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Predictors of falls in older survivors of breast and prostate cancer: A retrospective cohort study of surveillance, epidemiology and end results—Medicare health outcomes survey linkage

Min H. Huang *, Jennifer Blackwood, Monica Godoshian, Lucinda Pfalzer

Physical Therapy Department, School of Health Professions and Studies, University of Michigan-Flint, United States

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ABSTRACT

Objectives: To identify predictors of falls in older breast and prostate cancer survivors.
Methods: This retrospective cohort study analyzed population-based Surveillance, Epidemiology and End Results–Medicare Health Outcomes Survey (SEER-MHOS) linkage. Inclusion criteria were age >65 years at cancer diagnosis, first primary female breast or prostate cancer, cancer staging information available, completion of baseline MHOS during years 2–3 and follow-up MHOS during years 4–5 post-diagnosis, and falls information available. Data from 437 breast and 660 prostate cancer survivors were analyzed. Multivariable logistic regression was constructed to evaluate variables from baseline MHOS with relation to falls from follow-up MHOS. Model accuracy was assessed using area under receiver-operating-characteristic curve (AUC).
Results: At follow-up MHOS, 26% of breast and 22% of prostate cancer survivors reported falls in the past 12 months. In breast cancer, a history of falls (odds ratio (OR) = 4.95, 95% confidence interval (CI) = 2.44–10.04) and sensory impairment in feet (OR = 3.33, 95%CI = 1.51–7.32) were significant predictors of falls. In prostate cancer, a history of falls (OR = 3.04, 95%CI = 1.79–5.15), unmarried (OR = 1.82, 95%CI = 1.12–2.95), lower physical summary score of quality-of-life(OR = 0.96, 95%CI = 0.94–0.98), urinary incontinence (OR = 1.69, 95%CI = 1.08–2.65), older age at diagnosis (OR = 1.05, 95%CI = 1.01–1.09), and shorter time post-diagnosis (OR = 0.96, 95%CI = 0.93–0.99) were significant predictors of falls. AUC was 0.67 and 0.77 for breast and prostate cancer, respectively, indicating moderate accuracy of models in detecting fallers.
Conclusions: Asking older breast and prostate cancer survivors about falls in the past 12 months is imperative in fall prevention. Further examination of deficits specific to each cancer is necessary to assess fall risks.

1. Introduction

Falls are a serious public health problem and the leading cause of injury and death in older adults [1]. In 2014, there were estimated 29 million falls, resulting in seven million injuries and $31 billion in Medicare costs [1]. Late or long-term side effects of cancer and its treatments may increase fall risk in older cancer survivors [2–5]. Research of population-based data indicate that older cancer survivors had significantly higher fall rates than individuals without cancer (26% vs. 22% in one study [6] and 33% vs. 29% in another [7]). In older cancer survivors, falls are associated with lower health-related quality of life (HRQOL), and a significance decline in HRQOL over time [8,9]. Research about falls in older cancer survivors is needed to improve the quality of survivorship care [10].

Risk factors of falls are well-established in older adults living in the community [11–13]. Many of these factors, including dependence in activities of daily living [14,17] and a history of falls [16,17] have been linked to falls in older cancer survivors. However, other risk factors, such as age, polypharmacy, and opioid use were not predictive of falls in the oncology population [14,16,17]. A population-based study of older survivors with mixed cancer diagnoses reported that functional limitations, impaired standing balance, and self-reported balance difficulty were significant predictors of falls during a 2-year follow-up [14]. The study did not include a history of falls as a potential risk factor of falls in the analysis [14]. In another study of community-dwelling older cancer survivors, a history of falls in the past 12 months significantly predicted falls [15]. In contrast, demographics, comorbidity, balance and gait speed, impaired sensation in feet, multiple medications, time since cancer diagnosis, and chemotherapy were not predictive of falls in these survivors [15]. Taken together, studies about predictors of falls in older cancer survivors have revealed inconsistent findings [14,15,17]. Risk factor profiles for falls in this population remain to be investigated.

Previous studies of factors linked to falls in older cancer survivors predominantly used cross-sectional design, precluding the identification

* Corresponding author.
E-mail address: mhhuang@umflint.edu (M.H. Huang).

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of predictors for falls [17]. Additionally, while cancer sequelae emerge over time and differ widely across diagnoses [18,19], prior analyses were mostly based on mixed cancer types across the survivorship trajectory [8,17]. To address these limitations, this study aimed to evaluate factors predictive of falls in older breast or prostate cancer survivors. These two diagnoses were chosen because they are the leading cancer in older adults [20]. Our objective was to identify demographics, health and function and cancer-related variables at baseline that independently contribute to the prediction of falls at two-year follow-up.

2. Materials and methods

2.1. Data source

This study was approved by the Institutional Review Board of the University of Michigan-Flint. Surveillance, Epidemiology and End Results–Medicare Health Outcomes Survey (SEER-MHOS) linkage [21] was the data source for this study. SEER collects information related to cancer diagnosis, stage, time of diagnosis, histology, and treatment, except for chemotherapy and hormonal therapy [21]. MHOS gathers demographics and information about health problems, chronic conditions, function, symptoms, and health-related quality of life from Medicare Advantage (MA) plan beneficiaries [21]. Each year the MHOS was administered to 1000 randomly selected beneficiaries from each Medicare Advantage Organization (MAO) from 1998 to 2006, and the sample size for each MAO was increased to 1200 from 2007 [21,22]. Each cohort of SEER-MHOS was comprised of beneficiaries of MAO who were randomly sampled to complete MHOS at baseline, and resurveyed two years later [21–23]. In previous research, response rates were 64%–72% for baseline survey, and 76%–85% for follow-up survey [21]. The impact on the estimates of health status as a result of nonresponse bias was reported to be minimal [24]. The Centers for Medicare & Medicaid Services added questions about fall risks to MHOS starting from 2006 [22]. Therefore, only data from cohorts 9–14 (January 1st, 2006 – December 31st, 2013) with completed baseline and follow-up MHOS about fall risks were extracted for this study.

2.2. Design and Setting

This study was a retrospective cohort study analyzing national, population-based data.

2.3. Participants

Fig. 1 shows the study sample inclusion. Inclusion criteria were age ≥ 65 years at time of cancer diagnosis, first primary female breast or prostate cancer, cancer staging information available, completion of baseline MHOS during years 2–3 years post-cancer diagnosis and follow-up MHOS during years 4–5 post-diagnosis, and information about falls available from MHOS.

2.4. Main Outcome

Primary outcome was a report of falls in the past 12 months from follow-up MHOS. Falls information was obtained from the MHOS question: "A fall is when your body goes to the ground without being pushed. Did you fall in the past 12 months?" Responses to this question were coded as "0 = no" and "1 = yes" to create a dichotomous outcome.

2.5. Predictor variables

We chose variables based on previous research [11,14,17,25]. However, we were limited to information available in SEER-MHOS. The list of variables with detailed definition and coding is provided in Table 1. Variables were obtained from baseline MHOS, including demographics, variables related to health and function, and cancer-related variables.

Demographics included age at MHOS administration, race, marital status, education, and household income. Health- and function-related variables included calculated body mass index (BMI), number of comorbidities, number of dependence in six activities of daily living (ADL) (bathing, dressing, eating, getting in/out of chairs, walking, and using toilet), fatigue, depression, urinary incontinence, sensory impairments in feet, physical (PCS) and mental summary scores (MCS) of Veterans RAND 12-Item Health Survey (VR-12) [25]. VR-12 is a 12-item, generic, self-administered health survey used to measure health-related quality of life and disease burden. VR-12 evaluates eight physical and mental health domains (general health perceptions, physical function, role limitations due to physical and emotional problems, bodily pain, energy-fatigue, social function, and mental health). Scores from VR-12 items are summarized into the PCS and MCS [26]. Cancer-related variables were age at cancer diagnosis, time of baseline MHOS administration since cancer diagnosis, cancer stage [27], surgery, and radiation.

2.6. Statistical analysis

All analyses were conducted separately for each cancer type. Descriptive statistics were calculated to describe sample characteristics. According to Hosmer and Lemeshow [28], minimizing the number of variables in the multivariable regression model results in a model that is more numerical stable, more easily adopted for use, and less dependent on the observed data. To avoid overfitting the multivariable model and to build a parsimonious model that best fits the data, we used stepwise approach in selecting model variables [28] as described below: Step 1, univariable logistic regression was used to assess the association of each baseline variable with falls at follow-up. Variables with a p-value ≤0.25 from univariable regression were included as candidate variables for a first multivariable logistic regression model to identify independent predictors of falls. Step 2, we fitted the first multivariable model containing all variables identified from Step 1 univariable analyses. Variables with a p-value ≥0.05 in this multivariable model were removed, and we refitted a new model with the remaining variables. Step 3, variables that were removed from Step 2 were then rechecked one at a time for model inclusion by examining changes in magnitudes of variable coefficients and variable significance based on the Wald statistic p-value or the partial likelihood ratio test as appropriate. This process of removing, refitting and rechecking variables, cycling through Steps 2 and 3, was repeated until all important variables were retained in the multivariable model. Step 4, variables that were not selected at Step 1 were added into the multivariable model obtained at the conclusion of Step 3 to recheck for model inclusion [28]. We only fit main effect model without interactions as the final multivariable model. Multicollinearity was determined with covariate correlation matrix ($r \geq 0.6$) and variance inflation factor (VIF ≥4) [29]. Because age at MHOS administration and age at cancer diagnosis were highly correlated, only age at diagnosis was included in multivariable regression. We obtained Nagelkerke R^2 values to approximate the proportion of variance explained by variables in the final multivariable model. Model fit was assessed using Hosmer and Lemeshow test [28]. Receiver operating characteristic (ROC) curves were generated for the final multivariable logistic regression model. Area under ROC curve (AUC) was calculated to evaluate accuracy of the final multivariable model in detecting survivors with falls (AUC = 0.5, random chance; AUC = 0.7–0.9, moderate discrimination; and AUC = 1.0, perfect discrimination) [30]. To examine the relative contribution of each predictor in the final multivariable model, odds ratio (OR) of each variable was converted to Cohen's d for effect size using the equation: $d = \log(OR) \times \left(\frac{\sqrt{3}}{\pi}\right)$ [31]. Cohen's d of 0.2, 0.5, and 0.8 corresponded to small, medium, and large effect size, respectively [32]. Statistical analyses were performed using

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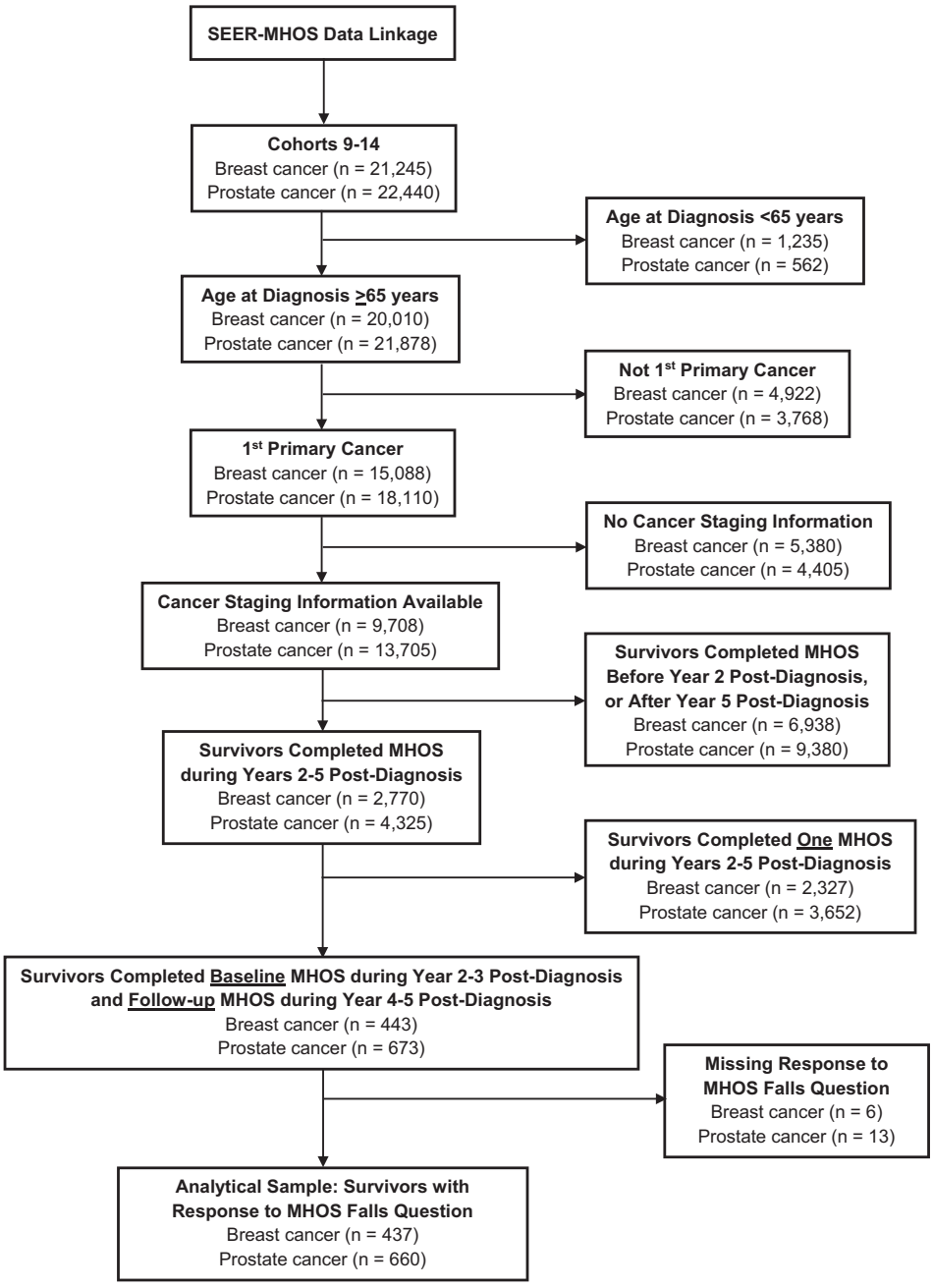

Fig. 1. Flowchart of study sample. The sample was from cohorts 9–14 (Medicare Health Outcomes Survey completed from January 2006 to December 2013) of the Surveillance, Epidemiology and End Results Program and Medicare Health Outcomes Survey (SEER-MHOS) data linkage. Survivors were excluded from the analysis if they did not meet the following criteria: age >65 years at time of cancer diagnosis, first primary female breast or prostate cancer, cancer staging information available, baseline MHOS completed during years 2–3 post-cancer diagnosis and follow-up MHOS completed during years 4–5 post-diagnosis, and response to MHOS falls question available.

IBM-SPSS 24 (IBM Corp., Armonk, NY). Two-sided significance level was $p < 0.05$.

3. Results

3.1. Sample characteristics

Baseline characteristics of survivors are displayed in Table 2 for breast ($n = 437$) and Table 3 for prostate cancer ($n = 660$). Average age at cancer diagnosis was 72.5 years (standard deviation (SD) = 6.26) in breast and 71.9 years (SD = 5.80) in prostate cancer. For both breast and prostate cancer, baseline MHOS was administered on average 24 months post-cancer diagnosis (SD = 6.7). Over 70% of survivors were white in both breast ($n = 325$) and prostate ($n = 477$) cancer. Most prostate cancer survivors were married at the baseline (74%). In contrast, only 43% of breast cancer survivors were married at the baseline. A majority of survivors had localized cancer stage (60% in breast and 87% in prostate cancer). Most breast cancer survivors received surgery (97%) and radiation (53%). Surgery and radiation was performed in 29% and 44% of prostate cancer survivors, respectively. At baseline, 22% ($n = 96$) and 18% ($n = 118$) of breast and prostate cancer survivors reported falls in the past 12 months, respectively. At 2-year follow-up, survivors with falls in the past 12 months increased to 26% ($n = 113$) in breast cancer and 22% ($n = 142$) in prostate cancer. Approximately 53% ($n = 48$) of breast cancer survivors and 48% ($n = 57$) of prostate cancer survivors with a history of falls at baseline also reported falls in

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Table 1
List of variables, detailed definition and coding.

Variable	Definition	Coding (response)
Gender	Gender reported in MHOS.	1 = Men 2 = Women
Race	Race was obtained from enrollment data base maintained by Center for Medicare and Medicaid Services.	1 = White 2 = Black or other race
Marital status	Marital status reported in MHOS.	1 = Married 2 = Unmarried (divorced, separated, widowed, or never married)
Education	Education level reported in MHOS.	1 ≤High school 2 = High school or some college 3≥ College
Household Income	Household income reported in MHOS.	1 ≤$30,000 2 = $30,000–$49,999 3≥ $50,000
Comorbidity	Total number of the following chronic conditions: arthritis, osteoporosis, emphysema/asthma/chronic obstructive pulmonary disease, angina, congestive heart failure, myocardial infarction, stroke, hypertension, diabetes, and low back pain.	
ADL dependence	Total number of ADL with difficulty (bathing, dressing, eating, getting in or out of chairs, walking, and using toilet) was based on response to the MHOS question: "Because of a health or physical problem, do you have any difficulty doing the following activities without special equipment or help from another person?" A response of "No, I do not have difficulty" corresponds to ADL independence. A response of "Yes, I have difficulty" or "I am unable to do this activity" corresponds to ADL dependence.	0 = no ADL dependence 1 = 1 ADL dependence 2 = 2 ADL dependence 3 = 3 ADL dependence 4 = 4 ADL dependence 5 = 5 ADL dependence 6 = 6 ADL dependence
Fatigue	Fatigue during the past 4 weeks was based on response to the MHOS question: "How much of the time during the past 4 weeks…Did you have a lot of energy?"	1 = No fatigue ("all of the time", "most of the time", or "of a good bit of the time") 2 = Yes fatigue ("some of the time", "a little of the time", or "of none of the time")
Depression	Depression was based on a positive response to either one of the two MHOS questions: "In the past year, have you had 2 weeks or more during which you felt sad, blue or depressed; or when you lost interest or pleasure in things that you usually cared about or enjoyed?", or "In the past year, have you felt depressed or sad much of the time?"	1 = No depression (no to both questions) 2 = Yes, with depression (yes to either question)
Urinary incontinence	Urinary incontinence was based on response to the MHOS question: "Many people experience problems with urinary incontinence, the leakage of urine. In the past 6 months, have you accidentally leaked urine?"	1 = No 2 = Yes
Sensory impairment in feet	Sensory impairment in feet was based on a positive response to any of the three MHOS questions: "During the past 4 weeks, how much of the time have you had any of the following problems with your legs and feet? (1) Numbness or loss of feeling in your feet", (2) "Tingling or burning sensation in your feet especially at night", or (3) "Decreased ability to feel hot or cold with your feet"	1 = Not impaired ("a little of the time", or "none of the time") 2 = Yes impaired ("all of the time", "most of the time", or "some of the time")
Cancer stage	Stage was determined by SEER summary stage 2000, derived from Collaborative Stage.	1 = In situ 2 = Localized 3 = Regional or distant
Radiation	Radiation therapy performed as part of the first course of cancer treatment from SEER.	1 = No radiation 2 = Yes, with radiation
Surgery	Surgery of primary site that removes and/or destroys tissue of the primary site performed as part of the initial work-up or first course of therapy from SEER.	1 = No surgery 2 = Yes, with surgery

Abbreviations: MHOS, Medicare Health Outcomes Survey; ADL, activities of daily living; SEER, Surveillance, Epidemiology, and End Results.

follow-up survey. Walking or balance difficulty was reported by 32% ($n = 141$) of breast and 24% ($n = 160$) of prostate cancer survivors at the baseline, and increased to 40% ($n = 178$) in breast and 29% ($n = 192$) in prostate cancer at the follow-up. Among survivors with walking or balance difficulty at the baseline, 33% ($n = 47$) and 43% ($n = 68$) reported falls at the follow-up in breast and prostate cancer, respectively.

3.2. Univariable analyses

Crude odds ratio (OR) for falls for each variable from univariable logistic regression is shown in Table 2 for breast cancer and Table 3 for prostate cancer. In both breast and prostate cancer, a history of falls, self-reported difficulty in balance or walking, higher comorbidity, lower PCS or MCS, and higher number of ADL dependence at baseline were significantly associated with higher fall risk at follow-up. In breast cancer, sensory impairment in feet also significantly increased fall risk. In prostate cancer, age at baseline MHOS administration, white race, being unmarried, depression, older age at cancer diagnosis, shorter time post-cancer diagnosis, and treatment without surgery were associated with higher fall risk.

3.3. Multivariable analyses

On the basis of results from univariable regression, candidate variables with a p-value ≤0.25 were entered into multivariable regression to evaluate independent predictors of falls through stepwise selection of variables. There was no collinearity between independent variables in multivariable models for either cancer.

Multivariable regression showed that in breast cancer, a history of falls in the past 12 months and sensory impairment in feet were independent predictors of falls (χ^2 (2)=31.1, $p < 0.001$) (Table 4). The model explained 21% (Nagelkerke R^2) of the variance in falls, and correctly classified 73% of survivors by their report of no falls or falls at the follow-up. AUC for the final multivariable model was 0.67, which was slightly below moderate accuracy in detecting breast cancer survivors with falls. Survivors with a history of falls at baseline were almost 5 times more likely to fall at follow-up than those without a history of falls (OR = 4.95, 95%CI = 2.44–10.04, $p < 0.001$). Sensory impairment in feet at baseline was associated with a three-fold increase of fall risk (OR = 3.33, 95%CI = 1.51–7.32, $p = 0.003$). Cohen's d was 0.38 for a history of falls and 0.29 for sensory impairment, indicating moderate effect size. Based on the final multivariable model, for breast cancer

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Table 2
Sample characteristics at baseline and crude odds ratio (OR) for falls from univariable logistic regression in breast cancer.

Variable	Breast				
	All	Falls at follow-up		Crude OR (95% CI)	*p*-value
		No ($n = 324$)	Yes (n = 113)		
History of falls	95	47	48	**4.37 (2.69–7.11)**	<0.001
Self-reported balance or walking difficulty	141	94	47	**1.81 (1.16–2.83)**	0.009
Age at baseline, year (SD)	75.1 (6.22)	74.9 (5.99)	75.7 (6.87)	1.02 (0.99–1.06)	0.231
White race	325	237	88	1.30 (0.78–2.13)	0.322
Divorced/separated/widows/never married	251	189	62	0.87 (0.57–1.35)	0.538
Education					
<High school	95	73	22	1.00	
High school or some college	266	196	70	1.19 (0.68–2.05)	0.545
≥College	68	49	19	1.29 (0.63–2.62)	0.488
Income					
≤$19,999	166	125	41	1.00	
$20,000–$39,999	136	102	34	1.02 (0.60–1.72)	
≥$40,000	57	39	18	1.41 (0.73–2.72)	
Body mass index (SD)	27.7 (5.83)	27.6 (5.62)	28.1 (6.45)	1.02 (0.98–1.05)	0.409
Comorbidity (SD)	2.5 (1.60)	2.4 (1.56)	3.0 (1.68)	**1.26 (1.10–1.45)**	0.001
Number of ADL dependence	0.8 (1.40)	0.5 (1.14)	1.6 (1.95)	**1.31 (1.14–1.52)**	<0.001
Depression	45	31	14	1.41 (0.72–2.76)	0.319
Urinary incontinence	219	148	71	2.27 (0.89–5.80)	0.086
Sensory impairment in feet	61	35	26	**2.56 (1.50–4.51)**	0.001
PCS (SD)	39 (11.7)	40 (11.3)	36 (12.6)	**0.97 (0.96–0.99)**	0.003
MCS (SD)	53 (10.3)	54 (9.6)	50 (11.7)	**0.97 (0.95–0.99)**	0.002
Age at cancer diagnosis, year (SD)	72.5 (6.26)	72.3 (6.01)	72.3 (6.01)	1.02 (0.99–1.05)	0.263
Time of baseline MHOS administration post-cancer diagnosis, m (SD)	24 (6.7)	24 (6.7)	25 (6.8)	1.02 (0.99–1.06)	0.194
Cancer stage					
In situ	72	56	16	1.00	
Localized	262	192	70	1.28 (0.69–2.37)	0.440
Regional/distant	103	76	27	1.24 (0.61–2.52)	0.547
Surgery	424	314	110	1.05 (0.28–3.95)	0.941
Radiation	233	179	54	0.71 (0.46–1.09)	0.113

Abbreviation: MHOS, Medicare Health Outcomes Survey; PCS, physical summary score of Veterans RAND 12-Item Health Survey (VR-12); MCS, mental summary score of VR-12; ADL, activities of daily living; CI, confidence interval; SD, standard deviation; OR, odds ratio.
ORs in bold text are statistically significantly different between survivors who reported no falls and who reported falls in the past 12 months at follow-up MHOS. The corresponding p-value for each variable was obtained from univariable logistic regression with falls at follow-up as primary outcome.

survivors with no risk factors, the probability of falls over 12 months would be 46%; and for breast cancer survivors with a history of falls and sensory impairment, the predicted probability of falls would increase to 93%.

In prostate cancer, the independent predictors in the final multivariable model were a history of falls, unmarried, lower PCS, urinary incontinence, older age at cancer diagnosis, and shorter time post-cancer diagnosis ($\chi^2(6)=105.1$, $p < 0.001$) (Table 5). The model explained 24% (Nagelkerke R^2) of the variance in falls, and correctly classified 81% of survivors by self-reported falls at the follow-up. AUC for the final multivariable model was 0.77, indicating moderate accuracy in identifying prostate cancer survivors with falls. Fall risk increased by three-fold in prostate cancer survivors with a history of falls (OR = 3.04, 95%CI = 1.79–5.15, $p < 0.001$), and by almost two-fold in those who were not married (OR = 1.82, 95%CI = 1.12–2.95, $p = 0.015$). Survivors with urinary incontinence were 1.69 times more likely to fall than those without incontinence (OR = 1.69, 95%CI = 1.08–2.65, $p = 0.021$). Cohen's d was 0.27 for a history of falls, indicating a moderate effect size, 0.14 for being unmarried and 0.13 for urinary incontinence, both corresponding to a small effect size. Lower PCS (OR = 0.96, 95% CI = 0.94–0.98, $p < 0.001$), older age at cancer diagnosis (OR = 1.05, 95%CI = 1.01–1.09, $p = 0.01$), shorter time post-cancer diagnosis (OR = 0.96, 95%CI = 0.93–0.99, $p = 0.011$) were associated with a slight increase in fall risk (4%–5%) and a very small effect size (Cohen's d = 0.01). Based on the final multivariable regression model, for prostate cancer survivors with baseline characteristics similar to those without falls during follow-up (i.e. no history of fall, being married, PCS = 43, no incontinence, aged 71.4 years at cancer diagnosis, and 25 months post-cancer diagnosis), the predicted probability of falls over 12 months would be 65%; and for prostate cancer survivors with baseline characteristics similar to those with falls during follow-up (i.e. a history of fall, being unmarried, PCS = 36, urinary incontinence, aged 73.7 years at cancer diagnosis, and 23 months post-diagnosis), the predicted probability of falls would increase to 88%.

4. Discussion

This study is the first to evaluate demographic, health and function, and cancer-related predictors of falls in older survivors who were within 5 years post-diagnosis of breast and prostate cancer, the most prevalent cancers in older adults [20]. Using national, population-based data, we demonstrated that a history of falls at baseline was an independent predictor of future falls in both breast and prostate cancer. Other independent predictors of falls differed between cancer types, highlighting the need to further examine deficits that may be specific to each cancer and its treatment. Asking about the history of falls in the past 12 months is the essential first step in fall risk screening as recommended by the American Geriatrics Society/British Geriatrics Society [11] and Centers for Disease Control and Prevention STEADI (Stopping Elderly Accidents, Deaths, & Injuries) Initiative [33]. Current findings suggest that integrating the geriatric care model into oncology practice [10,34] for screening, assessing, and managing fall risk may have important clinical implications in fall prevention for older breast and cancer survivors.

In previous studies, the proportion of cancer survivors with falls ranged widely across settings. Falls were reported in 18%–27% of inpatient survivors [35,36], 48% of survivors receiving palliative care [37], 59% of survivors living in the community [15], and 25%–26% of Medicare beneficiaries with any cancer diagnosis [6,8]. In this study, 22%–26% of survivors reported falls in the past 12 months at follow-up. Methods for measuring falls likely contributed to variations in fall rates across studies. Studies tracking falls prospectively by weekly phone calls [37]

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Table 3
Sample characteristics at baseline and crude odds ratio (OR) for falls from univariable logistic regression in prostate cancer.

Variable	Prostate				
	All	Falls at Follow-Up		Crude OR (95% CI)	*p*-Value
		No ($n = 516$)	Yes ($n = 144$)		
History of falls	118	61	57	**4.94 (3.22–7.60)**	<0.001
Self-reported balance or walking difficulty	160	92	68	**4.22 (2.83–6.30)**	<0.001
Age at baseline MHOS, year (SD)	74.5 (5.81)	73.9 (5.48)	76.1 (6.62)	**1.06 (1.03–1.10)**	<0.001
White race	477	361	116	**1.79 (1.12–2.78)**	0.013
Divorced/separated/widows/never married	171	119	52	**1.92 (1.29–2.85)**	0.001
Education					
<High school	134	112	22	1.00	
High school or some college	324	254	70	1.40 (0.83–2.38)	0.210
≥College	189	142	47	1.69 (0.96–2.96)	0.070
Income					
≤$19,999	136	107	29	1.00	
$20,000–$39,999	298	233	65	1.03 (0.63–1.69)	0.910
≥$40,000	152	114	38	1.23 (0.71–2.13)	0.460
Body mass index (SD)	27.5 (4.37)	27.4 (4.13)	27.9 (5.12)	1.03 (0.99–1.07)	0.195
Comorbidity (SD)	2.2 (1.70)	2.0 (1.68)	2.7 (1.70)	**1.25 (1.12–1.40)**	<0.001
Number of ADL dependence	**0.7 (1.43)**	**1.1 (0.05)**	**2.0 (1.63)**	**1.55 (1.38–1.75)**	<0.001
Depression	42	24	18	**2.88 (1.51–5.46)**	0.001
Urinary incontinence	285	200	85	**1.89 (1.00–3.58)**	0.050
Sensory impairment in feet	75	54	21	1.49 (0.87–2.57)	0.148
PCS (SD)	42 (11.5)	43 (11.2)	36 (10.8)	**0.95 (0.93–0.96)**	<0.001
MCS (SD)	52 (9.9)	53 (9.1)	50 (12.0)	**0.97 (0.95–0.98)**	<0.001
Age at cancer diagnosis, year (SD)	71.9 (5.80)	71.4 (5.47)	73.7 (6.57)	**1.07 (1.04–1.10)**	<0.001
Time of baseline MHOS administration post-cancer diagnosis, m (SD)	24 (6.7)	25 (6.7)	23 (6.4)	**0.95 (0.93–0.98)**	0.001
Cancer stage					
In situ	0[a]	0[a]	0[a]		
Localized	577	447	130	1.00	
Regional/distant	83	69	14	0.70 (0.38–1.28)	0.245
Surgery	193	164	29	**0.53 (0.34–0.83)**	0.005
Radiation	289	229	60	0.87 (0.60–1.26)	0.460

Abbreviation: MHOS, Medicare Health Outcomes Survey; PCS, physical summary score of Veterans RAND 12-Item Health Survey (VR-12); MCS, mental summary score of VR-12; ADL, activities of daily living; CI, 95% confidence interval; SD, standard deviation; OR, odds ratio.
ORs in bold text are statistically significantly different between survivors with and without falls in the past 12 months at follow-up MHOS. The corresponding *p*-value for each variable was obtained from univariable logistic regression with falls at follow-up as primary outcome.
[a] There were no prostate cancer survivors with the cancer stage "in situ".

or daily calendar [15] reported higher fall rates. In contrast, fall rates recorded retrospectively using questionnaires were lower [6,8]. Recall bias and underreporting [38] in MHOS data about falls is possible. Additionally, previous studies of Medicare beneficiaries included older survivors with any cancer [6,8]**.** Survivors of cancer with high symptoms and disease burden, such as lung cancer, may be more likely to fall [39]. Lastly, previous studies measured falls over different time frames, ranging from 3 months [16] to 2 years [14]**,** making comparisons of fall rates across studies difficult.

We demonstrated that a history of falls was an important predictor of falls, leading to a five-fold and three-fold increase of fall risk in breast and prostate cancer, respectively. This finding is consistent with previous research in the geriatric [11] and oncology populations across early to advanced cancer stages [14,15,37,40]. Winters-Stone et al. [41] investigated risk factors of falls in 59 breast cancer survivors (age = 59 ± 9.7 years) who were within 2 years of completing chemotherapy. They reported that a history of falls in the past year was not predictive of falls that occurred over a 6-month period [41]. Compared to the current study, the study by Winters-Stone et al. [41] had younger subjects, smaller sample size, and shorter follow-up time of falls. In another prospective study of prostate cancer survivors aged 65 years and over, a prior history of falls, but not balance performance was identified as an independent predictor of future falls over 12 months [42]. This study further supports that oncology clinicians need to ask about falls when treating older breast and prostate cancer survivors.

Current findings suggest that in breast cancer, patient-reported symptoms of sensory impairment in feet were predictive of future falls. Peripheral sensation is the most important sensory system in maintaining balance and preventing falls [43]. While this study could not determine the underlying etiology, previous studies indicate that impaired sensation is a risk factor for falls in older adults [44] and in

Table 4
Final multivariable regression model for predicting falls in breast cancer.*

Intercept and predictors	β Coefficient	SE	OR (95% CI)	*p*-value	Cohen's d
Intercept	−0.16	0.21			
History of falls	1.6	0.36	4.95 (2.44–10.04)	<0.001	0.38
Sensory impairment in feet	1.2	0.4	3.33 (1.51–7.32)	0.003	0.29

AUC (95% CI) = 0.67 (0.60–0.73), $\chi^2(2)=31.1$, $p < 0.001$
Abbreviation: PCS, physical summary score of Veterans RAND 12-Item Health Survey (VR-12); SE, standard error; OR, odds ratio; CI, confidence interval; AUC, area under receiver operating characteristic (ROC) curve.
Cohen's d for effect size was converted from OR using the equation: $d = \log(OR) \times (\frac{\sqrt{3}}{\pi})$ [33]. Positive values indicate the direction of predicting higher fall risk; negative values indicate the direction of predicting lower fall risk.
* The predicted probability of falls can be calculated using the following formula: $P(\text{fall}) = \exp.(-0.16 + \text{history of falls} \times 1.6 + \text{sensory impairment in fee} \times 1.2) / (1 + \exp.(-0.16 + \text{history of falls} \times 1.6 + \text{sensory impairment in fee} \times 1.2))$. Predictor value is one when present and zero when absent.

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Table 5
Final multivariable regression model for predicting falls in prostate cancer.*

Intercept and Predictors	β Coefficient	SE	OR (95% CI)	*p*-value	Cohen's d
Intercept	−1.54	1.52			
History of falls	1.11	0.27	3.04 (1.79–5.15)	<0.001	0.27
Unmarried	0.6	0.25	1.82 (1.12–2.95)	0.015	0.14
PCS	−0.04	0.01	0.96 (0.94–0.98)	<0.001	−0.01
Urinary incontinence	0.53	0.23	1.69 (1.08–2.65)	0.021	0.13
Age at cancer diagnosis	0.05	0.02	1.05 (1.01–1.09)	0.010	0.01
Time since cancer diagnosis	−0.04	0.02	0.96 (0.93–0.99)	0.011	−0.01

AUC (95% CI) = 0.77 (0.73–0.82), $\chi^2(6)=105.1$, $p < 0.001$

Abbreviation: PCS, physical summary score of Veterans RAND 12-Item Health Survey (VR-12); SE, standard error; OR, odds ratio; CI, confidence interval; AUC, area under receiver operating characteristic (ROC) curve.

Cohen's d for effect size was converted from OR using the equation: $d = \log(OR) \times \left(\frac{\sqrt{3}}{\pi}\right)$ [33]. Positive values indicate the direction of predicting higher fall risk; negative values indicate the direction of predicting lower fall risk.

* The predicted probability of falls can be calculated using the following formula: $P(\text{fall}) = \exp.(-1.54 + \text{history of falls} \times 1.11 + \text{unmarried} \times 0.6 + \text{PCS} \times (-0.04) + \text{urinary incontinence} \times 0.53 + \text{age at cancer diagnosis} \times 0.05 + \text{time since cancer diagnosis} \times (-0.04)) / (1 + \exp.(-1.54 + \text{history of falls} \times 1.11 + \text{unmarried} \times 0.6 + \text{PCS} \times (-0.04) + \text{urinary incontinence} \times 0.53 + \text{age at cancer diagnosis} \times 0.05 + \text{time since cancer diagnosis} \times (-0.04))$. Predictor value is one when present and zero when absent for dichotomous variables, including history of falls, unmarried, and urinary incontinence.

cancer survivors treated with neurotoxic chemotherapy [45,46]. Research has linked both sensory and motor symptoms of chemotherapy induced peripheral neuropathy with falls in cancer survivors [3,46]. Fall risk in cancer survivors is increased with higher cumulative dosage of chemotherapy and use of neurotoxic agents [45,46]. Long-term problems related to neuropathy for up to 9 years post-diagnosis have been reported in breast cancer survivors after the use of paclitaxel [47]. Identifying sensory impairment during survivorship care, particularly during and after the exposure to neurotoxic chemotherapy, is important in order to detect fall risk in older breast cancer survivors.

Similar to a previous study [42], we found that being unmarried was a significant predictor of falls in older prostate cancer survivors [42]. It has been suggested that marriage may offer health benefits in men in late adulthood [48,49]. Spousal relationship was found to encourages men to seek and access medical care before and after the diagnosis of prostate cancer [48]. In this connection, married prostate cancer survivors may be more likely to receive interventions that contribute to reduced fall risk.

Cancer negatively impacts HRQOL, particularly in physical health [50–52]. We confirmed that physical component summary (PCS) score of Veterans RAND 12-item Health Survey (VR-12) was an important predictor of falls in prostate cancer survivors. Previous research showed that in older survivors of mixed cancer diagnoses, physical domain of HRQOL was associated with falls, whereas walking speed, balance confidence, and balance performance were not [9]. In contrast to patient-reported outcomes in physical health, performance-based measures of physical function were not consistently linked to falls in prostate cancer survivors. A cross-sectional study of older prostate cancer survivors undergoing androgen deprivation therapy (ADT) reported that impairment in ADL and physical performance, including walking, balance, and chair stands, was associated with falls [53]. In another prospective study, after adjusting for covariates in multivariable analyses, physical performance measures for walking, balance, and strength were not predictive of falls in prostate cancer survivors, regardless of their use of ADT [42]. HRQOL tools are patient-reported outcome measures (PROM) used to evaluate perceived health, function, and disease burden [26]. PROM facilitate communication between patients, family, and clinicians to make informed healthcare decisions that are important to patients, and are particularly useful in the geriatric oncology population [54]. Our findings suggest that PCS from VR-12 may reveal valuable and patient-centered information about symptoms and function relevant to fall risk in older prostate cancer survivors.

Urinary incontinence is a complication of prostate cancer treatment [55] and a geriatric syndrome associated with prostate cancer [6]. Current findings confirm urinary incontinence as a fall risk factor in prostate cancer. Substantive evidence supported the link between urinary incontinence and falls in older adults [44,56,57] and cancer survivors [37,58]. Previous research reported that urinary incontinence was an independent factor associated with falls in women but not men, which likely resulted from a higher prevalence of incontinence in women (23%) than men (9%) [57]. In a prior SEER-MHOS study, prevalence of urinary incontinence was higher in breast and prostate cancer survivors compared to non-cancer controls [59]. In this study, urinary incontinence was an independent predictor of falls in prostate cancer, but not in breast cancer.

Age is a strong predictor of falls in older adults [44]. In advanced stage of cancer, age was not associated with falls, but brain metastasis, cancer-related pain, depression, and benzodiazepine dose were significant predictors of falls [36]. We found that in prostate cancer, the odds for falling increased by 5% with each additional year of age at cancer diagnosis. Chronological age alone is a significant factor in influencing clinical decision at cancer diagnosis [60]. With aging and increased comorbidity, older adults may not be able to tolerate toxicities from aggressive cancer treatment [60]. The interplay of age at cancer diagnosis and cancer treatment with relation to falls needs to be investigated further. The increase in fall risk associated with age at cancer diagnosis was very small in comparison to a history of falls, unmarried, or incontinence in prostate cancer. Screening for fall risk remains pertinent even among prostate cancer survivors who were older at time of cancer diagnosis.

We found that longer time post-cancer diagnosis at baseline showed a small but significant protection against falls in prostate cancer. It may be possible that prostate cancer survivors continued to improve health and function during years 2–3 post-diagnosis at baseline [61,62], and consequently had lower fall risk over time. Alternatively, survivors with better outcomes after cancer diagnosis may live longer, have less symptom burden and fewer comorbidities that contribute to higher fall risk. Healthier survivors would likely be alive to participate in MHOS at a later time post-cancer diagnosis.

Lastly, AUC in the final multivariable regression models was moderate in detecting survivors with falls in breast and prostate cancer. We did not aim to develop a prediction model for falls. However, current findings provide the foundation for future research in developing and evaluating risk prediction models that are specific to each cancer type and incorporate medical examination data, patient-reported outcomes and objective measurements. Prediction models with validated sensitivity, specificity, likelihood ratios, and other discriminative indices can guide fall prevention strategies in oncology practice.

This study has limitations. First, medication and cancer treatment information, particularly chemotherapy and hormonal therapy is not available from SEER-MHOS [21]. Second, falls was obtained by subjective report in response to questions in MHOS. Recall bias and underreporting of falls cannot be ruled out [38]. Third, every year Medicare Advantage beneficiaries are randomly sampled to participate in

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MHOS. Compared with other Medicare beneficiaries, participants in Medical Advantage plans have more risk factors and poorer function [63]. Generalization of findings needs to consider the characteristics of this population. Fourth, information from objective measurements, such as physical performance, balance skills, or gait speed, was not available in SEER-MHOS linkage. Lastly, we only analyzed data from breast and prostate cancer. Because the impact of cancer and its treatment is diverse across different diagnoses, risk factors profiles for falls likely differ in other cancer types.

5. Conclusions

In older breast and prostate cancer survivors, a history of falls in the past 12 months is an important predictor of future falls. Other fall predictors varied between the two cancer types. Oncology clinicians need to inquire about the history of falls and consider other fall risk factors unique to each cancer and its treatment. In breast cancer, particularly among survivors treated with neurotoxic chemotherapy, sensory examination is important in fall risk screening, in addition to asking about the history of falls. In prostate cancer, survivors who are unmarried and/or experience urinary incontinence post-diagnosis warrant further examination to manage fall risk, although a history of falls is the most important predictor of falls in this population.

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Authorship Contribution

Study concepts, data acquisition, analysis and interpretation: M.H. Huang, L. Pfalzer.

Quality control of data and algorithms: M.H. Huang, M. Godoshian.

Study design, statistical analysis and manuscript preparation: M.H. Huang.

Manuscript editing and review: M.H. Huang, J. Blackwood, M. Godoshian, L. Pfalzer.

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The authors declare no financial or non-financial interest in the study and materials presented in this manuscript.

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