Risk Factors for Multiple Falls in Men Over the Age of 65

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Background

Osteoporosis, defined as a bone mineral density that is 2.5 or more standard deviations below the population mean, is the most common bone disease in the U.S., with a prevalence of almost 20% in women over age 50 and 4.4% in men over age 50. Low bone mass, a risk factor for the development of osteoporosis, is prevalent in over 40% of adults over age 50. People with osteoporosis are at significantly higher risk of bone-fracture than those without it.[1] As the U.S. population ages, rates of osteoporosis and its associated medical expenditures are likely to increase, with annual medical expenditures associated with osteoporosis estimated to reach $25.3B by 2025.[2] Because of its high prevalence and associated cost, and because of the serious and often fatal effects of bone fracture for elderly adults,[3] monitoring osteoporosis is of great public health importance.

Most studies of osteoporotic fractures have focused only on post-menopausal women, as they represent the majority of adults with osteoporosis.[4] As a result, there are significant gaps in the medical literature about osteoporosis in men. It is important that these gaps are closed, as even though men have much lower rates of osteoporosis than women, men account for 30% of hip fractures globally, and mortality after bone fractures is higher in men than in women.[3]

The Osteoporotic Fractures in Men (MrOS) study is a prospective cohort study of men over age 65 (average age = 73.7 years, sample size = 5,994). It was designed to assess the significance of bone mass, bone geometry, lifestyle, anthropometric and neuromuscular measures, and fall propensity as risk factors for bone fracture in men. It also allows for assessment of the effect of bone fractures on quality of life for men, and of the association between osteoporosis and prostate disease. Participants complete a survey at baseline for potential risk factors, as well as demographic information and potential confounders. Objective measures of physical and mental health are also obtained at baseline. After the baseline survey, surveys are completed every 4 months with information about incident falls, fractures, prostate cancer, and death.[4]

Study Objective

This study aims to assess potential risk factors for experiencing more than one fall in a 12-month period for men over age 65. A logistic regression model was created using data from the MrOS study to predict risk of multiple falls and report odds ratios for each significant risk factor. To evaluate the validity of the study, we assessed for potential information bias due to missing data and assessed the model's discriminative ability in predicting multiple falls.

Methods

Seven-step purposeful variable selection, as described in Hosmer and Lemeshow,[5] was employed to select the variables used in the final prediction model discussed hereafter. Because of the sparse nature of the subjects' self-reported health on the five-point scale encoded in the original data set, this variable was re-coded as binary where those that reported their health as fair, poor, and very poor were given a 0 value, and those reporting otherwise were given a value of 1. Portland, OR, was used as the referent group for study site throughout the variable selection process simply because this is where our research team was based. For each model generated in the selection process, the data was subsetted first to only contain the variables under consideration, then observations with missing fields were censored to circumvent missingness and the need for missing data methods, which are beyond the scope of this investigation. Nonlinearity in continuous variables was identified graphically by plotting the smoothed scatter plot of predicted probability of falls against the linear variable (**Figure 1:** `Falls Risk as a Function of Continuous Variables`). Walking speed and grip strength were selected for the multiple fractional polynomial approach implemented in the 'mfp' package for R,[6] and walking speed transformed as the inverse square was found to be significant ($\alpha = 0.10$). While all possible interaction terms were investigated during step six of the purposeful selection process, only clinically relevant interaction terms were considered for addition to the preliminary final model. The Hosmer-Lemeshow test, as implemented in the 'ResourceSelection' R package,[7] showed a good fit ($p = 0.83$, $g = 378$). Model diagnostics were carried out using graphical assessment to identify poorly fit covariate patterns, utilizing the 'LogisticDx' R package.[8] Finally, while a censored model was generated that omits four poorly fit covariate patterns present in our final model, this model omitting certain variables is only to be used for comparative purposes, as there is no clinically relevant reason to omit these four observations.

Results

This analysis includes data for 5,994 men enrolled in the MrOS study. Table 1 (**Appendix 1:** Table 1) shows the sample sizes and distributions of characteristics of the overall sample, analytic sample, and excluded observations. The mean age at enrollment of the analytic sample was 73.1 (standard deviation [SD]: 5.6) years. A small proportion of the sample had a history of stroke (256, 5.0%), Parkinson's disease (32, 0.6%), and chronic obstructive pulmonary disease (COPD; 498, 9.8%) at baseline. A large proportion of the sample had a history of arthritis (2,353, 46.2%) at baseline. Most participants rated their baseline health as excellent or good (4,480, 88%) and the mean baseline body mass index (BMI) was 27.4 (SD: 3.8) kg/m^2.

Those in the analytic sample and excluded individuals statistically significantly differed by every characteristic included in the analysis. Notably, those who were excluded had a higher percentage of a history of stroke (9.8% vs. 5.0%), Parkinson's disease (2.2% vs. 0.6%), COPD (15.7% vs. 9.8%), arthritis (54.8% vs. 46.2%), were more likely to rate their health as fair, poor, or very poor (27.2% vs. 12.0%), were older (median 76.6 years vs. 73.1 years), had a lower PASE score (median 126.0 vs. 150.0), and lower average grip strength (mean 34.0 vs. 39.0 kg).

Table 2 (**Appendix 1:** Table 2) depicts the final model built for the association between baseline characteristics and the occurrence of more than one fall within a year of baseline and their respective log odds ratios (beta coefficients) and odds ratios. Included in the model are baseline age, history of stroke, Parkinson's disease, COPD, and arthritis, PASE score, subjective health rating, BMI, average grip strength, walk speed (transformed to the inverse squared walk speed), femoral neck bone mineral density, total body fat mass, and total body lean mass. Fit of the model is poor, with an area under the curve value of 66.3% (95% confidence interval [CI]: 64.1%-68.4%).

After adjusting for all covariates, a history of Parkinson's disease was associated with a 5-fold increased odds of having more than one fall within a year of baseline (95% CI: 2.38, 10.4) compared to those without Parkinson's disease. A history of COPD and arthritis were also significantly associated with an increased odds of having more than one fall within a year of baseline (1.58 [95% CI: 1.25, 2.0]; 1.47 [95% CI: 1.25, 1.73], respectively). While a history of stroke was associated with increased odds of having more than one fall within a year of baseline, it was not significant (1.37 [95% CI: 0.99, 1.87]).

Every one-year increase in age is associated with a 1.03-fold increased odds of having more than one fall within a year of baseline (95% CI: 1.01, 1.04); every 10-year increase in age is associated with a 1.30-fold increased odds of having more than one fall within a year of baseline (95% CI: 1.11, 1.52). Additionally, compared to an "Excellent" or "Good" subjective rating of health, a "Fair", "Poor", or "Very Poor" subjective rating of health is associated with a 1.36-fold increased odds of falling more than once within a year of baseline (95% CI: 1.08, 1.71). Every one-kg/m^2 increase in BMI is associated with a 7% decrease in the predicted odds of falling more than once within a year of baseline (95% CI: 2.9%, 11.8%); every 5-kg/m^2 increase in BMI is associated with a 32% decrease in the predicted odds of falling more than once within a year of baseline (95% CI: 13.9%, 46.6%).

Discussion

Our final logistic regression model, as highlighted in Table 2 (**Appendix 1:** Table 2), includes thirteen of the original sixteen covariates. Covariates included in the original MrOS study but not found to adequately predict multiple falls in the past year include history of diabetes, history of cancer, and corrected total hip BMD. Of the thirteen covariates in the final model, all but two were significantly associated with having more than one fall within a year of baseline given a 5% significance level. More specifically, covariates found to be significantly associated with having more than one fall within a year of baseline include age, history of Parkinson's Disease, COPD, or arthritis, subjective health rating, body mass index, average grip strength, inverse square walking speed, corrected femoral neck BMD, total body fat, and lean body mass. The insignificant covariates included history of strokes and PASE scores, with p-values of 0.053 and 0.059 respectively. However, despite both covariates being insignificant when controlling for other covariates, these variables contributed enough to the prediction of having more than one fall within a year of baseline to be considered valuable and included in the model.

We found a large odds ratio for the odds of multiple falls within a year of baseline among those with Parkinson's disease compared to those without Parkinson's disease (5.00, 95% CI: 2.38, 10.4). Falls are a major concern among those with Parkinson's disease, with 35-90% of patients reporting at least one fall, and recurrent falls making up 39% of all falls.[9] The results of this analysis highlight the need to continue exercise- and pharmaceutical-based interventions already common in clinical practice in order to reduce the occurrence of falls among individuals with Parkinson's disease. Changes in clinical practice are not recommended based on this analysis because, despite a large odds ratio, only 32 individuals (0.6%) in the analytic sample had a history of Parkinson's disease, which limits the strength of these findings.

Also of interest is the reduced predicted odds of multiple falls associated with an increase in BMI (0.93, 95% CI: 0.88, 0.97). This finding is in agreement with previous research, which has found that older men whose BMI increased from <25 kg/m^2 (normal/healthy BMI) in midlife to 25-29.9 kg/m^2 (overweight BMI) in older age had the lowest mortality risk among BMI changes assessed (hazard ratio [HR] 0.84, 95% CI: 0.75, 0.94).[10] Those whose BMI decreased had increased risk of mortality; for example, those whose midlife BMI of ≥ 30 kg/m^2 (obesity BMI) decreased to 25-29.9 kg/m^2 (overweight BMI) in older age had the highest mortality risk (HR 1.79, 95% CI: 1.12, 2.88).[10] Our finding of a decreased risk of falls with increasing BMI is supportive of suggestions for BMI gain after midlife, especially among those who were underweight or normal weight in midlife.

As can be seen from Table 1 (**Appendix 1:** Table 1), the analytic sample (N = 5,092) had significantly different demographic characteristics than the sample of excluded observations (N = 902) for every variable considered. Compared to the analytic sample, the excluded observations had a higher percentage of men over the age of 65 that had a history of stroke, Parkinson's Disease, COPD, and arthritis or gout. The excluded observations also had significantly lower PASE scores, lower BMI, lower average grip strength, and were older in age. As such, we inevitably expect these excluded observations to significantly impact our results if we are interested in the entire sample (N = 5,994). This could potentially hinder our ability to generalize results or even invalidate the model entirely, as the missing outcome data in the excluded observations could introduce biases into our model. Particularly, it is expected that excluded individuals might have experienced more falls than included individuals, thus resulting in a bias toward the null that attenuated observed associations. Lack of outcome information for these observations causes more uncertainty and leads to less precise estimates.

Further limitations of this analysis exist. The final model had poor discriminative ability, with an area under the receiver operating curve of 66.3%. As such, findings should be understood with caution and should not be used to predict individual risk of multiple falls. Additionally, the study population consisted mainly of healthy men, further reducing generalizability to other populations and to women.

Conclusion

We found a strong association between history of Parkinson's disease and low bone mineral density with odds of multiple falls within a year of baseline. These results reaffirm existing practices that are aimed at mitigating fall risk and fracture risk among elderly men with Parkinson's disease and low bone mineral density. Among those with Parkinson's disease, a clinical emphasis on exercise- and pharmaceutical-based interventions should be continued.[9] Additionally, among those with low bone mineral density, exercise- and pharmaceutical-based interventions have also found evidence of reducing fall risk and should be continued.[11]

Clinical recommendations based on these results extend to increasing BMI in underweight adults. This analysis found a 32% decrease in the predicted odds of multiple falls for every 5-kg/m^2 increase in BMI (indicative of an increase of one BMI category; i.e., from the overweight BMI category to the obesity class I category). As such, efforts to increase BMI, particularly among those who also exhibit other risk factors found in this analysis, should be emphasized.

Future research would benefit from analyzing medication use and history. Specifically, benzodiazepine use and other medications which affect balance or cognitive ability may prove useful in predicting falls. Data on prostate enlargement should also be considered, as this may increase the number of times a person gets up to use the restroom. Especially at night, increased trips to the bathroom may increase a person's risk of falls

Finally, the MrOS study now includes over 15 years of follow-up data; while this study used data from the first year of follow-up, studying risk of falls with data from more than one year of follow-up is suggested.

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Table 1

Table 1. Characteristics of the overall sample, analytic sample, and excluded observations

Characteristic	Overall, N = 5,994[1]	Excluded, N = 902[1]	Included, N = 5,092[1]	p-value[2]
More than one fall	786 / 5,224 (15%)	31 / 132 (23%)	755 / 5,092 (15%)	0.006
Age	73.7 (5.9)	76.6 (6.7)	73.1 (5.6)	<0.001
Stroke	344 / 5,994 (5.7%)	88 / 902 (9.8%)	256 / 5,092 (5.0%)	<0.001
Parkinsons	52 / 5,994 (0.9%)	20 / 902 (2.2%)	32 / 5,092 (0.6%)	<0.001
COPD	640 / 5,994 (11%)	142 / 902 (16%)	498 / 5,092 (9.8%)	<0.001
Arthritis or Gout	2,847 / 5,994 (47%)	494 / 902 (55%)	2,353 / 5,092 (46%)	<0.001
PASE Score	146 (68)	126 (70)	150 (67)	<0.001
Subjective Health Rating	857 / 5,992 (14%)	245 / 900 (27%)	612 / 5,092 (12%)	<0.001
Body Mass Index	27.4 (3.8)	27.1 (4.1)	27.4 (3.8)	<0.001
Average Grip Strength	39 (8)	34 (8)	39 (8)	<0.001
Walking Speed	1.20 (0.23)	1.09 (0.26)	1.22 (0.22)	<0.001
Corrected Femoral Neck BMD	0.78 (0.13)	0.76 (0.13)	0.79 (0.13)	<0.001
Total Body Fat	22 (7)	21 (7)	22 (7)	<0.001
Lean Body Mass	57 (7)	55 (8)	57 (7)	<0.001

[1] n / N (%); Mean (SD)

[2] Pearson's Chi-squared test; Wilcoxon rank sum test

Note. COPD, chronic obstructive pulmonary disease; PASE, Physical Activity Scale for the Elderly; BMD, bone mineral density; SD, standard deviation. Prevalence of stroke, Parkinson's disease, COPD, and arthritis/gout are reported. Prevalence "Fair", "Poor", or "Very Poor" subjective health rating is reported.

Table 2

Table 2. Multivariable adjusted log odds ratios and odds ratios for falling more than once within a year of baseline

	Log Odds Ratios			Odds Ratios		
Characteristic	**log(OR)[1]**	**95% CI[1]**	**p-value**	**OR[1]**	**95% CI[1]**	**p-value**
Age	0.03	0.01, 0.04	0.001	1.03	1.01, 1.04	0.001
Stroke	0.31	-0.01, 0.63	0.053	1.37	0.99, 1.87	0.053
Parkinsons	1.6	0.87, 2.3	<0.001	5.00	2.38, 10.4	<0.001
COPD	0.46	0.22, 0.69	<0.001	1.58	1.25, 2.00	<0.001
Arthritis or Gout	0.39	0.22, 0.55	<0.001	1.47	1.25, 1.73	<0.001
PASE Score	0.00	0.00, 0.00	0.059	1.00	1.00, 1.00	0.059
Subjective Health Rating	0.31	0.08, 0.53	0.007	1.36	1.08, 1.71	0.007
Body Mass Index	-0.08	-0.13, -0.03	0.001	0.93	0.88, 0.97	0.001
Average Grip Strength	-0.04	-0.05, -0.03	<0.001	0.96	0.95, 0.97	<0.001
Inverse Square Walking Speed	0.33	0.17, 0.51	<0.001	1.39	1.18, 1.66	<0.001
Corrected Femoral Neck BMD	1.0	0.33, 1.7	0.003	2.70	1.39, 5.22	0.003
Total Body Fat	0.05	0.02, 0.07	<0.001	1.05	1.02, 1.07	<0.001
Lean Body Mass	0.02	0.00, 0.04	0.034	1.02	1.00, 1.04	0.034

[1] OR = Odds Ratio, CI = Confidence Interval

Note. COPD, chronic obstructive pulmonary disease; PASE, Physical Activity Scale for the Elderly; BMD, bone mineral density. Reference groups: For Stroke, Parkinson's, COPD, Arthritis/Gout: individuals without these comorbidities. For Subjective Health Rating: "Fair", "Poor", or "Very Poor" subjective health rating.

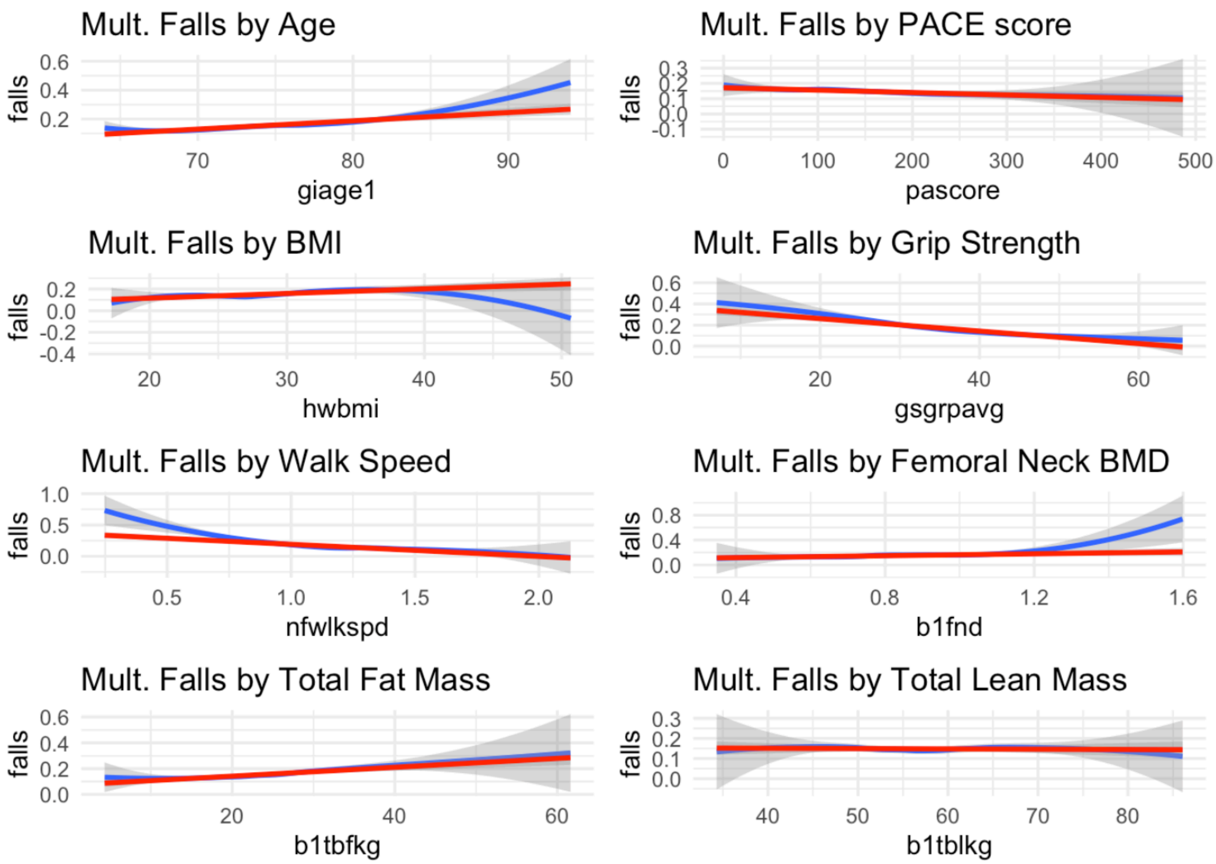

Figure 1. For each continuous variable present at step five, we fit the log odds of multiple falls across the range of values in the dataset linearly (red) and with a loess spline (blue).