21)	15 (35)	36 (55)	50%	4.6 (2.6, 8.1)	3.5 (1.8, 6.9) [§]
Benzodiazepine	32 (13)	10 (23)	19 (29)	48%	2.5 (1.4, 4.3)	1.9 (0.9, 3.8) [§]
Antipsychotic	19 (8)	8 (19)	16 (24)	56%	3.4 (1.8, 6.6)	2.7 (1.2, 5.8) [§]
Sedative/hypnotic	34 (14)	6 (14)	25 (38)	48%	2.5 (1.5, 4.4)	3.2 (1.7, 6.1) [§]
Anticonvulsant	13 (6)	5 (14)	11 (18)	55%	3.2 (1.5, 6.9)	2.3 (0.9, 5.6) [§]
Gabapentin/pregabalin	22 (9)	5 (12)	14 (21)	46%	2.2 (1.1, 4.2)	1.8 (0.8, 4.0) ^{//}
Opiate	45 (18)	10 (23)	36 (55)	51%	3.3 (2.0, 5.5)	3.4 (1.4, 8.1) ^{//}

Comorbidities	Non-Fallers N=250	Single Fallers N=43	Recurrent Fallers N=66	Fall Rate (any fall)	Odds Ratio (95% confidence interval)	
					Unadjusted	Adjusted*
Any didanosine	57 (23)	10 (23)	24 (36)	37%	1.5 (0.9, 2.5)	1.9 (1.03, 3.5) [¶]
Any stavudine	93 (37)	22 (51)	33 (50)	37%	1.7 (1.1, 2.7)	1.6 (0.9, 2.9) [¶]
Efavirenz	86 (34)	10 (23)	22 (33)	27%	0.8 (0.5, 1.3)	1.0 (0.5, 1.8)

CVD, cardiovascular disease;

* Adjusted for age, gender, CD4+ lymphocyte count; Adjusted for underlying treatment indication in addition to age, gender, CD4+ lymphocyte count;

[†]hypertension;

[‡]diabetes,

[§]psychiatric disease,

^{||}chronic pain, or

[¶]neuropathy (result of therapy rather than treatment indication)

Table 3

Odds of recurrent falls by functional assessment tools and individual components

Functional Component	Non-Fallers N=250 (%)	Single Fallers N=43 (%)	Recurrent Fallers N=66 (%)	Odds Ratio* (95% confidence interval)	
				Unadjusted	Adjusted†
Frailty (3 points)	7 (3)	6 (14)	14 (21)	9.4 (3.6, 24.3)	9.5 (3.6, 25.1)
Weakness	16 (6)	5 (12)	16 (24)	4.7 (2.2, 10.0)	4.6 (2.2, 10.0)
Slowness	2 (1)	3 (7)	3 (5)	5.9 (1.0, 36.1)	3.3 (0.7, 28.9)
Exhaustion	54 (22)	17 (40)	39 (59)	5.2 (3.0, 9.3)	5.4 (3.0, 9.9)
Shrinking	17 (7)	8 (19)	10 (15)	2.5 (1.1, 5.6)	2.4 (1.0, 5.6)
Low activity	159 (64)	30 (71)	60 (91)	5.7 (2.4, 13.8)	6.0 (2.4, 14.5)
Disability (SPPB 9 points)	17 (7)	12 (28)	16 (24)	4.4 (2.1, 9.3)	4.2 (2.0, 9.0)
Tandem difficulty‡	4 (2)	3 (7)	12 (18)	13.7 (4.2, 44.0)	15.6 (4.6, 53.1)
Sit-stand difficulty‡	27 (11)	14 (33)	16 (24)	2.6 (1.3, 5.3)	2.6 (1.3, 5.3)
4-m walk difficulty‡	3 (1)	3 (7)	1 (2)	1.3 (0.1, 12.4)	0.9 (0.1, 9.7)
400-m pace (mean m/sec ± SE)	1.52 ± 0.02	1.44 ± 0.06	1.33 ± 0.04	14.3 (4.8, 50.0)	10.0 (4.3, 50.0)

SPPB, short physical performance battery; SE, standard error;

* Odds ratio comparing non-fallers and recurrent fallers;

† Adjusted for age, gender, and CD4 lymphocyte count;

‡ 2 or less of 4 possible points

Table 4

Risk factors for recurrent falls from multivariate logistic regression models.

Parameter	Odds Ratio (95% CI)
Difficulty with tandem stand [*]	13.5 (3.0, 60.5)
Antidepressant use	3.7 (1.8, 7.7)
Exhaustion [†]	3.7 (1.8, 7.7)
Diabetes	3.6 (1.4, 9.4)
Female gender	3.5 (1.4, 8.8)
Shrinking [‡]	3.4 (1.2, 10.1)
Opiate use	3.1 (1.5, 6.5)
Current/prior didanosine	2.6 (1.2, 5.4)
Sedative use	2.5 (1.1, 5.5)

^{*}Inability to stand heel-to-toe for 3 seconds;

[†]Three to four times/week of feeling “everything I do is an effort” or “sometimes I just cannot get going”;

[‡]Unintentional weight loss of 10 pounds or decrease of 5% body weight in the last year