Research Article

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Associations of Postdiagnosis Physical Activity and Change from Prediagnosis Physical Activity with Quality of Life in Prostate Cancer Survivors

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Abstract

Background: This prospective study examined the associations between postdiagnosis physical activity and change from prediagnosis physical activity with quality of life (QoL) in prostate cancer survivors.

Methods: Prostate cancer survivors ($N = 830$) who participated in a case–control study with invasive stage ≥II disease were followed up to 2007 to capture QoL outcomes. At baseline and three time points postdiagnosis (2000–2007), interviews/questionnaires were used to collect data on physical activity, general QoL measured by the SF-36, and other treatment/lifestyle factors. Multivariable linear regression was used to test the relation between postdiagnosis physical activity and QoL as well as the change in physical activity over the diagnostic period and QoL.

Results: Both total and recreational physical activities were positively associated with physical QoL. Furthermore, when comparing changes in physical activity levels from pre- to postdiagnosis, men who consistently met physical activity guidelines had significantly higher physical [$\beta = 6.01$; 95% confidence interval (CI), 4.15–7.86] and mental ($\beta = 2.32$; 95% CI, 0.29–4.34) QoL scores compared with those who did not meet guidelines pre- or postdiagnosis. Furthermore, those who adopted and met guidelines had increased QoL, whereas those who relapsed experienced decreased QoL.

Conclusions: Postdiagnosis recreational physical activity is associated with better physical QoL in prostate cancer survivors. Moreover, prostate cancer survivors who maintain or adopt physical activity after diagnosis report substantially higher QoL than men who never exercised or stopped exercising after diagnosis.

Impact: Future intervention studies should focus on achieving and maintaining adherence to physical activity guidelines postdiagnosis in prostate cancer survivors. *Cancer Epidemiol Biomarkers Prev; 26(2); 179–87. ©2016 AACR.*

Introduction

Prostate cancer is the second most common cancer in men worldwide (1, 2). Early detection and improved treatment options have increased prevalence and decreased the mortality rate associated with prostate cancer (3). Because of the increase in 5-year survival rates, currently approximately 81% in Canada (4), men diagnosed with low-grade (stage I–II) prostate cancer, more likely than not, die from other causes, particularly after age 75 (5). In addition, PSA screening programs often overdetect low-grade cancers, which, for the most part, are indolent for long periods of time (6). In turn, overtreatment of potentially non–life threatening disease has burdened prostate cancer survivors and the health care system (7, 8). Consequently, priorities in prostate cancer control involve reducing the burdens of living beyond cancer diagnosis, improving health, overall functioning, care, quality of life (QoL; ref. 9), and addressing the specific needs of prostate cancer survivors (10).

Prostate cancer survivors who undergo surgery (11, 12) and receive treatments such as androgen deprivation therapy (13, 14) or radiotherapy (11, 15, 16) often experience worse QoL. Physical activity is an inexpensive, modifiable behavior that has been shown to improve QoL after diagnosis and may be associated with survival (17–20). Observational epidemiologic research (21–32) and randomized controlled exercise intervention trials (33–40) have shown that physical activity can improve QoL in prostate cancer survivors. No study to date, however, has examined the associations between changes in physical activity across the diagnostic period and QoL in prostate cancer survivors. Furthermore, only one study (27) explicitly examined different types of physical activity, including household and occupational physical activity and QoL. Moreover, previous observational research has had methodologic limitations associated with inadequate control for confounding and an inability to examine effect modification because of the small sample sizes.

The parent study was primarily designed to examine the associations of physical activity and survival in prostate cancer survivors (17). In this current analysis, we examined the role of both total postdiagnosis physical activity and each type of activity,

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including recreational, occupational, and household activity, and changes in physical activity over the diagnostic period on physical and mental QoL in prostate cancer survivors. In addition, this study had a large sample size that can explore multiple subgroup analyses.

Materials and Methods

Study design

A prospective cohort of prostate cancer survivors that originated from a population-based case–control study in Alberta, Canada, was conducted between November 1997 and December 2000 (41). All cases from the original case–control study were recontacted and followed up for postdiagnosis measurements and mortality outcomes to 2014. Details regarding this study have been published previously (17). Briefly, prostate cancer cases were histologically confirmed, invasive cases of stage II or greater prostate cancer and identified from the Alberta Cancer Registry, a population-based cancer registry. The prostate cancer survivors were <80 years of age, English speaking with no previous cancer diagnosis except for nonmelanoma skin cancer. Permission to contact prostate cancer cases for in-person interviews was obtained through the referring urologist. All surviving cases from the case–control study were recontacted by telephone for voluntary recruitment and provided written informed consent for the prostate cancer cohort follow-up study (2% rate of refusal). The cohort study began in 2000 when additional funding was obtained, to permit follow-up and further data collection from the cases. In addition, referring urologists were recontacted for additional missing medical data. This study received ethics approval from the Alberta Cancer Research Ethics Board and the Conjoint Health Research Ethics Board at the University of Calgary (Alberta, Canada).

Data collection

Through in-person interviews, conducted in the original case–control study, participants reported on their personal health history, prostate cancer screening history, prostate conditions, surgery history, family history of cancer, lifetime physical activity patterns prior to diagnosis, dietary intake during the reference year (year prior to cancer diagnosis), lifetime alcohol consumption history, smoking habits, current social support and motivation for lifestyle change, demographic characteristics, and adult height and weight at each decade from age 20 to 60 years. Anthropometric measurements were measured directly at the interview. In addition, as a part of the cohort follow-up study, survivors were interviewed to assess their physical activity behavior within the first two years after diagnosis. At the cohort follow-up interview, self-reported questionnaires on current QoL were completed by participants. At a second and third follow-up time points, approximately 2 years apart, self-administered questionnaires asking participants about their past 2 years of physical activity behavior as well as their current QoL were mailed to participants to complete. Furthermore, medical chart abstractions and vital status assessments were completed throughout the follow-up to capture updated medical information, treatments, and outcomes.

Physical activity assessment

Physical activity was assessed using the Lifetime Total Physical Activity Questionnaire (LTPAQ) and the Past Year Total Physical Activity Questionnaire (PYTPAQ) previously tested for reliability and validity (42, 43). Both the LTPAQ and the PYTPAQ record all types of physical activity (occupational, household, and recreational) as well as all parameters of activity (frequency, duration, and intensity) from childhood to the time of diagnosis. The LTPAQ was interview administered as part of the baseline case–control study, and the results from that study have been published (41). The participants were reinterviewed between 2000 and 2002 using the LTPAQ restricted to their activity done since the first interview, which had occurred between 1997 and 2000. Two additional assessments of physical activity were obtained through the self-administered PYTPAQ between 2002 and 2004 and 2004 and 2007. Hence, continuous levels of physical activity throughout the participant's life up until 2007 (when active data collection ceased) were obtained.

All physical activities (pre- and postdiagnosis) were assigned a metabolic equivalent (MET) value defined as a ratio of the associated metabolic rate for a specific activity as compared with the resting metabolic rate. These MET values were based on the Compendium of Physical Activities (44) and used with the reported frequency and duration of activity to derive the MET-hours/week/year for each type of activity. Moderate-to-vigorous recreational activity was defined as any activity >3 METs according to the Compendium of Physical Activities categorization (44). Moderate-to-vigorous total and recreational physical activity (hour/week/year) were derived to examine activity duration similar to general cancer survivorship physical activity guidelines (45, 46).

To assess the change in physical activity over the diagnosis period, a change score was derived using the difference between prediagnosis lifetime and average postdiagnosis physical activity. The average postdiagnosis physical activity variables contained up to three postdiagnosis time points. For those with missing assessments, because of nonresponse or death, the average physical activity levels were derived from available complete assessments. In addition, adherence to physical activity guidelines for cancer prevention and survivorship (150 minutes of moderate or 75 minutes of vigorous recreational physical activity; refs. 45, 46) over the diagnosis period was assessed, and behaviors were categorized as follows: consistently not meeting pre- and postdiagnosis (nonexercisers); not meeting prediagnosis to meeting guidelines postdiagnosis (adopters); meeting prediagnosis to not meeting guidelines postdiagnosis (relapsers); or consistently meeting guidelines pre- and postdiagnosis (maintainers). Active data collection ended in 2007; therefore, we utilized the physical activity cancer prevention and survivorship guidelines specific to aerobic physical activity.

QoL assessment

QoL assessments at up to three follow-ups were obtained through a single questionnaire, the RAND 36-Item Short Form Health Survey (SF-36) version 1.0. The SF-36 has been used in several settings, is one of the most widely used QoL questionnaires (47), and has been validated in colorectal cancer survivors (48). The SF-36 addresses eight domains of health status that have been summarized into a physical component summary (PCS) score and a mental component summary (MCS) score. Both scores range from 0 to 100; higher scores indicate better QoL. Accordingly, clinically meaningful QoL score differences reflect >5 point changes (49).

Statistical analysis

Descriptive statistics were performed on all variables to report study characteristics. Next, multivariable least squares linear regression was used in all analyses (all statistical linear regression assumptions, including distributional, homogeneity of variances, were verified). *A priori* variables deemed to be predictors of QoL were forced into the models: prostatectomy surgery (yes, no), postdiagnosis Charlson comorbidity score (0, 1, 2, $\geq$3; ref. 50), aggressive or nonaggressive disease (Gleason score >8 or stage >II cancer; ref. 51), type of treatment (none, hormone, radiotherapy, both hormone and radiotherapy), and age at diagnosis (years). The aforementioned variables were first tested for interaction. Furthermore, we tested the following covariates for potential confounding first, with univariate analyses ($P < 0.2$) and secondly through backward elimination: prediagnosis lifetime physical activity (MET-hour/week/year) to adjust for baseline differences, nonlinearity of age at diagnosis, family history of cancer (yes, no), PSA score at diagnosis ($\leq$4, >4 and $\leq$10, >10 and $\leq$20, >20), smoking status at diagnosis (never, former, current), total alcohol consumption at diagnosis (grams/year), region of residence (urban, rural), ethnicity (Caucasian, other), education (less than high school, high school, trade school, other non-university degree, university degree), marital status (married, other), weight at diagnosis (kg), body mass index (kg/m^2), daily caloric intake at diagnosis (kcal/day), lifestyle change postdiagnosis (yes, no), family support (yes, no), friend support (yes, no), and ever joined a support group (yes, no). In addition, recreational, occupational, and household physical activity types and other physical activity intensities were mutually adjusted to control for the effects of one type/intensity on another. All quantitative variables were centered at the median for ease of interpretation.

To investigate the associations between postdiagnosis physical activity and QoL, the first follow-up data (collected 2000–2002) for both physical activity and QoL were used. To determine changes in pre- and postdiagnosis physical activity and the influence on QoL, lifetime prediagnosis physical activity and average (over all available time points) postdiagnosis physical activity data were used to derive change scores and adherence groups. In addition, average (over all available time points) postdiagnosis QoL scores were derived for these analyses.

Sensitivity analyses were performed by removing survivors diagnosed with stage III/IV and IV metastatic cancer to account for disease severity differences. In addition, cases who died prior to completing all three postdiagnosis follow-ups were excluded in the physical activity change over the diagnostic period analysis to determine the impact of these data potentially missing not at random. Estimated rates of change of QoL scores, per unit of physical activity values and their corresponding 95% confidence intervals (CI) were reported in multivariable adjusted models. *A priori* hypotheses were assessed with a significance level of $P < 0.05$, using the statistical package Stata v.13.

Results

Descriptive statistics

There were initially 830 men who survived up until the first follow-up time point (2000–2002); 8 of those participants were missing first follow-up QoL data and 5 participants were missing first follow-up lifetime physical activity data, and therefore, the analytic sample was 817 for these analyses. The majority of the study participants were diagnosed with stage II cancer, married, and had at least one comorbidity postdiagnosis (Table 1). The mean age of the participants at the start of follow-up was 67.3 years. The sample had a postdiagnosis first follow-up total physical activity median of 78.7 MET-hour/week/year; however, the recreational physical activity median was only 11.1 MET-hour/week/year. Furthermore, their first follow-up mean PCS score was 40.8 (SD = 12.4) and MCS score was 50.8 (SD = 11.8), which were approximately symmetrically distributed.

Postdiagnosis physical activity and QoL at first follow-up

Final multivariable adjusted models found statistically significant associations between three postdiagnosis types of physical activity in relation to first follow-up PCS score (Table 2). Only one type of physical activity was significantly associated with MCS score. Recreational physical activity revealed the strongest associations (relative to the other types) with an estimated increase of 0.16 (95% CI, 0.12–0.20; $P < 0.001$) in PCS score and 0.05 (95% CI, 0.01–0.09; $P = 0.024$) for MCS score per MET-hour/week/year increase in physical activity volume. Although other physical activity types were not significantly associated with MCS score, associations appeared to be consistent in direction with estimated PCS score, except household physical activity, which was slightly negative. Furthermore, sensitivity analyses excluding stage III/IV and IV cancers ($n = 130$) did not appear to substantially influence these results.

Analyses restricted to duration (hour/week/year) of moderate-to-vigorous total and recreational physical activity are presented in Table 2. Recreational moderate-to-vigorous activity was positively associated with both PCS and MCS scores with estimated increases of 0.68 (95% CI, 0.50–0.85; $P < 0.001$) and 0.22 (95% CI, 0.03–0.40; $P = 0.021$) per hour of recreational activity, respectively. Total moderate-to-vigorous physical activity was also positively associated with PCS score with an estimated increase of 0.09 (95% CI, 0.05–0.13; $P < 0.001$) but not with MCS score ($\beta = -0.01$ [95% CI, -0.05–0.04; $P = 0.76$]). Interestingly, the sensitivity analysis excluding stage III/IV and IV cancers increased the recreational moderate-to-vigorous physical activity associations, but not those for total activity.

Change of physical activity over diagnostic period and QoL

The analysis evaluating changes of physical activity volume (MET-hour/week/year) between lifetime (prediagnosis) and postdiagnosis activity on average postdiagnosis QoL for up to three follow-ups revealed similar results to the postdiagnosis physical activity analysis (Table 3). Although recreational physical activity change was consistently associated with PCS score ($\beta = 0.15$; 95% CI, 0.11–0.19; $P < 0.001$ and MCS score $\beta = 0.06$; 95% CI, 0.02–0.11; $P = 0.006$), total and occupational activity change were only associated with PCS score. Similarly, household activity did not impact the PCS or MCS scores significantly. Excluding stage III/IV and IV cancers or those who died before completing all three follow-ups did not materially change results.

Table 3 also presents physical activity change focused on moderate-to-vigorous total and recreational activity, which indicated associations with recreational activity and both PCS and MCS QoL scores with estimated increases of 0.72 (95% CI, 0.54–0.90; $P < 0.001$) and 0.35 (95% CI, 0.15–0.55; $P = 0.001$) per hour of activity performed. Total physical activity was once again statistically significantly associated with PCS score ($\beta = 0.11$; 95% CI, 0.07–0.16; $P < 0.001$) but not MCS score ($\beta = 0.04$; 95% CI, -0.01–0.09; $P = 0.15$). Nonetheless, in the sensitivity analysis

Table 1. Characteristics for prostate cancer survivors ($N = 817$), in the Prostate Cancer Cohort Study, Alberta, Canada, 1997–2014

Study characteristics[a]	*N* (%)
Gleason score at diagnosis	
≤7	312 (38.2%)
>7	505 (61.8%)
PSA value at diagnosis	
<4	75 (9.2%)
4–10	297 (36.4%)
>10–20	193 (23.6%)
>20	252 (30.8%)
Stage of cancer	
II (T1/T2, N0, M0)	630 (77.1%)
III (T3, N0, M0)	57 (7.0%)
III/IV (T3, NX, MX)	75 (9.2%)
IV[b]	55 (6.7%)
Primary treatment[c]	
Prostatectomy	240 (29.4%)
Hormone therapy[d]	517 (63.3%)
Radiotherapy	359 (43.9%)
Relationship status	
Married/common law	689 (84.3%)
Other	128 (15.7%)
Education level	
University degree	140 (17.2%)
Other non-university degree	170 (20.8%)
Trade degree	166 (20.3%)
High school diploma	86 (10.5%)
Less than high school diploma	255 (31.2%)
Race	
Caucasian	780 (95.5%)
Other	37 (4.5%)
Region of residence	
Urban	482 (59.0%)
Rural	335 (41.0%)
Postdiagnosis Charlson comorbidity score	
0	71 (8.7%)
1	218 (26.7%)
2	214 (26.2%)
3+	314 (38.4%)
First-degree family history of prostate cancer	
Yes	166 (20.3%)
No	651 (79.7%)
Smoking status	
Current smoker	114 (14.0%)
Former smoker	465 (56.9%)
Never smoker	238 (29.1%)
	Median (Q1, Q3)
Total lifetime alcohol intake (g/year)[e]	1,909.2 (588.4, 4,507.3)
Dietary caloric intake (kcal/day)	2,008.3 (1,644.4, 2,474.5)
Prediagnosis lifetime total physical activity[f]	143.7 (98.1, 198.3)
Prediagnosis lifetime recreational physical activity[f]	12.4 (6.7, 21.3)
Prediagnosis lifetime occupational physical activity[f]	107.9 (58.0, 160.4)
Prediagnosis lifetime household physical activity[f]	17.8 (9.2, 29.9)
First follow-up total physical activity[f]	78.7 (44.2, 126.9)
First follow-up recreational physical activity[f]	11.1 (3.0, 25.1)
First follow-up occupational physical activity[f]	2.9 (0.0, 50.0)
First follow-up household physical activity[f]	33.1 (12.5, 56.0)
Second follow-up total physical activity[f]	71.6 (35.1, 132.9)
Second follow-up recreational physical activity[f]	13.5 (2.0, 32.6)
Second follow-up occupational physical activity[f]	0.0 (0.0, 41.8)
Second follow-up household physical activity[f]	25.9 (7.6, 49.7)
Third follow-up total physical activity[f]	62.0 (28.3, 106.7)
Third follow-up recreational physical activity[f]	13.5 (0.0, 32.9)
Third follow-up occupational physical activity[f]	0.0 (0.0, 12.9)
Third follow-up household physical activity[f]	21.9 (5.8, 47.5)

(Continued on the following column)

Table 1. Characteristics for prostate cancer survivors ($N = 817$), in the Prostate Cancer Cohort Study, Alberta, Canada, 1997–2014 (Cont'd)

Study characteristics[a]	*N* (%)
	Mean (SD)
Age at diagnosis (years)	67.3 (7.4)
Body mass index (kg/m^2)	28.0 (3.8)
First follow-up PCS score	40.8 (12.4)
First follow-up MCS score	50.8 (11.8)
Second follow-up PCS score	40.8 (12.2)
Second follow-up MCS score	50.5 (11.7)
Third follow-up PCS score	40.1 (12.0)
Third follow-up MCS score	51.0 (11.6)

[a]Baseline (captured at diagnosis) characteristics ($N = 817$) unless otherwise stated. Second follow-up ($n = 595$) and third follow-up ($n = 495$).
[b]IV included: T4, N0, M0; T4, N0/NX, M0/MX; any T, N1, M0/MX; any T, any N, M1; any T, NX, MX.
[c]Not mutually exclusive (could have more than one treatment).
[d]Included bilateral orchiectomy, luteinizing hormone-releasing hormone agonists, nonsteroidal antiandrogens.
[e]66 never-drinkers.
[f]Units: MET hr/wk/yr.

excluding participants diagnosed with stage III/IV and IV cancers, recreational activity associations were slightly heightened; however, this finding was not seen in the total activity analysis, nor in the analysis excluding those who did not complete all three follow-ups.

Finally, the change in behavior over the diagnostic period according to the physical activity cancer survivorship guidelines (46) relative to PCS and MCS scores is presented. This analysis provides more definitive physical activity change according to existing cancer survivorship guidelines. First, the median prediagnosis and postdiagnosis physical activity levels for each cancer survivorship guideline adherence group were produced (Fig. 1). Maintainers and adopters increased physical activity levels, whereas relapsers and nonexercisers reduced physical activity levels from prediagnosis to postdiagnosis. In multivariable analyses (Table 4), prostate cancer survivors who were characterized as adopters experienced an increase of PCS score by 4.80 (95% CI, 2.82–6.78; $P < 0.001$) and MCS score by 2.26 (95% CI, 0.09–4.43; $P = 0.041$) relative to nonexercisers. Furthermore, maintainers showed the strongest results with increased PCS score of 6.01 (95% CI, 4.15–7.86; $P < 0.001$) and MCS score of 2.32 (95% CI, 0.29–4.34; $P = 0.025$) relative to nonexercisers. Interestingly, relapsers had nonstatistically significant worse scores. Slight attenuations were shown in the analysis excluding stage III/IV and IV cancers and participants that did not complete all follow-ups due to death, specifically in MCS scores for adopters and maintainers; however, point estimates and CIs remained fairly unchanged. Evidence of statistical interactions were not present in these analyses; therefore, estimated PCS and MCS scores for the entire study population were reported.

Discussion

This study found that postdiagnosis physical activity was associated with PCS scores in prostate cancer survivors. Specifically, the positive association between recreational physical activity and PCS score was consistent across analyses; however, the magnitude of the association of physical activity on PCS score was relatively small (49). Total, occupational and household activities were not associated with QoL at the first

Table 2. Associations between postdiagnosis first follow-up physical activity and postdiagnosis first follow-up QoL in prostate cancer survivors in Alberta, Canada, in 1997–2002

Type of physical activity	Physical activity median (min, max)	PCS score[a]			MCS score[b]		
		β	95% CI	*P*	β	95% CI	*P*
All activity (MET-hr/wk/yr)							
Total sample ($N = 817$)							
Total	79 (0, 491)	0.04	0.02–0.05	<0.0001	0.01	0–0.02	0.19
Recreational[c]	11 (0, 120)	0.16	0.12–0.20	<0.0001	0.05	0.01–0.09	0.024
Occupational[c]	3 (0, 445)	0.02	0.01–0.03	0.001	0.01	−0.01–0.02	0.22
Household[c]	33 (0, 314)	0.01	−0.01–0.03	0.14	−0.01	−0.03–0.01	0.26
Excluding stage III/IV and IV ($n = 687$)[d]							
Total	79 (0, 491)	0.03	0.02–0.04	<0.0001	0.01	−0.01–0.02	0.20
Recreational[c]	11 (0, 120)	0.16	0.12–0.20	<0.0001	0.05	0.01–0.10	0.024
Occupational[c]	3 (0, 445)	0.02	0–0.03	0.023	0.01	−0.01–0.02	0.24
Household[c]	33 (0, 314)	0.01	−0.01–0.03	0.20	−0.01	−0.04–0.01	0.33
Moderate-to-vigorous activity (hr/wk/yr)							
Total sample ($N = 817$)							
Total	28 (0, 113)	0.09	0.05–0.13	<0.0001	−0.01	−0.05–0.04	0.76
Recreational[c]	2 (0, 28)	0.68	0.50–0.85	<0.0001	0.22	0.03–0.40	0.021
Excluding stage III/IV and IV ($n = 687$)[d]							
Total	28 (0, 113)	0.08	0.04–0.13	<0.0001	−0.01	−0.06–0.04	0.78
Recreational[c]	2 (0, 28)	0.71	0.53–0.88	<0.0001	0.25	0.05–0.45	0.015

NOTE: All models adjusted for age at diagnosis, aggressive versus nonaggressive prostate cancer, prostate cancer treatment (none, hormone only, radiotherapy only, or both hormone and radiation therapy), prostatectomy, postdiagnosis Charlson co-morbidity score, level of education, and prediagnosis lifetime physical activity.
[a]Additionally adjusted for smoking status.
[b]Additionally adjusted for whether or not they joined a support group postdiagnosis and whether they had family support or not.
[c]Mutually adjusted for other physical activity types and intensities (for moderate-to-vigorous activity analysis).
[d]Stage IV cancers: 55; stage III/IV cancers: 75.

follow-up. It is also interesting to note that mean first follow-up PCS scores were 10 points lower than MCS scores. Adherence to cancer survivorship physical activity guidelines resulted in 5- and 6-point increases in average PCS scores for prostate cancer survivors who were adopters and maintainers relative to nonexercisers. These results were clinically relevant. Both

Table 3. Associations between physical activity change (prediagnosis minus average postdiagnosis scores) over the diagnosis period and average postdiagnosis QoL in prostate cancer survivors in Alberta, Canada, in 1997–2007

Type of physical activity	Physical activity change score: median (min, max)	PCS score[a]			MCS score		
		β	95% CI	*P*	β	95% CI	*P*
All activity (MET hr/wk/yr)							
Total sample ($N = 817$)							
Total	−60 (−425, 246)	0.04	0.03–0.05	<0.0001	0.01	0–0.03	0.07
Recreational[b]	0 (−83, 120)	0.15	0.11–0.19	<0.0001	0.06	0.02–0.11	0.006
Occupational[b]	−76 (−390, 258)	0.04	0.02–0.05	<0.0001	0.02	0–0.03	0.05
Household[b]	10 (−87, 279)	0.02	0–0.04	0.08	0	−0.03–0.02	0.51
Excluding stage III/IV and IV ($n = 687$)[c]							
Total	−60 (−426, 246)	0.04	0.02–0.05	<0.0001	0.01	0–0.03	0.15
Recreational[b]	0 (−83, 120)	0.16	0.12–0.20	<0.0001	0.09	0.04–0.14	<0.0001
Occupational[b]	−76 (−390, 258)	0.03	0.01–0.04	0.001	0.02	0–0.04	0.09
Household[b]	10 (−87, 279)	0.02	0–0.05	0.05	−0.02	−0.05–0.01	0.16
Excluding those who died before third follow-up ($n = 559$)[d]							
Total	−56 (−426, 246)	0.04	0.02–0.05	<0.001	0.02	0–0.04	0.019
Recreational[b]	0 (−83, 120)	0.14	0.10–0.18	<0.001	0.08	0.03–0.13	0.001
Occupational[b]	−72 (−390, 258)	0.03	0.01–0.04	0.001	0.02	0–0.04	0.07
Household[b]	10 (−66, 222)	0.03	0–0.05	0.027	0	−0.03–0.03	0.94
Moderate-to-vigorous activity (hr/wk/yr)							
Total sample ($N = 817$)							
Total	−17 (−83, 60)	0.11	0.07–0.16	<0.0001	0.04	−0.01–0.09	0.15
Recreational[b]	0 (−20, 21)	0.72	0.54–0.90	<0.0001	0.35	0.15–0.55	0.001
Excluding stage III/IV and IV ($n = 687$)[c]							
Total	−17 (−83, 60)	0.10	0.05–0.15	<0.0001	0.02	−0.03–0.08	0.38
Recreational[b]	0 (−20, 21)	0.81	0.62–1.00	<0.0001	0.45	0.23–0.68	<0.0001
Excluding those who died before third follow-up ($n = 559$)[d]							
Total	−16 (−83, 60)	0.11	0.06–0.16	<0.0001	0.05	−0.01–0.11	0.08
Recreational[b]	0 (−20, 21)	0.70	0.51–0.89	<0.0001	0.43	0.21–0.66	<0.0001

NOTE: All models adjusted for age at diagnosis, aggressive versus nonaggressive prostate cancer, prostate cancer treatment, prostatectomy, PSA value at diagnosis, postdiagnosis Charlson comorbidity score, and prediagnosis lifetime physical activity.
[a]Additionally adjusted for BMI and smoking status.
[b]Mutually adjusted for other physical activity types and intensities (for moderate-to-vigorous activity analysis).
[c]Stage IV cancers: 55; stage III/IV cancers: 75.
[d]152 participants died before second follow-up; 106 participants died between second and third follow-up.

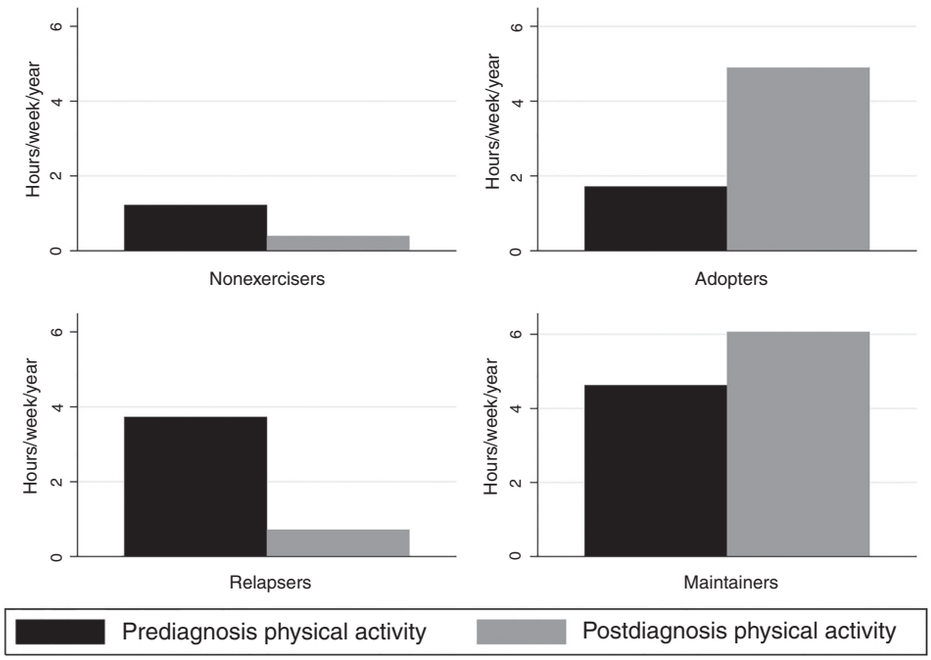

Figure 1.
Change in moderate-to-vigorous recreational physical activity guideline adherence groups over the diagnostic period in prostate cancer survivors in Alberta, Canada (2000–2007).

relapsers and nonexercisers had reduced physical activity levels postdiagnosis (Fig. 1). Future interventions should consider strategies to improve adherence to current exercise and cancer guidelines prior to and after prostate cancer diagnosis.

Our results illustrated a positive association between physical activity and QoL in prostate cancer survivors, similar to other cohort studies (26, 27). However, the studies differed in their methods for physical activity and QoL assessment; therefore, comparisons between studies are somewhat difficult. For example, in the Health Professionals Follow-up Study (24), prostate cancer–specific QoL was measured, and physical activity was significantly associated with vitality/hormonal functioning scores. On the other hand, four exercise intervention studies (52–55) measured generic QoL using PCS and MCS scores. One of these interventions (55) found statistically significant and clinically relevant effects with PCS score (similar to our study); however, three studies (52, 53, 55) found significant associations with MCS score. However, to our knowledge, our study is the first to measure change in lifetime physical activity prior to and after prostate cancer diagnosis in relation to QoL.

The lack of association in total activity may be attributed to the increased duration of occupational and household physical activities in the average day for those who were employed postdiagnosis. Retired men who had an occupational score of zero (Tables 2 and 3) would not have contributed to these associations and therefore, may have spent more time performing recreational activities. We also considered the possibility that cancer survivors with progressing disease or diminishing health would experience a decrease in their QoL and in turn, exercise less. To minimize this bias, we performed sensitivity analyses excluding men with stage III/IV and IV cancer at diagnosis, as well as those who died before completing all three postdiagnosis assessments. Regardless, we continued to observe positive associations between recreational physical activity and PCS scores.

Reverse causation was of less concern with the change in physical activity analysis. Men who were maintainers and adopters had the highest QoL scores. Furthermore, slightly stronger effects were observed for analyses restricted to moderate-to-vigorous recreational physical activity. Nonetheless, given that a majority of our sample had stage II prostate cancer at diagnosis and only a small portion of the sample was confirmed to be stage IV ($n = 55$), we cannot be certain whether disease severity did not have an impact on the physical activity and QoL relationship.

There are multiple proposed mechanisms by which physical activity has been linked to physical and mental QoL. First, in prostate cancer exercise intervention studies, fatigue (56, 57), cardiorespiratory fitness (57), walking speed (56), upper body strength (56), and lower body functional performance (58) has been identified as possible mediators between exercise intervention and different aspects of QoL. Furthermore, marital status, time since diagnosis, and use of bisphosphonates (58) have been described as moderators. In epidemiologic studies, physical activity has been shown to reduce adiposity (27, 59) and inflammation (60), which can account for increased physical functioning. Furthermore, physical activity decreases secretion of insulin (61), enhances sex hormone regulation (59), and in turn, increases insulin resistance and QoL (62). Specifically, improved sex hormone regulation may lead to decreased erectile dysfunction and improved marital relations (62–64). Therefore, modifiable behaviors like physical activity can reduce these burdens. With respect to mental QoL, physical activity has been associated with increased regulation of neurotransmitters associated with mood (65), improved self-esteem, self-efficacy, and reduced anxiety (66), all aspects of psychological functioning. More work is needed to confirm these mechanisms specific to changes in recreational physical activity over the course of the diagnostic period in prostate cancer survivors.

There are some inherent limitations that need to be considered when interpreting these results. First, this was an observational study and, therefore, subject to bias. Measurement

Table 4. Change in moderate-to-vigorous recreational physical activity based on meeting the cancer survivorship guidelines (150 minutes/week) over the diagnostic period (pre- and average postdiagnosis) and average postdiagnosis QoL in prostate cancer survivors in Alberta, Canada, in 1997–2007

Moderate-to-vigorous recreational physical activity guideline adherence (hr/wk/yr)	No. in group	PCS score			MCS score		
		β	95% CI	*P*	β	95% CI	*P*
Total sample ($N = 817$)							
Nonexercisers	272	Referent			Referent		
Adopters	173	4.80	2.82–6.78	<0.0001	2.26	0.09–4.43	0.041
Relapsers	149	−0.04	−2.10–2.01	0.97	−0.35	−2.60–1.89	0.76
Maintainers	223	6.01	4.15–7.86	<0.0001	2.32	0.29–4.34	0.025
Excluding stage III/IV and IV cases ($n = 687$)[a]							
Nonexercisers	224	Referent			Referent		
Adopters	142	4.71	2.60–6.81	<0.0001	2.12	−0.30–4.54	0.09
Relapsers	125	−0.28	−2.46–1.89	0.80	−0.64	−3.13–1.86	0.62
Maintainers	196	6.03	4.09–7.96	<0.0001	2.34	0.12–4.56	0.039
Excluding those who died before third follow-up ($n = 559$)[b]							
Nonexercisers	151	Referent			Referent		
Adopters	128	4.75	2.54–7.00	<0.0001	1.89	−0.66–4.46	0.15
Relapsers	99	0	−2.37–2.36	0.99	−0.41	−3.15–2.33	0.77
Maintainers	181	5.76	3.74–7.78	<0.0001	2.19	−0.15–4.52	0.07

NOTE: All models adjusted for age at diagnosis, aggressive versus nonaggressive prostate cancer, prostate cancer treatment, prostatectomy, PSA value at diagnosis, and postdiagnosis Charlson comorbidity score.

[a]Stage IV cancers: 55; stage III/IV cancers: 75.

[b]152 participants died before second follow-up; 106 participants died between second and third follow-up.

bias in physical activity assessment may exist, which could attenuate the results. However, these data were collected first, by in-person interviews and additionally by self-reported questionnaires; therefore, measurement bias was minimized. Also, measurement and adjustment for sedentary behavior in all analyses would strengthen these results by further isolating physical activity levels. Furthermore, in the physical activity change analysis, we used a change score and are limited in our generalizability of interpretations to individual participants. Change scores are not related to individual baseline values; although we did adjust for prediagnosis physical activity, in general, we cannot differentiate between participant-specific changes in their physical activity levels. However, the analysis examining adherence to physical activity cancer survivorship guidelines addresses these concerns by evaluating physical activity against a standard. Another limitation arises from missing data due to mortality. However, sensitivity analyses excluding those who died before the third follow-up did not materially change the results. Finally, we restricted our study sample to patients with ≥stage II cancers aged <80 years of age; therefore, we can only generalize our results to these cancer populations.

There are implicit strengths that should also be noted. First, this study included a large population-based sample of prostate cancer survivors with a follow-up of 10 years for QoL outcomes. The assessment of physical activity was comprehensive as all parameters of physical activity (i.e., frequency, duration, and intensity) of three separate physical activity types (i.e., recreational, occupational, and household) were captured. Furthermore, using the PCS and MCS scores, rather than individual QoL domains, reduced the issue of multiple testing while providing summary scores of physical and mental QoL. Moreover, the pre- and postdiagnosis physical activity measurements enabled us to examine associations with change in physical activity over the diagnostic period in prostate cancer survivors. Finally, several potential effect modifiers and confounding variables were considered for this analysis to reduce the chance of spurious results and to identify potential subgroups within the population.

Conclusion

This study provided insights regarding the types of physical activity that impact QoL in prostate cancer survivors. Objective measurements of physical activity by accelerometry or fitness trackers are warranted in this population to reduce any suspicions of measurement error and further confirm the benefits of recreational physical activity on QoL. Health professionals should emphasize the importance of recreational physical activity to their patients as a modifiable and a possible behavioral change for most prostate cancer survivors. Interpretations may need to be tailored to prediagnosis physical activity level to ensure prostate cancer survivors can achieve recommended physical activity thresholds. Future research should focus on sedentary behavior to determine efficacy of increased physical activity postdiagnosis in a phase III trial or health promotion program.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Authors' Contributions

Conception and design: K.S. Courneya, S.E. McGregor, C.M. Friedenreich
Development of methodology: M.S. Farris, K.S. Courneya, C.M. Friedenreich
Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.): K.A. Kopciuk, C.M. Friedenreich
Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis): M.S. Farris, K.A. Kopciuk, K.S. Courneya, Q. Wang, C.M. Friedenreich
Writing, review, and/or revision of the manuscript: M.S. Farris, K.A. Kopciuk, K.S. Courneya, S.E. McGregor, Q. Wang, C.M. Friedenreich
Administrative, technical, or material support (i.e., reporting or organizing data, constructing databases): C.M. Friedenreich
Study supervision: C.M. Friedenreich
Other (co-investigator on the grants that obtained the follow-up information, including the timing of the data collection as well as the information to be collected, and a member of the thesis committee of M.S. Farris and worked closely with her on these analyses): K.A. Kopciuk

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References

1. Siegel R, DeSantis C, Virgo K, Stein K, Mariotto A, Smith T, et al. Cancer treatment and survivorship statistics, 2012. CA Cancer J Clin 2012; 62:220–41.
2. Torre LA, Siegel RL, Ward EM, Jemal A. Global cancer incidence and mortality rates and trends-an update. Cancer Epidemiol Biomarkers Prev 2016;25:16–27.
3. Aziz NM. Cancer survivorship research: challenge and opportunity. J Nutr 2002;132:3494S–503S.
4. Canadian Cancer Society's Advisory Committee on Cancer Statistics. Canadian Cancer Statistics 2012. Toronto, ON: Canadian Cancer Society; 2012.
5. Moyer VA; U.S. Preventive Services Task Force. Screening for prostate cancer: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med 2012;157:120–34.
6. Draisma G, Boer R, Otto SJ, van der Cruijsen IW, Damhuis RAM, Schröder FH, et al. Lead times and overdetection due to prostate-specific antigen screening: estimates from the European Randomized Study of Screening for Prostate Cancer. J Natl Cancer Inst 2003;95:868–78.
7. Chodak GW, Thisted RA, Gerber GS, Johansson JE, Adolfsson J, Jones GW, et al. Results of conservative management of clinically localized prostate cancer. N Engl J Med 1994;330:242–8.
8. Albertsen PC, Fryback DG, Storer BE, Kolon TF, Fine J. Long-term survival among men with conservatively treated localized prostate cancer. JAMA 1995;274:626–31.
9. Hall IJ, Lee Smith J. Evolution of a CDC public health research agenda for low-risk prostate cancer. Am J Prev Med 2015;49:S483–8.
10. Richards M, Corner J, Maher J. The National Cancer Survivorship Initiative: new and emerging evidence on the ongoing needs of cancer survivors. Br J Cancer 2011;105 Suppl 1:S1–S4.
11. Punnen S, Cowan JE, Chan JM, Carroll PR, Cooperberg MR. Long-term health-related quality of life after primary treatment for localized prostate cancer: results from the CaPSURE registry. Eur Urol 2015;68:600–8.
12. Eisemann N, Nolte S, Schnoor M, Katalinic A, Rohde V, Waldmann A. The ProCaSP study: quality of life outcomes of prostate cancer patients after radiotherapy or radical prostatectomy in a cohort study. BMC Urol 2015;15:28.
13. Dacal K, Sereika SM, Greenspan SL. Quality of life in prostate cancer patients taking androgen deprivation therapy. J Am Geriatr Soc 2006; 54:85–90.
14. Alibhai SM, Breunis H, Timilshina N, Naglie G, Tannock I, Krahn M, et al. Long-term impact of androgen-deprivation therapy on physical function and quality of life. Cancer 2015;121:2350–7.
15. Brassell SA, Elsamanoudi SI, Cullen J, Williams ME, McLeod DG. Health-related quality of life for men with prostate cancer–an evaluation of outcomes 12–24 months after treatment. Urol Oncol 2013;31:1504–10.
16. Yamamoto S, Fujii Y, Masuda H, Urakami S, Saito K, Kozuka T, et al. Longitudinal change in health-related quality of life after intensity-modulated radiation monotherapy for clinically localized prostate cancer. Qual Life Res 2014;23:1641–50.
17. Friedenreich CM, Wang Q, Neilson HK, Kopciuk KA, McGregor SE, Courneya KS. Physical activity and survival after prostate cancer. Eur Urol 2016 Jan 7. [Epub ahead of print].
18. Richman EL, Kenfield SA, Stampfer MJ, Paciorek A, Carroll PR, Chan JM. Physical activity after diagnosis and risk of prostate cancer progression: data from the cancer of the prostate strategic urologic research endeavor. Cancer Res 2011;71:3889–95.
19. Kenfield SA, Stampfer MJ, Giovannucci E, Chan JM. Physical activity and survival after prostate cancer diagnosis in the health professionals follow-up study. J Clin Oncol 2011;29:726–32.
20. Bonn SE, Sjolander A, Lagerros YT, Wiklund F, Stattin P, Holmberg E, et al. Physical activity and survival among men diagnosed with prostate cancer. Cancer Epidemiol Biomarkers Prev 2015;24:57–64.
21. Galvao DA, Newton RU, Gardiner RA, Girgis A, Lepore SJ, Stiller A, et al. Compliance to exercise-oncology guidelines in prostate cancer survivors and associations with psychological distress, unmet supportive care needs, and quality of life. Psychooncology 2015 Jun 18. [Epub ahead of print].
22. Blanchard CM, Courneya KS, Stein K. Cancer survivors' adherence to lifestyle behavior recommendations and associations with health-related quality of life: results from the American Cancer Society's SCS-II. J Clin Oncol 2008;26:2198–204.
23. Mosher CE, Sloane R, Morey MC, Snyder DC, Cohen HJ, Miller PE, et al. Associations between lifestyle factors and quality of life among older long-term breast, prostate, and colorectal cancer survivors. Cancer 2009;115: 4001–9.
24. Phillips SM, Stampfer MJ, Chan JM, Giovannucci EL, Kenfield SA. Physical activity, sedentary behavior, and health-related quality of life in prostate cancer survivors in the health professionals follow-up study. J Cancer Surviv 2015;9:500–11.
25. Humpel N, Iverson DC. Depression and quality of life in cancer survivors: is there a relationship with physical activity? Int J Behav Nutr Phys Act 2007;4:65.
26. Santa Mina D, Guglietti CL, Alibhai SMH, Matthew AG, Kalnin R, Ahmad N, et al. The effect of meeting physical activity guidelines for cancer survivors on quality of life following radical prostatectomy for prostate cancer. J Cancer Surviv 2014;8:190–8.
27. Santa Mina D, Matthew AG, Trachtenberg J, Tomlinson G, Guglietti CL, Alibhai SM, et al. Physical activity and quality of life after radical prostatectomy. Can Urol Assoc J 2010;4:180–6.
28. Demark-Wahnefried W, Clipp EC, Morey MC, Pieper CF, Sloane R, Snyder DC, et al. Physical function and associations with diet and exercise: Results of a cross-sectional survey among elders with breast or prostate cancer. Int J Behav Nutr Phys Act 2004;1:16.
29. Dahn JR, Penedo FJ, Molton I, Lopez L, Schneiderman N, Antoni MH. Physical activity and sexual functioning after radiotherapy for prostate cancer: beneficial effects for patients undergoing external beam radiotherapy. Urology 2005;65:953–8.
30. Keogh JW, Shepherd D, Krageloh CU, Ryan C, Masters J, Shepherd G, et al. Predictors of physical activity and quality of life in New Zealand prostate cancer survivors undergoing androgen-deprivation therapy. NZ Med J 2010;123:20–9.
31. Chipperfield K, Fletcher J, Millar J, Brooker J, Smith R, Frydenberg M, et al. Predictors of depression, anxiety and quality of life in patients with prostate cancer receiving androgen deprivation therapy. Psychooncology 2013; 22:2169–76.
32. Chipperfield K, Fletcher J, Millar J, Brooker J, Smith R, Frydenberg M, et al. Factors associated with adherence to physical activity guidelines in patients with prostate cancer. Psychooncology 2013;22:2478–86.
33. Teleni L, Chan RJ, Chan A, Isenring EA, Vela I, Inder WJ, et al. Exercise improves quality of life in androgen deprivation therapy-treated prostate cancer: systematic review of randomised controlled trials. Endocr Relat Cancer 2016;23:101–12.
34. Segal RJ, Reid RD, Courneya KS, Malone SC, Parliament MB, Scott CG, et al. Resistance exercise in men receiving androgen deprivation therapy for prostate cancer. J Clin Oncol 2003;21:1653–9.
35. Segal RJ, Reid RD, Courneya KS, Sigal RJ, Kenny GP, Prud'Homme DG, et al. Randomized controlled trial of resistance or aerobic exercise in men receiving radiation therapy for prostate cancer. J Clin Oncol 2009;27:344–51.

36. Galvao DA, Taaffe DR, Spry N, Joseph D, Newton RU. Acute versus chronic exposure to androgen suppression for prostate cancer: impact on the exercise response. J Urol 2011;186:1291–7.
37. Galvao DA, Spry N, Denham J, Taaffe DR, Cormie P, Joseph D, et al. A multicentre year-long randomised controlled trial of exercise training targeting physical functioning in men with prostate cancer previously treated with androgen suppression and radiation from TROG 03.04 RADAR. Eur Urol 2014;65:856–64.
38. Hasenoehrl T, Keilani M, Sedghi Komanadj T, Mickel M, Margreiter M, Marhold M, et al. The effects of resistance exercise on physical performance and health-related quality of life in prostate cancer patients: a systematic review. Support Care Cancer 2015;23:2479–97.
39. Chipperfield K, Brooker J, Fletcher J, Burney S. The impact of physical activity on psychosocial outcomes in men receiving androgen deprivation therapy for prostate cancer: a systematic review. Health Psychol 2014; 33:1288–97.
40. Keogh JW, MacLeod RD. Body composition, physical fitness, functional performance, quality of life, and fatigue benefits of exercise for prostate cancer patients: a systematic review. J Pain Symptom Manage 2012;43:96–110.
41. Friedenreich CM, McGregor SE, Courneya KS, Angyalfi SJ, Elliott FG. Case-control study of lifetime total physical activity and prostate cancer risk. Am J Epidemiol 2004;159:740–9.
42. Friedenreich CM, Courneya KS, Bryant HE. The lifetime total physical activity questionnaire: development and reliability. Med Sci Sports Exerc 1998;30:266–74.
43. Friedenreich CM, Courneya KS, Neilson HK, Matthews CE, Willis G, Irwin M, et al. Reliability and validity of the Past Year Total Physical Activity Questionnaire. Am J Epidemiol 2006;163:959–70.
44. Ainsworth BE, Haskell WL, Leon AS, Jacobs DR Jr, Montoye HJ, Sallis JF, et al. Compendium of physical activities: classification of energy costs of human physical activities. Med Sci Sports Exerc 1993;25:71–80.
45. Kushi LH, Doyle C, McCullough M, Rock CL, Demark-Wahnefried W, Bandera EV, et al. American Cancer Society Guidelines on nutrition and physical activity for cancer prevention: reducing the risk of cancer with healthy food choices and physical activity. CA Cancer J Clin 2012; 62:30–67.
46. World Health Organization. Recommended population levels of physical activity for health. Geneva, Switzerland: World Health Organization; 2010.
47. Pucci GC, Rech CR, Fermino RC, Reis RS. Association between physical activity and quality of life in adults. Rev Saude Publica 2012;46:166–79.
48. Antonescu I, Carli F, Mayo NE, Feldman LS. Validation of the SF-36 as a measure of postoperative recovery after colorectal surgery. Surg Endosc 2014;28:3168–78.
49. Jaeschke R, Singer J, Guyatt GH. Measurement of health status. Ascertaining the minimal clinically important difference. Control Clin Trials 1989; 10:407–15.
50. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373–83.
51. McGregor SE, Courneya KS, Kopciuk KA, Tosevski C, Friedenreich CM. Case-control study of lifetime alcohol intake and prostate cancer risk. Cancer Causes Control 2013;24:451–61.
52. Daubenmier JJ, Weidner G, Marlin R, Crutchfield L, Dunn-Emke S, Chi C, et al. Lifestyle and health-related quality of life of men with prostate cancer managed with active surveillance. Urology 2006;67:125–30.
53. Winger JG, Mosher CE, Rand KL, Morey MC, Snyder DC, Demark-Wahnefried W. Diet and exercise intervention adherence and health-related outcomes among older long-term breast, prostate, and colorectal cancer survivors. Ann Behav Med 2014;48:235–45.
54. McGowan EL, North S, Courneya KS. Randomized controlled trial of a behavior change intervention to increase physical activity and quality of life in prostate cancer survivors. Ann Behav Med 2013; 46:382–93.
55. Park SW, Kim TN, Nam JK, Ha HK, Shin DG, Lee W, et al. Recovery of overall exercise ability, quality of life, and continence after 12-week combined exercise intervention in elderly patients who underwent radical prostatectomy: a randomized controlled study. Urology 2012; 80:299–305.
56. Buffart LM, Galvao DA, Chinapaw MJ, Brug J, Taaffe DR, Spry N, et al. Mediators of the resistance and aerobic exercise intervention effect on physical and general health in men undergoing androgen deprivation therapy for prostate cancer. Cancer 2014;120:294–301.
57. Kalter J, Kampshoff CS, Chinapaw MJ, van Mechelen W, Galindo-Garre F, Schep G, et al. Mediators of exercise effects on HRQoL in cancer survivors after chemotherapy. Med Sci Sports Exerc 2016;48:1859–65.
58. Buffart LM, Newton RU, Chinapaw MJ, Taaffe DR, Spry NA, Denham JW, et al. The effect, moderators, and mediators of resistance and aerobic exercise on health-related quality of life in older long-term survivors of prostate cancer. Cancer 2015;121:2821–30.
59. McTiernan A. Mechanisms linking physical activity with cancer. Nat Rev Cancer 2008;8:205–11.
60. Petersen AM, Pedersen BK. The anti-inflammatory effect of exercise. J Appl Physiol 2005;98:1154–62.
61. Werner H, Bruchim I. The insulin-like growth factor-I receptor as an oncogene. Arch Physiol Biochem 2009;115:58–71.
62. Khera M. Male hormones and men's quality of life. Curr Opin Urol 2016; 26:152–7.
63. Pereira RF, Daibs YS, Tobias-Machado M, Pompeo AC. Quality of life, behavioral problems, and marital adjustment in the first year after radical prostatectomy. Clin Genitourin Cancer 2011;9:53–8.
64. Ramsey SD, Zeliadt SB, Blough DK, Moinpour CM, Hall IJ, Smith JL, et al. Impact of prostate cancer on sexual relationships: a longitudinal perspective on intimate partners' experiences. J Sex Med 2013;10: 3135–43.
65. Erickson KI, Miller DL, Roecklein KA. The aging hippocampus: interactions between exercise, depression, and BDNF. Neuroscientist 2012;18:82–97.
66. Phillips SM, McAuley E. Physical activity and quality of life in breast cancer survivors: the role of self-efficacy and health status. Psychooncology 2014;23:27–34.