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Falls and frailty in prostate cancer survivors: current, past and never users of androgen deprivation therapy

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Abstract

BACKGROUND/OBJECTIVES—In prostate cancer survivors (PCS), androgen deprivation therapy (ADT) causes muscle loss, weakness, and fatigue, that may not reverse with cessation of treatment and that could increase the risk of falls and frailty. We compared the prevalence of and association between falls and frailty among PCS who were current, past or never users of ADT.

DESIGN—Cross-sectional study

SETTING—Mail and electronic survey

PARTICIPANTS—PCS (N=280; mean age: 72±8 years)

MEASUREMENTS—Cancer history, falls and frailty status (robust, pre-frail or frail) using traditional and obese phenotypes.

RESULTS—Current (37%) or past (34%) ADT users were more than twice as likely to have fallen in the previous year compared never users (15%) (p=0.002). ADT users had twice as many recurrent falls (p <0.001) and more fall-related injuries than unexposed men (p=0.01). Current (43%) or past (40%) ADT users were more likely to be classified as pre-frail or frail than never users (15%) (p<0.001), and the prevalence of obese pre-frailty + frailty was even greater among current (59%) or past (62%) ADT users compared to never users (25%) (p<0.001). Traditional and obese frailty significantly increased the likelihood of reporting falls in the previous year (OR: 2.15; 95% CI: 1.18, 3.94 and OR: 2.97; 95% CI: 1.62, 5.58, respectively) and was also associated with increased risk of recurrent falls (OR: 3.10; 95% CI: 1.48, 6.5 and OR: 3.99; 95% CI: 1.79, 8.89, respectively).

CONCLUSIONS—Current, as well as past exposure to ADT is linked to a higher risk of falls and frailty compared to no treatment. Prostate cancer survivors should be appropriately counseled on fall prevention strategies while approaches to reduce the frailty phenotype should be considered.

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Keywords

prostate cancer; survivorship; androgens; falls; frailty

INTRODUCTION

Prostate cancer is the most common cancer in men and strikes predominantly in older age[1]. Nearly half (45%) of all prostate cancer survivors (PCS) will receive treatment with androgen deprivation therapy (ADT) as part of their primary therapy, for biochemical recurrence, or due to metastatic spread[2]. ADT is associated with serious adverse consequences that might increase rates of falls[3–6], frailty[3] and dysfunction[3, 7] and contribute to morbidity and mortality from non-cancer causes. Recent development of higher potency inhibitors of androgen signaling is rapidly expanding the use of ADT[4, 6, 8, 9] accelerating the urgency to mitigate serious, life-altering side effects of these drugs.

Falls and falls-related injuries are the costliest and most life-threatening injuries among older persons, resulting in age-related fractures, traumatic brain injury, internal organ damage, hospitalization, disability and death[10, 11]. ADT may accelerate physical changes experienced by older adults that are conceptualized as frailty - a cycle of inactivity, slowing and weakening that cascades into falls, dysfunction and disability. The Frailty Phenotype, a cluster of 5 components (shrinking, weakness, slowness, exhaustion, and inactivity), is an approach to quantify frailty and is predictive of hospitalization, development of disability, and falls in older adults without cancer[12, 13]. ADT is associated with the development of individual frailty components, including muscle loss,[14, 15] weakness,[7] fatigue,[16] slow walking speed[7, 16] and inactivity[17,18]. While traditionally conceived as a wasting disorder, there is increasing recognition of the contribution of obesity to similar negative health outcomes as frailty and thus some have proposed an obese frailty phenotype, substituting obesity for shrinking[17]. Since ADT is also linked with excess fat gain[18], androgen deprived men may also be at risk for obese frailty.

The goals of this study were to better describe the prevalence of and associations among ADT use, falls and frailty. Since it is thought that limited or intermittent courses of ADT may minimize side effects while maintaining therapeutic efficacy, we also compared fall and frailty rates between current and past users of ADT. We hypothesized that fall and frailty rates would significantly differ across patterns of ADT use (current, past or never), with rates being highest among current users, lowest among never users and intermediate among past users. We further hypothesized that independent of demographic variables (e.g., age) and clinical history (e.g., disease severity), ADT use would be significantly associated with frailty in PCS and that ADT use and frailty would each be significantly associated with falls among PCS.

MATERIAL AND METHODS

The study and procedures were approved by Oregon Health & Science University Institutional Review Board. All men consented to participate in the study prior to completing the survey.

Study Design and Sample

Men were identified through a search of hospital tumor registry cases with a prostate cancer diagnosis within the last 10 years (i.e., 2005–2015) and a survey was mailed electronically or by post to potentially eligible men (N=909). Based on his use of ADT, confirmed through the electronic health record, a man was categorized as a never, current (dose received ≤ 12 months) or past (no treatment for >12 months) user of ADT.

Data Collection

Men completed a questionnaire about their demographics, cancer and treatment history, falls history, and frailty status. Falls over the last year were determined using an accepted and standardized definition[19]. If a man reported 1 or more falls he was considered a “faller”, with further classification as a “single” faller if men reported having only one fall or a “recurrent” faller if men reported 2 or more falls. For fallers, follow-up questions were asked about fall number and injuries. Frailty was assessed using the self-report FRAIL scale to ascertain the presence of five frailty criteria: fatigue, resistance, ambulation, illness, and loss of weight in order to categorize men as Robust (0 criteria), Pre-Frail (1–2 criteria), and Frail (3 or more criteria)[20]. The International Association of Aging recommends the FRAIL scale as a simple, scalable approach to assess frailty in large groups of people and accurately predicts frailty in community samples[20–22]. The weight loss criterion (>5% of loss of body weight in the past year) is the measure for the traditional frailty component of “shrinking”, an indicator of sarcopenia. While ADT is associated with muscle loss, it is associated with a proportionately greater gain of fat mass[18] that may contribute to morbidity[23] and fall risk[24]. Thus, as Bylow and others have done we also re-categorized frailty into an obese frail phenotype substituting obesity (BMI > 30 kg/m^2) for the weight loss criterion[3].

Statistical Analysis

To compare the incidence of falls and prevalence of frailty components across ADT exposure groups, Pearson’s Chi-squared were conducted on categorical variables (e.g. no falls vs. 1 fall vs. 2+ falls or on frailty components) and ANOVA on continuous variables (e.g. number of falls). Characteristics associated with falls and frailty among PCS was identified using multinomial logistic regression and logistic regression models. Relevant clinical and demographic variables were included as control variables. Multinomial logistic regression allowed us to compare those who reported no falls vs. 1 fall vs. 2+ falls and to compare robust vs. pre-frail vs. frail for both the traditional and obese frailty phenotypes. When used as a predictor, frailty was limited to robust vs. any frailty due to sample size restrictions as no participants were frail and had only one fall. Logistic regression was used to compare no falls vs. any falls and robust vs. any frailty. All significance values were set at $p<0.05$ and odds ratios (w/95% CI’s) were used to quantify effect size.

RESULTS

Out of 909 mailings to potentially eligible participants, 318 men completed the survey, a response rate of 35%. Only the date of cancer diagnosis was available on all potentially eligible participants. Survey respondents did not significantly differ in their average time since diagnosis from men who did not respond (mean: 5.0 ± 2.7 years vs. 5.3 ± 2.4 years,

respectively, p=0.15). Only men who provided consent to access their electronic health records to verify cancer-related information were included in analyses (n=280). The median age of the sample was 71 (range: 49 to 94) with never ADT users slightly younger than current and past ADT users (Table 1). Current and past ADT users had a higher BMI, with over twice the proportion of men classified as obese compared to never users. Never users were more likely to have received surgery but least likely to have had radiation therapy than current and past ADT users. Current ADT users had the highest rates of metastatic disease, while past and never ADT users had a similar extent of disease.

Over twice as many current (37%) or past (34%) ADT users experienced one or more falls in the past year compared to never users (15%), with ADT users experiencing four times the rate of recurrent falls (2+ falls) compared to never users (p<0.01; Table 2). ADT users had significantly more falls resulting in injuries than never users (p=0.01), experiencing more bruises, scrapes, and fractures related to their fall.

When using the traditional frailty phenotype, a significantly higher proportion of current (40%) or past (43%) ADT users were classified as pre-frail or frail compared to men never on treatment (15%) (Table 3; p<0.0001), with over 2-fold or 10-fold higher rates of pre-frailty and frailty, respectively. The prevalence of obese pre-frailty and frailty was even greater and significantly different between current (59%) or past (62%) ADT users compared never users (25%) (p<0.0001). Significantly more ADT users met the frailty criteria of ambulation, resistance, fatigue and obesity compared to never users.

In order to isolate the independent contribution of ADT use to falls and frailty over and above disease severity, other treatments and age all regression models were adjusted for these factors. In Table 4, we examine the contribution of ADT use to phenotypes of traditional and obese frailty. Both current and past ADT exposure was associated with near 3-fold higher odds of any frailty compared to never users (p<0.05). The prevalence of frailty did not significantly differ between current and past ADT users. ADT exposure increased the odds of any frailty vs. no frailty, approaching significance (p=0.06 to p=0.10), with 9-fold higher frailty rates among ADT users compared to never users. When using the obese frailty phenotype, the odds of having obese pre-frailty and obese frailty were 3 to 19 times higher, respectively, among current or past ADT users than never users (all p<0.05).

In Table 5, we examine the contribution of ADT and frailty (traditional and obese phenotypes) to the risk of falls. After adjustment for disease status and other confounders, the odds of being a faller (1+ falls) was statistically elevated among ADT users with ADT exposure associated with a 5-fold higher likelihood of having recurrent falls in the past year compared to men not exposed to ADT (p<0.01). Traditionally-defined frailty significantly increased the likelihood of being a faller (odds ratio (OR): 2.15; 95% confidence intervals (CI): 1.18, 3.93) or a recurrent faller (OR: 2.97; 95% CI: 1.62, 5.59), but did not increase the odds of a single fall. When replacing traditional frailty with obese frailty as a predictor variable, the likelihood of being a faller or recurrent faller increased nearly an order of magnitude.

DISCUSSION

Consistent with our hypotheses, our study provides suggestive evidence that ADT may lead to recurrent and injurious falls that could be explained in part by worsening frailty. However, contrary to our expectation that fall risk would lessen if ADT were stopped, fall rates were similar between current and past users of ADT. We also report that ADT users are more than twice as likely to have some degree of frailty than men not on ADT using traditional frailty criteria developed and validated in older adults. Rates of frailty climb substantially among ADT users when using a contemporary frailty phenotype that considers obesity in lieu of sarcopenia as a frailty criterion. As with falls, past ADT users had similarly high frailty rates as current ADT users, suggesting little reversal of ADT side effects with discontinuation. Unsurprisingly then, we also observed that development of traditional or obese frailty was associated with a significantly higher risk of being a faller or recurrent faller.

In our study, men exposed to ADT, whether currently or in the past, had fall rates well over twice as high as in men never exposed to ADT who had similar fall rates to that reported in a large population-based sample of similarly aged men[25]. Wu (2016) also recently reported that Taiwanese prostate cancer patients on ADT were twice as likely to have a fall compared to patients not on ADT[26], but they were unable to control for potential differences in disease severity and did not differentiate between current and past ADT users. On the other hand, our study was able to confirm that ADT independently predicted falls and that stopping ADT may not ameliorate fall risk. A particularly salient finding in our study was the high proportion of recurrent fallers among men on ADT. Between 22%-24% of current and past ADT users were recurrent fallers, compared to 5% of men not on ADT, which is comparable to the 6% reported for recurrent fallers among the broader population of older men[25]. Recurrent falls lead to higher rates of nursing home admission and mortality and worse quality of life than single falls[19, 27] and may be a symptom of frailty and poor physical and mental health status[28, 29]. When we adjusted regression models for disease severity, treatment and age, current or past ADT users had a six-fold higher likelihood of recurrent falls than never users and frailty or obese frailty was associated with a 3–4 fold higher odds of falling than no frailty. These findings strongly suggest that ADT is not merely a proxy indicator of disease severity or overall health status, but is having an independent influence on fall risk, potentially through frailty. Frailty has been linked to higher falls risk, particularly recurrent falls, among both older women and older men[30]. In fully adjusted models we found 2–3 fold increases in the odds of being a faller or recurrent faller, respectively, among men at risk of (pre-frail) or with frailty using the traditional phenotype and even higher odds ratios when considering obese frailty. Obese frailty may be a better predictor of falls in our sample than traditional frailty because obese frailty still captures the weakness associated with ADT-induced sarcopenia, but then also captures excess adiposity that is linked to poor balance[24, 31].

Based on our findings patients placed on ADT should be monitored for early onset fall and frailty risk and for recurrent falls that increase the odds for a fall-related injury[32]. We observed significantly elevated numbers of injurious falls among men exposed to ADT compared to men not on treatment. Our findings are similar to those tracked via adverse event reports in recent clinical trials of new androgen inhibitors where men on additional

second line ADT agents (e.g., abiaterone, enzalutamide) were more likely to have a fall result in an injury including fracture, joint injury and hematoma compared to men on a single ADT agent + placebo[5, 6, 33]. Another new finding in our study was that the falls and frailty were similarly elevated among men who received ADT within the last 12 months compared to men who had ADT treatment further out. While men with metastatic prostate cancer are most likely to receive continuous treatment with ADT, men treated for loco-regional disease may only be prescribed ADT for a finite period of time following adjuvant therapy and men with biochemical recurrence may be placed on an intermittent regimen of ADT to balance PSA suppression with symptom relief[2]. Our data indicate that past use of ADT carries a similar risk for falls and frailty as current use, suggesting that there may be little reversal of the body composition changes, fatigue and mobility deficits that begin with initiation of androgen suppression. Though our survey focused on capturing prior or current ADT use rather than frequency of ADT dosing, our data suggest that cessation of ADT may not ameliorate side effects enough to alter fall and frailty risk long-term. Until future, prospective studies that follow falls and frailty throughout varying courses ADT are conducted, oncology and primary care providers may wish to assess and monitor for falls and frailty risk in patients with a history of ADT exposure.

Our cross-sectional survey-based study had limitations including our inability to establish causation between ADT use and falls or frailty. We used a survey approach to obtain a reasonable sample size to evaluate falls, which may lead to over or under reporting of outcomes, though we verified cancer history and ADT use against patient electronic medical records. More difficult to extract from the medical record were accurate data on the duration of and compliance with ADT, thus we did not include these measures in our analysis. Falls data in large samples are always obtained by self-report but the retrospective reporting of falls may result in underreporting of overall prevalence that would be independent of ADT use. Though we controlled for disease severity in analyses, we cannot completely ignore the possibility that cancer itself influences fall and frailty risk since ADT is prescribed to men whose cancer has progressed. A future prospective falls study would offer the advantage of linking the occurrence of falls to timing and trajectories of ADT use, disease progression and fall risk factors. Frailty was also self-reported in our study using a validated survey[20–22], but is often assessed using a combination of self-report and performance-based measures. Men may have minimized their limitations and thus underreported frailty but we would expect this bias to be similar across ADT groups. Also of note is that we did not measure testosterone levels and did not distinguish past ADT users by duration of exposure, though 12 months without ADT is regarded as sufficient for recovery of testosterone[34]. It is possible that subsets of patients that are exposed to a short course ADT and recover their testosterone levels return to a pre-therapy level of fall risk, and this could be evaluated in future studies.

In summary, our findings provide evidence that ADT is associated with a higher risk of falls, recurrent falls, frailty and obese frailty and that risk for these poor health outcomes does not diminish when ADT is discontinued. These findings have important implications for the clinical management of men exposed to ADT for prostate cancer in both the oncology and general practice settings. Clinicians may consider evaluating men receiving ADT currently or in the past for fall risk using current fall prevention guidelines[32] and screen for frailty using the FRAIL scale or using simple clinical assessments, such as chair rise and sit, usual

walk speed, presence of fatigue and BMI. To date there are no trials of any strategy to reduce falls or the frailty phenotype in PCS because these problems have not been well recognized nor sufficiently characterized. Strategies, such as exercise, could prevent or reverse frailty related to ADT, interrupting the downward trajectory toward disability and dependence. In fact, several studies have shown that exercise can improve individual frailty components in PCS on ADT[35], such as increased leg strength and muscle mass, but we do not yet know whether and what type of exercise can change several frailty components enough to reduce overall frailty status. We also need to understand the optimal timing of exercise training to prevent falls and frailty in PCS while optimally managing their disease with ADT.

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References

1. American Cancer Society. Cancer Facts & Figures 2015. Atlanta: American Cancer Society; 2015. p. 54
2. Connolly RM, Carducci MA, Antonarakis ES. Use of androgen deprivation therapy in prostate cancer: indications and prevalence. Asian J Androl. 2012; 14:177–186. [PubMed: 22231299]
3. Bylow K, Hemmerich J, Mohile SG, Stadler WM, Sajid S, Dale W. Obese Frailty, Physical Performance Deficits, and Falls in Older Men with Biochemical Recurrence of Prostate Cancer on Androgen Deprivation Therapy: A Case-control Study. Urology. 2011; 77:934–940. [PubMed: 21269665]
4. Scher HI, Fizazi K, Saad F, et al. Increased survival with enzalutamide in prostate cancer after chemotherapy. N Engl J Med. 2012; 367:1187–1197. [PubMed: 22894553]
5. Penson DF, Armstrong AJ, Concepcion R, et al. Enzalutamide Versus Bicalutamide in Castration-Resistant Prostate Cancer: The STRIVE Trial. Journal of Clinical Oncology. 2016; 34:2098–2106. [PubMed: 26811535]
6. Shore ND, Chowdhury S, Villers A, et al. Efficacy and safety of enzalutamide versus bicalutamide for patients with metastatic prostate cancer (TERRAIN): a randomised, double-blind, phase 2 study. The Lancet Oncology. 2016; 17:153–163. [PubMed: 26774508]
7. Galvao DA, Taaffe DR, Spry N, Joseph D, Turner D, Newton RU. Reduced muscle strength and functional performance in men with prostate cancer undergoing androgen suppression: a comprehensive cross-sectional investigation. Prostate Cancer Prostatic Dis. 2009; 12:198–203. [PubMed: 18852703]
8. Beer TM, Armstrong AJ, Rathkopf DE, et al. Enzalutamide in metastatic prostate cancer before chemotherapy. N Engl J Med. 2014; 371:424–433. [PubMed: 24881730]
9. Bahl A, Masson S, Birtle A, Chowdhury S, de Bono J. Second-line treatment options in metastatic castration-resistant prostate cancer: A comparison of key trials with recently approved agents. Cancer Treatment Reviews. 2014; 40:170–177. [PubMed: 23958310]
10. Frost HM. Should fracture risk-of-fracture analyses include another major risk factor? The case for falls. J Clin Densitom. 2001; 4:381–383. [PubMed: 11748343]
11. Centers for Disease Control and Prevention. Falls among older adults: An overview. Available fromhttp://www.cdc.gov/ncipc/factsheets/adultfalls/htm

12. Bandeen-Roche K, Xue QL, Ferrucci L, et al. Phenotype of frailty: characterization in the women's health and aging studies. J Gerontol A Biol Sci Med Sci. 2006; 61:262–266. [PubMed: 16567375]
13. Vermeulen J, Neyens J, van Rossum E, et al. Predicting ADL disability in community-dwelling elderly people using physical frailty indicators: a systematic review. BMC Geriatrics. 2011; 11:33. [PubMed: 21722355]
14. Smith MR, Saad F, Egerdie B, et al. Sarcopenia during androgen-deprivation therapy for prostate cancer. J Clin Oncol. 2012; 30:3271–3276. [PubMed: 22649143]
15. Galvao DA, Spry NA, Taaffe DR, et al. Changes in muscle, fat and bone mass after 36 weeks of maximal androgen blockade for prostate cancer. BJU Int. 2008; 102:44–47. [PubMed: 18336606]
16. Schwartz AL. Fatigue in long-term cancer survivors. Oncology (Williston Park). 2009; 23(27):33–24.
17. Porter Starr KN, McDonald SR, Bales CW. Obesity and Physical Frailty in Older Adults: A Scoping Review of Lifestyle Intervention Trials. Journal of the American Medical Directors Association. 2014; 15:240–250. [PubMed: 24445063]
18. Hamilton EJ, Gianatti E, Strauss BJ, et al. Increase in visceral and subcutaneous abdominal fat in men with prostate cancer treated with androgen deprivation therapy. Clin Endocrinol (Oxf). 2011; 74:377–383. [PubMed: 21118287]
19. Tinetti M, Williams C. Falls, injuries due to falls, and the risk of admission to a nursing home. N Engl J Med. 1997; 337:1279–1284. [PubMed: 9345078]
20. Morley JE, Malmstrom TK, Miller DK. A simple frailty questionnaire (FRAIL) predicts outcomes in middle aged African Americans. J Nutr Health Aging. 2012; 16:601–608. [PubMed: 22836700]
21. Díaz de León González E, Gutiérrez Hermosillo H, Martinez Beltran JA, et al. Validation of the FRAIL scale in Mexican elderly: results from the Mexican Health and Aging Study. Aging Clin Exp Res. 2016; 28(5):901–8. [PubMed: 26646253]
22. Woo J, Yu R, Wong M, et al. Frailty Screening in the Community Using the FRAIL Scale. Journal of the American Medical Directors Association. 2015; 16:412–419. [PubMed: 25732832]
23. Saylor PJ, Smith MR. Metabolic Complications of Androgen Deprivation Therapy for Prostate Cancer. The Journal of Urology. 2013; 189:S34–S44. [PubMed: 23234628]
24. Winters KM, Snow CM. Body composition predicts bone mineral density and balance in premenopausal women. J Womens Health Gend Based Med. 2000; 9:865–872. [PubMed: 11074952]
25. Karlsson MK, Ribom EL, Nilsson J-Å, et al. International and ethnic variability of falls in older men. Scandinavian Journal of Public Health. 2014; 42:194–200. [PubMed: 24259542]
26. Wu F-J, Sheu S-Y, Lin H-C, Chung S-D. Increased Fall Risk in Patients Receiving Androgen Deprivation Therapy for Prostate Cancer. Urology. 2016 Epub ahead of print.
27. Boyé NDA, Mattace-Raso FUS, Van Lieshout EMM, Hartholt KA, Van Beeck EF, Van der Cammen TJM. Physical performance and quality of life in single and recurrent fallers: Data from the Improving Medication Prescribing to Reduce Risk of Falls study. Geriatrics & Gerontology International. 2015; 15:350–355. [PubMed: 24730545]
28. Ku Y-C, Liu M-E, Tsai Y-F, Liu W-C, Lin S-L, Tsai S-J. Associated Factors for Falls, Recurrent Falls, and Injurious Falls in Aged Men Living in Taiwan Veterans Homes. International Journal of Gerontology. 2013; 7(2):80–84.
29. Nevitt MC, Cummings SR, Kidd S, Black D. Risk factors for recurrent nonsyncopal falls. A prospective study. JAMA. 1989; 261:2663–2668. [PubMed: 2709546]
30. Kojima G. Frailty as a Predictor of Future Falls Among Community-Dwelling Older People: A Systematic Review and Meta-Analysis. Journal of the American Medical Directors Association. 16:1027–1033.
31. Odessa A, Patricia Y, Mario I, et al. Hip but Not Thigh Intramuscular Adipose Tissue is Associated with Poor Balance and Increased Temporal Gait Variability in Older Adults. Current Aging Science. 2014; 7:137–143. [PubMed: 24998419]
32. Panel on Prevention of Falls in Older Persons American - Geriatric Society, British Geriatrics Society. Summary of the Updated American Geriatrics Society/British Geriatrics Society Clinical Practice Guideline for Prevention of Falls in Older Persons. Journal of the American Geriatrics Society. 2011; 59:148–157. [PubMed: 21226685]

33. Graff JN, Baciarello G, Armstrong AJ, et al. Efficacy and safety of enzalutamide in patients 75 years or older with chemotherapy-naive metastatic castration-resistant prostate cancer: results from PREVAIL. Annals of Oncology. 2016; 27:286–294. [PubMed: 26578735]

34. Dai B, Qu Y-Y, Kong Y-Y, et al. Kinetics of testosterone recovery in clinically localized prostate cancer patients treated with radical prostatectomy and subsequent short-term adjuvant androgen deprivation therapy. Asian Journal of Andrology. 2013; 15:466–470. [PubMed: 23708460]

35. Gardner JR, Livingston PM, Fraser SF. Effects of Exercise on Treatment-Related Adverse Effects for Patients With Prostate Cancer Receiving Androgen-Deprivation Therapy: A Systematic Review. J Clin Oncol. 2014; 34(2):335–46.

Table 1

Demographic and clinical characteristics of prostate cancer patients by androgen deprivation therapy (ADT) exposure. Data are expressed as mean (SD) for continuous data or % of sample for categorical data.

Characteristic	Current ADT (N=119) Mean (SD)	Past ADT (N=62) Mean (SD)	Never ADT (N=99) Mean (SD)	p-value
Age (yrs.)	72.5 (7.8)	72.9 (8.0)	69.7 (7.6)	0.01
BMI (kg/m^2)	29.2 (4.8)	29.0 (6.0)	26.8 (3.9)	<0.01*
BMI category (%)				
Underweight & Normal	17.5%	29.0%	29.3%	
Overweight	41.6%	30.6%	54.5%	<0.01*
Obese	40.8%	40.3%	16.2%	
Race[a]				
White	91.7%	98.4%	97.0%	
African American	2.5%	0.0%	1.0%	
Asian	1.7%	1.6%	0.0%	
Native American/Alaskan Native	0.8%	0.0%	0.0%	0.58
Native Hawaiian/Pacific Islander	0.0%	0.0%	1.0%	
Hispanic (%)	1.7%	0.0%	2.1%	0.55
Time since diagnosis (months)	56.2 (53.2)	71.0 (39.1)	65.2 (41.2)	0.10
Disease severity				<0.01*
Loco-regional (%)	56.3%	87.1%	86.9%	
Biochemical recurrence (%)	13.4%	11.3%	13.1%	
Metastatic disease (%)	30.3%	1.1%	0%	
Received surgery (%)	36.1%	37.7%	81.6%	<0.01*
Received radiation therapy (%)	75.8%	85.5%	26.3%	<0.01*
Received chemotherapy (%)	9.3%	5.1%	2.0%	0.07

*p-value <0.001

[a]Percentages do not add up to 100% due to some men identifying as “more than one race” or “other race”

Table 2

Patterns of falls in past year reported by prostate cancer patients by androgen deprivation therapy (ADT) exposure. Data are expressed as mean (SD) for continuous data or % of sample for categorical data.

Characteristic	Current ADT (N=119) Mean (SD)	Past ADT (N=62) Mean (SD)	Never ADT (N=99) Mean (SD)	p-value
Faller Status (%)				
No falls	62.9%	66.7%	84.8%	
1 fall	12.9%	11.7%	10.1%	<0.01*
2+ falls	24.2%	21.7%	5.1%	
Number of falls (all participants)	1.0 (2.0)	1.2 (4.4)	0.3 (1.1)	0.09
Number of injurious falls (all participants)	0.4 (0.8)	0.5 (1.0)	0.1 (0.4)	0.01
Type of injury				
Bruise	16.1%	15.0%	5.0%	0.04
Scrape	11.3%	15.0%	3.0%	0.01
Joint	1.6%	0.0%	0.0%	0.17
Head	3.2%	0.8%	1.0%	0.40
Fracture	6.5%	2.5%	0.0%	0.04

* p-value <0.001

Table 3

Frailty patterns self-reported by prostate cancer patients by androgen deprivation therapy (ADT) exposure. Data are expressed as % of sample.

Characteristic	Current ADT (N=120)	Past ADT (N=62)	Never ADT (N=99)	p-value
Frailty Phenotype (%)				
Robust	60.0%	56.9%	85.1%	
Pre-frail	29.6%	32.8%	13.8%	<0.01 *
Frail	10.4%	10.3%	1.1%	
Obese Frailty Phenotype[a] (%)				
Robust	37.9%	41.4%	74.7%	
Pre-frail	47.4%	43.1%	24.2%	<0.01 *
Frail	14.7%	15.5%	1.1%	
Frailty Component (%)				
Resistance	15.3%	16.4%	3.1%	<0.01
Exhaustion	19.5%	24.2%	8.2%	0.02
Ambulation	27.6%	25.4%	3.2%	<0.01 *
Illness	3.3%	4.8%	0.0%	0.12
Weight loss	10.9%	8.2%	5.1%	0.30
Obesity[a]	40.8%	40.3%	16.2%	<0.01 *

* p-value <0.001

[a] Obese frailty phenotype calculated by substituting weight loss component of original frailty phenotype with obesity component = BMI ≥ 30 kg/m^2.

Table 4

Odds ratios for frailty and obese frailty among prostate cancer survivors (N=280)[a]

Characteristic	Frailty Phenotype Odds ratio (95% CI)	p-value	Obese Frailty Phenotype[b] Odds ratio (95% CI)	p-value
Pre-Frailty vs. Robust[c]				
Current ADT (vs. no ADT)	2.24 (0.86, 5.85)	0.10	3.83 (1.662 8.83)	<0.01*
Past ADT (vs. no ADT)	2.35 (0.89, 6.17)	0.08	2.63 (1.10, 6.25)	0.03
Current ADT (vs. Past)	0.96 (0.43, 2.15)	0.91	1.46 (0.65, 3.26)	0.36
Frailty vs. Robust[c]				
Current ADT (vs. no ADT)	8.53 (0.84, 86.51)	0.07	18.95 (1.96, 183.10)	0.01
Past ADT (vs. no ADT)	9.34 (0.92, 95.33)	0.06	16.30 (1.69, 157.42)	0.02
Current ADT (vs. Past)	0.91 (0.26, 3.24)	0.88	1.16 (0.38, 3.58)	0.79
Any Frailty vs. Robust[d]				
Current ADT (vs. no ADT)	2.86 (1.16, 7.20)	0.02	4.48 (2.03, 10.24)	< 0.01*
Past ADT (vs. no ADT)	2.71 (1.12, 6.76)	0.03	3.25 (1.42, 7.58)	<0.01*
Current ADT (vs. Past)	0.95 (0.45, 2.01)	0.89	1.38 (0.64, 2.97)	0.41

* p<0.001

[a] All models adjusted for age, time since diagnosis, disease severity, and receipt of surgery, radiation therapy, and/or chemotherapy.

[b] Frailty calculated using obesity (BMI 30 kg/m^2) in place of weight loss

[c] Parameter estimates derived from multinomial logistic regression to compare each frail and pre-frail versus robust

[d] Parameter estimates derived from binary logistic regression to compare any frailty (frail+pre-frail) versus robust

Table 5

Odds ratios for having 1 fall, 2 or more falls, or 1 or more falls in past year among prostate cancer survivors (N=281)[a].

Characteristic	1 Fall vs. No Fall Odds Ratio 95% CI	p-value	2+ Falls vs. No Fall Odds Ratio 95% CI	p-value	Faller vs. Non-Faller Odds Ratio 95% CI	p-value
Model 1[b]						
Age	1.03 (0.98, 1.09)	0.23	1.04 (0.99, 1.09)	0.13	1.04 (1.00, 1.08)	0.08
Time since diagnosis	1.00 (0.99, 1.01)	0.37	1.01 (1.00, 1.02)	0.04	1.01 (1.00, 1.01)	0.05
Biochemical recurrence (vs. loco-regional disease)	0.60 (0.15, 2.39)	0.47	0.88 (0.30, 2.59)	0.82	0.76 (0.29, 1.84)	0.56
Metastatic (vs. loco-regional disease)	0.79 (0.23, 2.75)	0.71	0.80 (0.27, 2.35)	0.68	0.79 (0.31, 1.87)	0.60
Past chemotherapy	0.71 (0.08, 6.58)	0.76	2.07 (0.51, 8.43)	0.31	1.48 (0.39, 5.00)	0.54
Past radiation	1.12 (0.43, 2.88)	0.82	1.72 (0.73, 4.05)	0.21	1.42 (0.72, 2.82)	0.31
Past surgery	0.61 (0.26, 1.63)	0.33	0.61 (0.26, 1.42)	0.25	0.62 (0.31, 1.22)	0.17
Model 2[c]						
Past ADT (vs. no ADT)	0.93 (0.27, 3.13)	0.90	5.42 (1.60, 18.39)	<0.01	2.29 (0.95, 5.70)	0.06
Current ADT (vs. no ADT)	1.09 (0.34, 3.45)	0.89	5.86 (1.75, 19.65)	<0.01	2.54 (1.10, 6.08)	0.03
Current ADT (vs. past ADT)	1.17 (0.39, 3.47)	0.78	1.08 (0.47, 2.51)	0.86	1.11 (0.54, 2.32)	0.78
Model 3[d]						
Frail + Pre-frail (vs. robust)	1.27 (0.54, 2.99)	0.59	3.10 (1.49, 6.46)	<0.01	2.15 (1.18, 3.94)	0.01
Obese Frail + Pre-frail (vs. robust)	2.07 (0.90, 4.77)	0.09	3.99 (1.79, 8.89)	<0.01*	2.97 (1.62, 5.59)	<0.01*

*p-value < 0.001

[a]Models for 1 fall vs. no fall and 2+ falls vs. no falls were run together using multinomial logistic regression, while models for faller (at least one fall in the last year) vs. non-faller were run using binary logistic regression

[b]Models ran with age and clinical variables

[c–d]Models ran with age and clinical variables followed by [c]ADT exposure or [d]Frailty Phenotype and Obese Frailty Phenotype