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Falls in Older Adults with Multiple Myeloma

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Abstract

Objective—To examine the prevalence of falls, factors associated with falls and the relationship between falls and survival in older adults with multiple myeloma.

Methods—In an analysis of the Surveillance, Epidemiology and End Results (SEER)-Medicare Health Outcomes Survey (MHOS) linked database, we examined 405 older adults with MM and 513 matched non-cancer controls. The primary outcome was self-reported within the past 12 months. Age, race, gender, symptoms and comorbidities were self-reported in the MHOS. Survival was calculated from SEER data.

Results—Of the patients with MM, 171 were within 1 year of diagnosis (cohort 1) and 234 were 1 year post-diagnosis (cohort 2). Patients in cohort 1 and 2 were more likely to have fallen than controls (26% and 33% vs 23%, $p=0.012$). On multivariate analysis, among patients with myeloma (combined cohorts 1&2), factors associated with falls included self-report of fatigue [aOR 2.52 (95% CI 1.34–4.93)], depression [aOR 1.90 (95% CI 1.14–3.18)], or poorer general health [aOR 1.86 (95% CI 1.05–3.36)]. Falls were not associated with survival.

Conclusions—Older adults with MM have a greater prevalence of falls than matched controls. Self-reported fatigue, depression and poorer general health are associated with greater odds of falls.

Keywords

Falls; Multiple Myeloma; Cancer; Elderly; Geriatric Assessment

INTRODUCTION

Falls are a common cause of morbidity and mortality among older adults. About one in three adults over age 65 fall each year.(1) Older adults with cancer have a greater risk for falls than their peers without cancer; those who report falls experience poorer quality of life and are at greater risk for severe toxicity from chemotherapy.(2–5) Despite these observations, falls among older adults with cancer are a relatively understudied event, and little is known regarding the prevalence, sequelae, or factors predictive of falls in this population.(6,7)

Multiple myeloma (MM) is a cancer of older adults, with a median age of 69 at diagnosis. Geriatric issues, including comorbidities or dependence in daily activities, are common and have been associated with poorer prognosis in older adults with MM.(8,9) However, the prevalence of falls, another geriatric syndrome, and their association with prognosis is unknown. Symptoms of MM and sequelae of its treatment, including bone loss, pain, functional decline and peripheral neuropathy, are highly prevalent, and could be associated with a higher risk for falls and injurious falls.(10–13)

In the present study, we sought to determine the prevalence of falls in older patients with MM, to compare this rate with a cohort of matched controls without cancer, to examine factors associated with falls, and assess the relationship between falls and overall survival.

PATIENTS AND METHODS

Data source

This study was performed under a protocol approved by the Washington University School of Medicine Human Subjects Committee. The data sources for this study were the Medicare Health Outcomes Survey (MHOS) and the Surveillance, Epidemiology, and End Results (SEER)-MHOS linked databases.(14) The MHOS, implemented in 1998, annually collects self-reported symptoms, functional status, and health-related quality of life (HRQOL) from Medicare beneficiaries who are enrolled in Medicare Advantage health plans. In the SEER-MHOS linked dataset, data from the MHOS are linked to demographics, tumor characteristics, and survival for those with a cancer diagnosis and reside in the coverage area of one of 14 registries participating in the SEER-MHOS linkage.

At the time of analysis, the SEER-MHOS data release included all participants who completed the initial survey 1998–2009. Subsequent follow-up surveys were available through 2011. An item inquiring about falls, “Did you fall in the past 12 months,” was added to the MHOS survey in 2006, thus, this analysis includes only MHOS participants who completed the survey from 2006–2011.

For this analysis, three cohorts were analyzed. Cohort 1 included MHOS participants whom completed the survey near the time of MM diagnosis (+/- 1 year), to approximate a baseline status. Cohort 2 included MHOS participants who only completed the survey 1 year or more following MM diagnosis. Each participant was only included in the analyses once using data from the MHOS survey nearest to MM diagnosis. Cohort 3 was a cohort of case-control matched MHOS participants without cancer. Controls were matched (3:1) to Cohort 1 by age, gender, and race.

Statistical Analysis

All data was analyzed using SAS enterprise guide 5.1. Case-control selection was performed using the PROC SURVEYSELECT function as previously described.(15) The characteristics of each cohorts were compared using ANOVA or Pearson Chi-square test as appropriate. Bivariate Logistic Regression was performed to determine what factors were associated with falling in patients with MM (Cohorts 1 and 2). We limited the selection of candidate variables to limit the compounding risk of Type I errors. A multivariate analysis was then

performed with variables significantly ($p < 0.05$) associated with falls in the univariate analysis. A survival analysis was performed using Cox Regression analysis to determine if falls were associated with survival, controlling for age and gender, in patients with newly diagnosed MM (cohort 1). Cohort 2 was not associated for the association between falls and survival given the numerous confounders potentially present in patients who had experienced toxicity of treatment, symptoms of advancing cancer and the outcome of falls. Full explanations of variables and coding are available in Supplementary Table 1.

RESULTS

We identified 1,889 MHOS surveys from 1,229 unique MM patients in the SEER-MHOS dataset from 1998 to 2011. Of these patients, 485 completed the falls question at least once. One hundred-seventy-one patients completed the falls question near the time of MM diagnosis and were included in Cohort 1; an additional 234 completed the question one or more years following MM diagnosis and were included in Cohort 2. One million, eight hundred and twelve thousand, six hundred and twenty-nine non-cancer MHOS surveys were available with the falls question completed; 513 of these were included in Cohort 3 as matched-controls for Cohort 1.

Compared to non-cancer controls, MM patients were significantly more likely to report falls. Twenty-three percent of non-cancer controls reported falls in the one-year prior, compared to 26% of MM patients in Cohort 1 and 33% in Cohort 2 ($p = 0.012$). Characteristics of the three cohorts are summarized in Table 1. Among patients with MM (Cohorts 1 and 2) who reported falls, nearly one-third (30%) reported that they had not discussed their falls with their healthcare provider.

Fatigue, depression, poorer general health, numbness in feet, COPD, and cardiac disorders were all associated with increased odds of prior falls on univariate analysis. On multivariate analysis only fatigue, depression, poorer general health, and depression were significantly associated with a report of falls. Patients reporting fatigue had over a two-fold increase in odds of falling [aOR = 2.52 (95% CI = 1.34–4.93); $p = 0.005$] compared to those without. Patients reporting depression had a 90% increase in odds of falling [aOR = 1.90 (95% CI = 1.14–3.18); $p = .014$]. Patients reporting poorer general health had an 86% increase in odds of falling [aOR = 1.86 (95% CI = 1.05–3.36); $p = .037$]. Results from the analyses of factors associated with falls are detailed in Table 2.

At the time of the analysis, 67% of the newly diagnosed MM population (Cohort 1) had expired. Estimated median survival was 41 months (95% CI 33–51 months). In this cohort, prior falls were not significantly associated with survival on univariate or multivariate analysis. Results from the survival analyses are detailed in Table 3.

DISCUSSION

In the present study, we sought to determine the prevalence of falls in older patients with MM, to compare this rate with a cohort of matched controls without cancer, to examine factors associated with falls, and assess the relationship between falls and overall survival. We found that, in older patients recently diagnosed with MM, prior falls were more

prevalent than in matched non-cancer controls, and there was an even higher prevalence of falls in the past year for patients surveyed more than a year subsequent to diagnosis. We found that older adults with MM who reported fatigue, poorer general health or depression had greater odds of reporting a prior fall. We did not find an association between prior falls and survival in our analysis.

To our knowledge, this is the first report demonstrating that older adults with myeloma report a higher rate of prior falls than matched non-cancer controls. MM is associated with an increased risk of falling, occurring in over one-quarter of patients surveyed within a year of their MM diagnosis, and one-third of patients surveyed more than a year after diagnosis. Several studies have shown higher odds of falls in cancer survivors.(5,10) Huang et al showed that the rate of falls was higher in patients with lung and prostate cancer who were surveyed 1 or more years after diagnosis, compared to those surveyed before diagnosis.(16) This increased prevalence of falls in patients with MM post-diagnosis is intriguing, and will require prospective study to understand the relative contribution of toxicity of therapy and symptoms of disease to the increased risk of falls over time.

Falls are potentially preventable, particularly when individuals at greater risk are targeted for intervention.¹⁷ Identification of factors associated with prior falls will inform future predictive models. In this study, depression was significantly associated with falls in this population. Patients reporting depressed mood had a 90% greater odds of reporting a prior fall [aOR 1.90 (95% CI 1.14–3.18)]. This is similar to associations between depression and falls (aORs of 2.4–2.5) reported in other populations of both people with cancer and non-cancer populations.(18,19) Appropriate referral for psychosocial services and adequate treatment of depression are essential in this vulnerable populations.

In our study, self-reported fatigue was associated with increased odds of reporting a prior fall [aOR 2.52 (95% CI 1.34–4.93)]. While two prior studies found no significant association between fatigue and falls in patients with cancer,(20,21) another did find a significant association between fatigue and falls in older adults with cancer.(22) In studies of individuals without cancer, fatigue alone is associated with falls, as is phenotypic frailty, of which self-reported exhaustion is a component.(23–25) The association between fatigue and falls may be directly linked through neuromuscular mechanisms. In one mechanistic study, participants walked on an inclined treadmill, and after fatiguing, older participants exhibited increased sway, slower reaction time, decreased lower leg strength and increased fall risk. (26)

Participants who reported that, overall, their health was fair or poor were 86% more likely to fall [aOR 1.86 (95% CI 1.05–3.36)]. This survey item is nonspecific, asking “In general, would you say your health is: excellent/very good/good/fair/poor?” Respondents may have been taking into account comorbidities or functional status, both of which have been associated with falls in prior studies.(11,22,27–29)

It is notable that the prevalence of numbness in the feet increased from 37% in patients surveyed at the time of diagnosis (cohort 1) to 63% in patients post-diagnosis (cohort 2). Peripheral neuropathy is a common toxicity of MM therapies, particularly thalidomide and

bortezomib.(30–33) Unfortunately, data on patient treatment is not available in this dataset. Numerous studies in other malignancies have shown an association between neurotoxic chemotherapy and falls.(11–13,34) We did find a statistically significant association between neuropathy and falls in univariate analysis, but not on multivariate.

As older adults undergoing cancer therapy receive the majority of their healthcare in the oncology setting, it is imperative that fall-risk be addressed during clinical follow-ups. However, falls assessments are not commonplace; in the current study, nearly one-third of patients who reported a prior fall had not talked with their doctor about falls or walking problems. Guerard *et al* showed in a cohort of over 500 older adults with cancer, while almost 25% had fallen in the prior 6 months, a fall was documented in the medical record in only 10% of those who had fallen, and only 6% were referred for intervention.(35) Because prior falls are strongly predictive of future falls,(36) this highlights a tremendous opportunity for more comprehensive and coordinated care to be provided to our older patients in the oncology clinic.(37)

The strengths of this study include its large sample size derived from an invaluable data source linking clinically confirmed myeloma diagnoses with patient-reported outcomes spanning multiple domains of function, emotional status, comorbidities and quality of life. This dataset also allows comparison to matched controls, allowing comparison of similar individuals without multiple myeloma.

This study also has several limitations. Self-report of falls as an outcome is frequently noted to be unreliable. In a cross-sectional study of falls in older adults with cancer by Overcash *et al*, participants were asked whether they had fallen in the prior 3 months, whether they had fallen since diagnosis, and whether they had fallen in the prior 12 months. More participants reported falls in the prior 3 months than in the prior 12 months, indicating that recall can be unreliable.(38) Consensus groups recommend that falls be assessed prospectively with falls calendars, grounded in a validated definition of falls to minimize subjective bias in what events would constitute a fall.(39)

Another potential limitation of this study is that all participants were Medicare Advantage recipients, potentially limiting generalizability. Some have argued that enrollment of lower cost enrollees was incentivized in Medicare Advantage, potentially selecting for lower risk participants.(40) However, that would suggest that the general population of older patients with MM enrolled in traditional fee-for-service Medicare may be even more vulnerable and may have an even greater risk for falls than that seen in our study. Finally, claims data are not available in the SEER-MHOS database, so additional analyses of treatment, ascertainment of injurious falls and healthcare utilization are not possible. Future study will be required to understand the impact of myeloma treatments and their toxicities, such as neuropathy, on the risk of falls in older adults with myeloma. In addition, further study is needed to understand the impact of falls on patients' quality-of-life and the incidence of fall-related injuries.

CONCLUSION

In conclusion, older adults with MM are at greater risk of falls than their matched peers without MM, and are associated with self-reported depression, fatigue or poorer health. Complications of MM may put them at higher risk of injury resulting from a fall. Despite this, falls assessments are not commonplace during oncology clinical follow-ups, and falls are underreported by the patients in the clinic. Simple but accurate screening assessments are needed to increase implementation of fall-prevention into oncology practices.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Patient Characteristics

	Cohort 1 MM at Diagnosis (n=171)	Cohort 2 MM Post-Diagnosis (n=234)	Cohort 3 Non-Cancer Controls* (n=513)	
Continuous Variables	<i>M (SD)</i>	<i>M (SD)</i>	<i>M (SD)</i>	<i>p</i>
Age	76.4 (8.1)	73.9 (10.6)	76.4 (8.1)	0.001
Categorical Variables	%	%	%	<i>p</i>
Falls	26	33	23	0.012
Race				
White	71	66	71	0.258
Black	15	20	15	
Other	14	14	14	
Gender				
Male	48	58	48	0.026
Female	52	42	52	
Fatigue				
Yes	62	72	53	<0.001
No	38	29	47	
General Health				
Excellent/Very Good/Good	51	35	66	<0.001
Fair/Poor	49	65	34	
Depression				
Yes	27	29	27	0.889
No	73	71	73	
Numbness in Feet				
Yes	37	63	42	<0.001
No	63	38	58	
COPD/Emphysema/Asthma History				
Yes	15	12	17	0.217
No	85	88	83	
Cardiac History				
Yes	21	26	22	0.500
No	79	74	78	
Stroke History				
Yes	10	8	11	0.541
No	90	92	90	

* - Matched to Cohort 1 by age, race, and gender

Table 2
Logistic Regression Analysis of Factors Associated with Falls in Patients with Multiple Myeloma

Independent Variables	Univariate				Multivariate			
	OR	95% CI	Wald χ^2	p	aOR	95% CI	Wald χ^2	p
Age (per year)	1.01	0.98–1.03	0.211	0.646	-	-	-	-
Gender								
Male	REF							
Female	1.25	0.82–1.92	1.07	0.302	-	-	-	-
Fatigue								
No	REF							
Yes	4.52	2.60–8.31	26.14	<0.001	2.640	1.41–5.15	8.72	0.003
Depression								
No	REF							
Yes	2.77	1.74–4.41	17.91	<0.001	1.87	1.13–3.13	5.85	0.016
General Health								
Excellent/Very Good/Good	REF							
Fair/Poor	3.41	2.12–5.60	24.69	<0.001	1.78	1.01–3.19	3.85	0.05
Numbness in Feet								
No	REF							
Yes	1.96	1.27–3.06	9.07	0.003	1.24	0.75–2.04	0.71	0.40
COPD/Emphysema/Asthma History								
No	REF							
Yes	1.91	1.05–3.43	4.57	0.033	1.37	0.69–2.67	0.83	0.36
Cardiac History								
No	REF							
Yes	1.63	1.00–2.62	3.94	0.047	1.22	0.72–2.06	0.55	0.46
Stroke History								
No	REF							
Yes	1.39	0.66–2.83	0.80	0.371	-	-	-	-

OR, Odds Ratio; CI, Confidence Intervals; aOR, adjusted Odds Ratio; REF, reference level

Bolded figures are statistically significant.

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Table 3
Cox Regression Analysis of Mortality in Patients with Newly Diagnosed Multiple Myeloma

Independent Variables	Univariate				Multivariate			
	HR	95% CI	Wald χ^2	p	aHR	95% CI	Wald χ^2	p
Age (per year)	1.05	1.02–1.07	11.88	<0.001	1.05	1.02–1.07	12.18	<0.001
Gender								
Male	REF							
Female	0.73	0.50–1.06	2.74	0.098	0.75	0.51–1.09	2.28	0.131
Falls								
No	REF							
Yes	1.30	0.86–1.97	1.57	0.211	1.44	0.95–2.18	2.91	0.088

HR, Hazard Ratio; CI, Confidence Intervals; aHR, adjusted Hazard Ratio

Bolded figures are statistically significant