

Physical activity for men receiving androgen deprivation therapy for prostate cancer: benefits from a 16-week intervention

S. Nicole Culos-Reed · John W. Robinson · Harold Lau · Lynette Stephenson · Melanie Keats · Steve Norris · Greg Kline · Peter Faris

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Abstract

Goals of work Prostate cancer patients receiving androgen deprivation therapy (ADT) are vulnerable to a number of potentially debilitating side effects, which can significantly impact quality of life. The role of alternate therapies, such as physical activity (PA), in attenuating these side effects is largely understudied for such a large population. Thus, the purpose of this study was to investigate the effects of PA intervention for men receiving ADT on PA behavior, quality of life, and fitness measures.

Patients and methods One hundred participants were randomized into an intervention ($n=53$) or a wait-list control group ($n=47$), with 11 dropping out of the intervention group and 23 dropping out of the wait-list control group prior to post-testing. The intervention consisted of both an individually tailored home-based aerobic and light resistant training program and weekly

group sessions. PA, quality of life, fitness, and physiological outcomes were assessed pre and post the 16-week intervention.

Results Significant increases in PA, supported by changes in girth measures and blood pressure, support the beneficial impact of the intervention. Positive trends were also evident for depression and fatigue. However, due to the high dropout rate, these results must be interpreted with caution. **Conclusions** PA effectively attenuates many of the side effects of ADT and should be recommended to prostate survivors as an alternate therapy. Determining the maintenance of this behavior change will be important for understanding how the long-term benefits of increased activity levels may alleviate the late effects of ADT.

Keywords Cancer · Prostate · Physical activity · Quality of life · Survivorship

S. N. Culos-Reed (✉) · L. Stephenson · S. Norris
Faculty of Kinesiology, University of Calgary,
2500 University Drive NW,
Calgary, AB T2N 1N4, Canada
e-mail: nculosre@ucalgary.ca

J. W. Robinson
Department of Psychosocial Resources,
Tom Baker Cancer Centre,
Calgary, Canada

J. W. Robinson · H. Lau
Department of Oncology, Faculty of Medicine,
University of Calgary,
2500 University Drive NW,
Calgary, AB T2N 1N4, Canada

J. W. Robinson
Program in Clinical Psychology, University of Calgary,
2500 University Drive NW,
Calgary, AB T2N 1N4, Canada

G. Kline
Department of Endocrinology, Faculty of Medicine,
University of Calgary,
2500 University Drive NW,
Calgary, AB T2N 1N4, Canada

P. Faris
Community Health Sciences, University of Calgary,
2500 University Drive NW,
Calgary, AB T2N 1N4, Canada

M. Keats
School of Health and Human Performance, Dalhousie University,
6230 South Street,
Halifax, NS B3H 3J5, Canada

Introduction

Although the projected incidence rate remains relatively high, the mortality rate for prostate cancer in North America is decreasing. As a result of an increase in prevention and early detection programs as well as improved treatment regimes, the 5-year survival rate has increased significantly over the past few decades, reaching 91% and 99% for early stage prostate cancer in Canada and the USA, respectively [1, 2]. Accordingly, there has been a notable shift in the focus of cancer research towards survivorship and quality of life (QOL) [3].

Androgen deprivation therapy (ADT) has become the prevalent therapy with advanced prostate cancer and is now also commonly used as an adjunctive therapy in patients undergoing radiation for localized cancer or those with increasing prostate-specific antigen (PSA) levels [4]. Unfortunately, QOL is often adversely impacted by ADT. Specifically, ADT has a significant negative impact on QOL, especially with regards to physical function and psychosocial issues [5–7]. These side effects may include anemia, cholesterol and lipid changes, depression, impaired sexual function, fatigue, hot flashes, osteoporosis, fractures, body composition changes (i.e., increased body fat and decreased lean body mass), and other potential changes such as muscle/joint pain [8].

As such, the interest in the association between modifiable behaviors, such as physical activity (PA), and QOL within the prostate cancer survivor population has been heightened. Although PA research within the prostate cancer population is limited, a few recent studies have offered support for an inverse association between PA and several adverse medical, physical, and psychosocial outcomes [9–15]. Importantly, each of these studies report moderately significant findings in favor of PA attenuating treatment side effects (e.g., fatigue, sexual dysfunction, and reduced QOL) and potential recurrence.

Although the majority of these studies have been observational, three recent randomized controlled trials (RCT) have investigated the effects of a structured PA program on treatment-related symptoms in prostate patients and survivors. Windsor et al. used an RCT to determine whether a home-based aerobic exercise intervention would reduce the amount of treatment-related fatigue for men receiving external beam radiotherapy [13]. The exercise intervention group reported increased physical function and no change in fatigue levels usually associated with the treatment. Conversely, the control group reported significant increases in fatigue during the 4-week treatment period, which diminished 4 weeks post-treatment but failed to return to baseline levels. Moreover, those who reported higher levels of fatigue also reported poorer QOL related to physical well-being.

Second, the work of Segal et al. found a 12-week resistance training intervention in men receiving ADT was effective in reducing fatigue and improving QOL and overall muscular strength [14]. Galvao et al. extended Segal's work by examining the physical, functional, and physiological effects of a 20-week resistance training program for men receiving ADT [15]. Findings from this study further support the role of resistance exercise in preserving composition and improving physical function in prostate cancer patients. Any effort to attenuate the negative side effects associated with ADT is desirable, and these studies have provided promising evidence of the role of PA in mitigating some of the ADT-related side effects.

While the preliminary data is encouraging, recent reviews have consistently noted a number of limitations associated with the work of PA and cancer patients/survivors. Specifically, there is a dearth of PA intervention studies outside of breast cancer, a lack of physiological outcomes, and few assessments of exercise programs that include components other than aerobic conditioning [16–18]. Duplication of the current positive findings in prostate cancer and further investigation into these physiological and psychosocial outcomes is justified. Accordingly, the primary purpose of this study was to assess the impact of a PA intervention on PA behavior with prostate cancer survivors receiving ADT. Changes in QOL, fitness, and physiological measures were also assessed. We hypothesized that a 16-week PA intervention, including both a home-based and a weekly group session, would be effective in increasing PA levels, enhancing QOL, and improving fitness and physiological measures as compared to a wait-list control condition.

Methods

Participants

Approval was obtained from the appropriate ethical committees, and all participants provided written informed consent prior to participation. The participants in this study were 100 prostate cancer survivors receiving long-term ADT (at least 6 months' treatment duration). They were randomized into either the PA intervention ($n=53$) or the 1-year wait-list control group ($n=47$). Participants were recruited over a 3-month period prior to each of the staggered group start dates. There were a total of five groups between 2004 and 2006. As participants were randomized at each recruitment wave over the 2 years, an uneven randomization into the two groups resulted (i.e., 53 vs 47). Eligibility criteria were as follows: (a) any man diagnosed with prostate cancer (any stage), who may or may not have had previous treatment and was expected to

receive ADT for at least 6 months; and (b) physician's clearance to participate in a hybrid exercise program consisting of aerobic, strength, and flexibility components. Exclusionary criteria were (a) any co-morbid condition that would restrict the participant's ability to enter the program (e.g., heart disease, emphysema, and arthritis) or (b) high risk of osteoporotic fracture due to long-term steroid use or T-score less than -2.5 on screening bone mineral densitometry (BMD) dual energy x-ray absorptiometry scan [19]. Refer to Fig. 1 for participant assignment and flow in the RCT.

Procedure

Following a preliminary telephone screening (prostate cancer diagnosis and on ADT confirmed; physical activity readiness questionnaire administered), participants attended a baseline testing session where the study procedures were explained. Following the completion of the baseline measures (QOL and fitness), participants were randomized into either the intervention or wait-list control group. All participants were provided with a copy of the informed consent and the appropriate laboratory requisitions (blood work and BMD). A post-assessment replicating the pre-assessment measures immediately followed the 16-week intervention, and the same follow-up assessments were completed 2 and 6 months post-intervention. Both groups (i.e., intervention and control) completed all assessments, with exception of the BMD tests which were only required for the pre-assessment and final follow-up. This manuscript focuses upon the immediate, post-intervention results. The follow-up results will be presented elsewhere upon completion of analyses.

Intervention

The intervention group was enrolled in a 16-week exercise program designed to promote daily PA. The prostate active

living series program includes both a home-based portion and weekly group sessions. An individualized PA program was provided by a certified fitness professional in a group-based session (week 1). Exercises were tailored to ability but primarily consisted of walking, stretching, and light resistance exercises (i.e., theraband), which the participant could perform at home. Additionally, exercise equipment (physio ball and theraband) was provided to each participant to encourage and facilitate his home-based PA program (suggested three to five times per week at moderate intensity).

In an effort to enhance social support and utilize group dynamics known to effectively promote PA participation [e.g., 20, 21], participants were also asked to attend weekly booster sessions in a group-based format for the duration of the 16-week intervention and monthly sessions thereafter to the completion of the follow-up assessments. These sessions were conducted in a fitness center. The format of these 1.5-hour sessions included both an activity portion (1 h) and an educational/discussion portion (1/2 h). The activity included a group-based workout, similar to their home-based program (i.e., walking, light resistance work with the band, and core strengthening work with the ball), whereby individualized feedback was provided by a certified fitness specialist. The education and group discussion focused on common concerns facing new exercisers with a new topic each week, including goal setting, monitoring behavior, overcoming barriers, role of a positive attitude and social support, relapse prevention, and the role of nutrition. The discussion periods provided a unique opportunity for the men to share their experiences regarding the integration of PA into their daily lifestyle, obstacles that they may be facing, as well as receive education on known factors that impact adherence.

Measures

Attendance

Booster session attendance was tracked on a recording sheet by the fitness instructor.

Pre-assessment and post-assessment laboratory investigations

Pre-assessment screening measures included screening bone mineral density test, blood work (complete blood count, electrolytes, PSA, total testosterone, fasting glucose, ferritin, magnesium, total protein, parathyroid hormone, luteinizing hormone, follicle stimulating hormone, estradiol, and 25-hydroxy-vitamin D), and urinary N-telo-peptide to assess bone turnover. For purposes of analyses, PSA

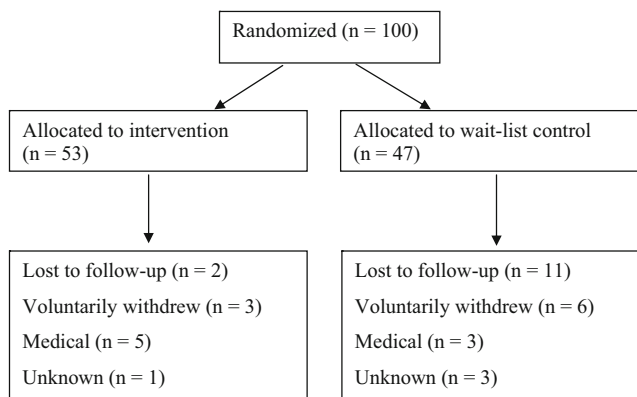


Fig. 1 Participant flow

level changes from pre to post assessment were examined (see attached Table 2).

Psychological questionnaires

Each participant completed a battery of self-report psychological instruments to assess QOL and demographics, including marital status, education, employment, and income. The following instruments were used in assessing QOL:

European Organization for the Research and Treatment of Cancer, Quality of Life Study Group (EORTC QLQ C30) [22]

This 30-item scale includes several domains important in assessing QOL for cancer in general. The domains assessed include physical function, emotional state, social interaction, global health status/QOL, and several symptom scales (e.g., nausea, sleep disturbance, loss of appetite, constipation, diarrhea, and financial impact). This instrument has been well proven in its validity and reliability with reliability coefficients ranging from 0.54 to 0.86 pre-treatment and from 0.522 to 0.89 during treatment [22–25]. The QOL subscale (two items) was used in this study.

Expanded prostate cancer index composite (EPIC) [26]

Based on the original prostate cancer index [27], this instrument assesses function and bother in three organ systems: sexual, urinary, and bowel; and has recently expanded to include possible effects of ADT. The test re-test reliability and internal consistency is reported to be high for the urinary, bowel, sexual, and hormonal domain summary scores ($r \geq 0.80$, $\alpha \geq 0.82$) [26]. The summary of functional scales was used in subsequent analyses.

Fatigue severity scale (FSS) [25, 28]

The FSS is widely used to assess fatigue in a variety of chronic medical conditions, including prostate cancer. Using a seven-point scale, nine items of fatigue are assessed to provide a unitary measure of fatigue. This instrument has been shown to have good internal consistency in both cancer ($\alpha=0.96$) and healthy controls ($\alpha=0.88$).

The center for epidemiological studies depression scale (CES-D)

This 20-item questionnaire has become one of the best known and most widely used surveys for depression [29]. Having undergone extensive reliability and validity testing in a variety of populations, the CES-D has been utilized within the PA domain and found to correlate well with QOL measures [30].

PA behavior

The frequency of past behavior was assessed by Godin's leisure score index (LSI) of the Godin leisure time exercise questionnaire [31]. The LSI is a three-item measure assessing the frequency of mild, moderate, and strenuous bouts of exercise performed for at least 15 min in duration during free time in a typical week. In this study, participants were asked to recall their exercise levels over the past 12 weeks. The LSI has been successfully used with adult cancer patients and survivors [32, 33], and an independent evaluation confirmed its reliability and validity compare to nine other self-report measures of exercise [34].

Physical activity and fitness assessments

PA and fitness assessments included standardized measures which followed the Canadian physical activity fitness and lifestyle appraisal protocol [35]. Measures included baseline physiological parameters (resting heart rate and blood pressure), functional and aerobic capacity (6-min walk test), grip strength (grip dynamometer), and flexibility (modified sit and reach).

Anthropometric assessment

Weight and height was measured to assess the participant's body mass index (BMI). Additionally, waist and hip circumference were measured to compute the waist to hip girth ratio, used to indicate body fat distribution.

Data analysis

All analyses used the statistical package provided by Statistical Package for the Social Sciences (version 14.0). Descriptive statistics included frequencies and percentages for attendance and demographic variables, including marital status, education level, annual family income, and employment status. Change scores were calculated to examine change in the variables from pre to post-intervention (significance value set at $p < .05$). Intention-to-treat (last observation carried forward) repeated measures analysis of variances were used to examine the effect of the PA intervention on fitness, PA behavior, and psychosocial variables. Due to the nature of the intervention, five separate groups completed the program over the course of 2 years. There were no group differences with regard to any of the demographic, medical, or PA variables at pre-intervention (two-sided t tests, all $p > .05$). Thus, subsequent analyses consider all intervention and wait-list control participants in two groups.

Results

Program participation

Participant demographics are shown in Table 1. In summary, the mean age of the participants was 67.6 years (SD=8.6), 88% were married, and 61% were retired. Attendance for the intervention group was 77.8% (participants attended on average 12/16 sessions). Of the original 100 participants, 34% dropped out before post-testing (post-testing $n=66$). The majority of the dropouts (67%) were in the wait-list control group, and discriminant function analysis showed that those who did not attend post-testing were older and had higher depression scores. Of the intervention subjects who withdrew, two were lost to follow-up, three voluntarily dropped out, five withdrew for medical reasons, and one withdrew for unknown reasons. In contrast, for the control group, 11 were lost to follow-up, six voluntarily dropped out, three were medically related, and three dropped for unknown reasons. Independent sample t tests (two-sided) indicated that there were no

other statistically significant differences between the adherers and the dropouts.

Primary outcome: PA behavior

LSI scores pre- to post-intervention showed a significant interaction effect, ($F(1,60)=3.15, p=.004$), with the intervention group reporting increased PA levels (pre $M=26.36$ to post $M=45.05$; 71% increase) and the controls decreased levels (pre $M=35.86$ to post $M=31.14$; 13% decrease) from pre- to post-intervention (see Table 2).

Secondary outcomes

Fitness Measures Significant main effects for time were seen in the fitness indicator of blood pressure (systolic $M=148.9$ mmHg at time 1, $M=139.9$ mmHg at time 2, $p=.004$; diastolic $M=88.6$ mmHg at time 1, $M=83.0$ mmHg at time 2, $p=.0005$). Significant interaction effects were also seen in waist and neck girth (waist, $p=.044$; neck, $p=.019$). Inspection of the means revealed negative changes in the control participants from pre- to post-intervention. No other fitness parameters revealed significant changes.

Quality of Life No significant changes were seen in either the QOL subscale ($\alpha=0.74$) from the EORTC-30 or the hormone symptom scale ($\alpha=0.74$) of the EPIC (see Table 2 for details). Of note, the physical function scale showed poor reliability ($\alpha=0.37$) and is therefore not included in the QOL analyses. The mean scores for this subscale for the intervention group were $M=92.20$ at time 1, $M=91.71$ at time 2, and for the control group, were $M=95.20$ at time 1 and $M=96.00$ at time 2.

Physiological Measures No significant changes were seen in PSA levels from time 1 to time 2 in either group (see Table 2 for details).

Exploratory analyses

The impact of age and medical factors (i.e., stage of disease and duration on treatment) were examined on PA levels and QOL. There were no significant differences between younger vs older participants, or for stage of disease.

Discussion

Although support for the benefits of PA for cancer survivors in general is growing, reviews have consistently noted the need to assess the effectiveness of PA specific to varying cancer types and treatment protocols [16, 18, 36,

Table 1 Participant demographics

	Intervention group	Control group
<i>N</i>	53	47
Mean age (SD)	67.2 (8.8)	68.0 (8.4)
Age range	46–82	49–86
Educational level, <i>n</i> (%)		
Some high school	12 (23.1)	7 (14.9)
Completed high school	10 (19.2)	6 (12.8)
Some university/college	8 (15.4)	12 (25.5)
Completed university/college	17 (32.7)	11 (23.4)
Some/completed graduate school	5 (9.6)	11 (23.4)
Employment status, <i>n</i> (%)		
Full-time	16 (30.2)	5 (10.6)
Retired	30 (56.6)	31 (66.0)
Disability/sick leave	3 (5.7)	1 (2.1)
Other	4 (7.6)	10 (21.2)
Annual income, <i>n</i> (%)		
<\$20,000	4 (8.3)	3 (6.8)
\$20,000–39,999	13 (27.1)	14 (31.8)
\$40,000–59,999	7 (14.6)	14 (31.8)
\$60,000–79,000	9 (18.8)	6 (13.6)
>\$80,000	15 (31.3)	7 (15.9)
Marital status, <i>n</i> (%)		
Married/common law	47 (88.7)	41 (87.2)
Divorced/separated	3 (5.7)	4 (8.5)
Never married	3 (5.7)	1 (2.1)
Widowed	–	1 (2.1)

Table 2 Effect of exercise intervention on outcome variables

Variable	Group	<i>N</i>	Pre (SD)	Post (SD)	Change (SD)	Pre- to post-time effect (<i>p</i>)	Time×group effect (<i>p</i>)
Leisure score index	Int.	38	26.36 (26.72)	45.05 (30.45)	18.69 (33.88)	.002	.004
	Cont.	24	35.87 (36.31)	31.14 (29.30)	−4.73 (23.00)	.324	
Body mass index (kg/m ²)	Int.	41	28.86 (2.51)	28.63 (2.39)	−0.23 (1.02)	.152	.225
	Cont.	22	28.29 (4.48)	29.04 (5.35)	0.75 (4.97)	.488	
Heart rate (bpm)	Int.	38	78.13 (13.15)	76.32 (11.75)	−1.81 (14.62)	.449	.582
	Cont.	19	70.32 (10.35)	70.58 (12.42)	0.26 (10.34)	.913	
Systolic BP (mmHg)	Int.	40	148.85 (17.31)	139.98 (22.79)	−8.87 (20.93)	.011	.774
	Cont.	22	141.09 (17.76)	133.77 (16.79)	−7.32 (19.28)	.090	
Diastolic BP (mmHg)	Int.	40	88.63 (10.64)	83.05 (11.04)	−5.58 (11.36)	.004	.833
	Cont.	22	82.23 (7.42)	76.05 (7.96)	−6.18 (9.67)	.007	
Walk distance (m)	Int.	36	650.03 (143.46)	674.78 (209.37)	24.75 (169.97)	.388	.926
	Cont.	20	701.80 (151.35)	730.60 (183.98)	28.80 (127.54)	.325	
Sit and reach (cm)	Int.	36	20.88 (9.37)	22.12 (8.89)	1.24 (6.30)	.245	.648
	Cont.	18	21.46 (10.18)	23.50 (12.44)	2.04 (5.31)	.122	
Neck girth (cm)	Int.	40	39.87 (2.25)	39.51 (2.40)	−0.36 (1.81)	.221	.019
	Cont.	22	39.41(2.72)	40.21 (3.17)	0.71 (1.77)	.046	
Waist girth (cm)	Int.	40	103.04 (6.57)	102.51 (6.57)	−0.53 (4.68)	.484	.044
	Cont.	22	101.41 (12.41)	103.47 (13.06)	2.06 (4.84)	.059	
Hip girth (cm)	Int.	40	105.68 (7.36)	105.82 (7.02)	0.14 (5.83)	.880	.414
	Cont.	22	107.41 (9.70)	108.73 (9.15)	1.32 (4.50)	.184	
General QOL (EORTC-30)	Int.	40	70.42 (17.39)	73.12 (15.96)	2.70 (0.92)	.269	.194
	Cont.	25	71.33 (18.65)	69.00 (15.12)	−2.33 (0.88)	.436	
Hormone symptoms (EPIC)	Int.	36	62.22 (17.54)	65.87 (15.94)	3.65 (14.11)	.130	.074
	Cont.	22	67.27 (15.49)	64.14 (14.26)	−3.13 (13.09)	.275	
Fatigue (FSS)	Int.	37	4.49 (1.45)	4.15 (1.58)	−0.34 (1.60)	.211	.429
	Cont.	24	4.50 (1.33)	4.46 (1.12)	−0.04 (1.10)	.870	
Depression (CES-D)	Int.	37	8.62 (7.94)	8.22 (6.66)	−0.4 (4.70)	.603	.279
	Cont.	24	6.71 (6.38)	7.67 (8.56)	0.96 (4.86)	.344	
PSA (ug/L)	Int.	39	1.14 (2.39)	1.27 (2.60)	0.13 (1.34)	.619	.491
	Cont.	27	0.82 (2.06)	0.74 (2.51)	−0.08 (0.97)	.408	

37]. Research on PA for attenuating the side effects of ADT for prostate cancer in particular is currently understudied.

The primary purpose of this study was to assess the effectiveness of a PA program, combining both a home-based portion and weekly group sessions, on the PA levels of prostate cancer survivors receiving ADT. Secondary measures of interest included the intervention effects on associated fitness changes, QOL, and physiological outcomes. As predicted, the intervention was successful in significantly increasing PA behavior, which was further supported by concomitant changes in various fitness and body composition measures.

Specifically, PA behavior (LSI scores) significantly increased (71%) in the intervention group from pre- to post-intervention; whereas, control group participants, though not statistically significant, decreased by 13% in their self-reported activity levels. This drop in activity levels is not uncommon in cancer survivors, as previous research notes that both breast and colorectal cancer survivors often fail to return to pre-diagnosis activity levels

following treatment [32, 33]. These PA changes were also supported with small yet statistically significant improvements in blood pressure, and both neck and waist girth. Although blood pressure improved significantly for both groups over time and therefore cannot be attributed to the intervention, significant negative changes in neck girth and borderline significant negative changes in waist girth were evident for the control group from pre- to post-testing. Even small changes in body composition measures are considered clinically relevant. Specifically, these measures may be reflective of the usual weight gain associated with ADT in the control vs the intervention participants. At pre-testing, both groups were similar in average BMI calculations (i.e., intervention group=28.86, controls=28.29) and would be considered in the overweight category [38]. After the program, the intervention participants had a slight decrease in average BMI; whereas, the controls showed an average increase to 29.04, which is just below the line distinguishing overweight from obesity [38]. As Brown et al. suggest in their nutrition and PA guidelines during and after cancer

treatment, moderate PA both during and after treatment will help to achieve appropriate body composition (i.e., increased lean muscle mass and decreased body fat), and losing any weight, whether the ideal weight is even attained, will be beneficial to the survivor [39].

Our secondary purposes were to examine concomitant changes in QOL and physiological outcomes. Our lack of statistically significant findings for QOL outcomes was both surprising and contrary to previous research. In Segal's resistance training intervention for prostate cancer survivors receiving ADT, significant improvements were found for the intervention group after 12 weeks of a structured program; whereas, scores declined for the controls [14]. Possible explanations for the lack of significant findings include that different QOL measurements were used in each study, and it may be possible that the EORTC-30 is not as sensitive to QOL change in such a short timeframe as the functional assessment of cancer therapy-prostate (FACT-P). Second, initial average QOL scores are quite high (70.41 at time 1 and 73.13 at time 2 out of 100) in our intervention group, and a non-significant finding may point to a potential ceiling effect. In addition, the physical function subscale of the EORTC did not achieve adequate reliability ($\alpha=0.37$) and thus could not be examined within subsequent analyses. This is traditionally the aspect of QOL that shows the most positive association with PA, and thus relying on a two-item global QOL scale may have attenuated the findings.

Similarly, our non-significant change found in participant fatigue and depression scores is contrary to the literature. Specifically, extensive research has previously shown PA interventions to be effective in diminishing these cancer-related side effects [e.g., 14, 16, 18, 40–42]. Within prostate cancer specifically, Segal's resistance training study also demonstrated significant reductions in fatigue, with less interference from fatigue on activity and roles in daily life [14]. However, average fatigue scores for the intervention group did drop from 4.49 at pre-test to 4.15 at post-test. On the other hand, the controls remained almost unchanged (4.50 at pre-test and 4.46 at post-test). With severe fatigue being defined as a score of 4.5 or greater, the controls were consistently high; whereas, the intervention group shows a diminishing trend from high towards moderate fatigue levels. Once again, it is possible that the FSS used in our study is not as responsive as the FACT-P fatigue scale used in Segal's work [14]. Nevertheless, any relief from fatigue is beneficial, and for prostate survivors suffering from fatigue following ADT, engaging in a PA program appears to be an effective alternate therapy to combat this debilitating symptom.

In regards to depression, this outcome was not explicitly measured in Segal's, Galvao's, or Windsor's prostate cancer studies [13–15]. Our results, however, indicate a minor

decrease in total depression scores for our intervention group from 8.62 to 8.22 and an increase from 6.71 to 7.67 in our controls from pre- to post-intervention. Any score above 16 is said to indicate clinical depression, so it appears that our cases remain at moderate levels of depression during the intervention, while our controls increase slightly within a moderately depressed range. Although no conclusions can be drawn from our non-significant results, it would be interesting to see if the observed trend is replicated in future prostate cancer and exercise studies. It may be that PA is found to be more preventative (i.e., depression scores do not worsen) than therapeutic (i.e., depression scores improve) for depression levels within prostate cancer patients receiving ADT.

Finally, rising PSA levels have become a widespread biomarker for potential prostate cancer growth or recurrence and are encouraged to be included as an outcome in all prostate cancer studies [43, 44]. Similar to Segal and Galvao's work, no significant alterations were found in PSA levels [14, 15]. However, these findings are also consistent with studies in cancer-free men, where PA levels have not been shown to reduce PSA levels [e.g., 45]. It remains important to further investigate the long-term effect of PA and lifestyle behaviors on PSA levels as it relates to recurrence and survival.

Limitations

With the high dropout rate (34%), our statistical power was reduced, and using an intention-to-treat analysis may have given inadequate numbers to detect significant changes. In theory, 100% adherence would be needed to assess the effectiveness of an intervention, and as Courneya et al. have previously found, exercise adherence has proven a significant problem in cancer survivor trials. Specifically, they noted that adherence rates have ranged from 60% to 85% for either supervised or home-based PA regimes [46, 47]. Thus, our 77.8% adherence rate, coupled with our 34% drop out rate, inevitably had significant implications on our findings.

Accordingly, we suggest that the use of a true control group in future RCTs of PA in cancer survivors should be reconsidered. Moreover, recent exercise and cancer reviews have noted the need to pay more attention to motivation and adherence issues in future trials [37, 48]. As such, utilizing a comparison arm, which provides participants with some benefit (e.g., comparison of two types of PA— aerobic vs weight training), may be appropriate. As the literature clearly supports PA for cancer survivors, examining the benefits of various modes, frequencies, or intensities of exercise programs within different groups should be utilized in future work.

Additional limitations to our study include the potential for sample selection bias, as prostate cancer survivors

interested in or already achieving an active lifestyle may be more likely to participate. The program was also multi-modal, incorporating PA, education, and group support. Thus, the findings cannot be attributed to the effects of activity alone. Future work must examine the relative benefits of these components independently. Furthermore, potential confounding variables such as disease status or specific physiological measures (e.g., anemia) were not obtained. Finally, the intervention length (16 weeks) may have not been sufficient for significant changes in all the outcome measures, thereby limiting the conclusiveness of our findings.

Strengths

Despite these limitations, there are several strengths to this study. The unique design of the intervention arm (i.e., combination of a home-based and weekly group session program) specific to the needs of prostate cancer survivors was successful in providing the tools and social support necessary to alter PA behavior within 16 weeks and provided additional fitness benefits. Overall, the findings do support current literature that altering PA behavior for cancer survivors may alleviate some of the treatment-related side effects. Finally, the prescription of a moderate aerobic activity with light resistance training program contributes to the limited studies employing exercise regimes other than aerobic conditioning alone.

Summary and future directions

In summary, the results of our RCT show a significant increase in PA levels and concomitant changes in some fitness measures. Analysis of the follow-up data with this study will be important for determining the maintenance of this behavior change, which remains a large gap in the cancer literature [49]. Overall, regular PA should be recommended, as Alibhai et al. suggest in their review [50], as adjuvant therapy to minimize the effects of ADT in men with prostate cancer.

References

- American Cancer Society (2006) Fact sheets: prostate cancer. ACS, Georgia
- National Cancer Institute of Canada (2006) Canadian cancer statistics 2006. NCIC, Ontario
- Baker F, Denniston M, Smith T, West MM (2005) Adult cancer survivors: how are they faring? *Cancer* 104(11 Suppl):2565–2576
- Widmark A, Klepp O, Solberg A, Damber J-E, Angelsen A, Fransson P, Lund J-A, Tasdemir I, Hoyer M, Wildund F, Fossa S-D (2009) Endocrine treatment with or without radiotherapy, in locally advanced prostate cancer (SPCG-7/SFUO-3): an open randomised phase III trial. *Lancet* 373:301–308
- Dacal K, Sereika SM, Greenspan SL (2006) Quality of life in prostate cancer patients taking androgen deprivation therapy. *J Am Geriatr Soc* 54:85–90
- Eton DT, Lepore SJ (2002) Prostate cancer and health-related quality of life: a review of the literature. *Psycho-oncology* 11:307–326
- Fowler FJ, Collins MM, Corkery EW, Elliott DB, Barry MJ (2002) The impact of androgen deprivation on quality of life after radical prostatectomy for prostate carcinoma. *Cancer* 95:287–295
- Moyad MA (2005) Promoting general health during androgen deprivation therapy (ADT): a rapid 10-step review for your patients. *Urol Oncol* 23:56–64
- Dahn J, Penedo FJ, Molton I, Lopez L, Schneiderman N, Antoni MH (2005) Physical activity and sexual functioning after radiotherapy for prostate cancer: beneficial effects for patients undergoing external beam radiotherapy. *Urology* 65:953–958
- Demark-Wahnefried W, Clipp EC, Morey MC, Pieper CF, Sloane R, Snyder DC et al (2004) 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* 1(1):16–21
- Giovannucci EL, Liu Y, Leitzmann MF, Stampfer MJ, Willett WC (2005) A prospective study of physical activity and incident and fatal prostate cancer. *Arch Intern Med* 165:1005–1010
- Ornish D, Weidner G, Fair WR, Marlin R, Pettengill EB, Raisin CJ et al (2005) Intensive lifestyle changes may affect the progression of prostate cancer. *J Urol* 174:1065–1070
- Windsor PM, Nicol KF, Potter J (2004) A randomized, controlled trial of aerobic exercise for treatment-related fatigue in men receiving radical external beam radiotherapy for localized prostate carcinoma. *Cancer* 101:550–557
- Segal RJ, Reid RD, Courneya KS, Malone SC, Parliament MB, Scott CG et al (2003) Resistance exercise in men receiving androgen deprivation therapy for prostate cancer. *J Clin Oncol* 21(9):1653–1659
- Galvao DA, Nosaka K, Taaffe DR, Spry N, Kristjanson LJ, McGuigan MR, Suzuki K, Yamaya K, Newton RU (2006) Resistance training and reduction of treatment side effects in prostate cancer patients. *Med Sci Sports Exerc* 38:2045–2052
- Galvao DA, Newton RU (2005) Review of exercise intervention studies in cancer patients. *J Clin Oncol* 23(4):899–909
- McTiernan A (2004) Physical activity after cancer: physiologic outcomes. *Cancer Invest* 22(1):68–81
- Stevinson C, Lawlor DA, Fox KR (2004) Exercise interventions for cancer patients: systematic review of controlled trials. *Cancer Causes Control* 2004(15):1035–1056
- Bae DC, Stein BS (2004) The diagnosis and treatment of osteoporosis in men on androgen deprivation therapy for advanced carcinoma of the prostate. *J Urol* 172(6 Pt 1):2137–2144
- Carron AV, Hausenblas HA, Mack D (1996) Social influence and exercise: a meta-analysis. *J Sport Exerc Psychol* 18:1–16
- McAuley E, Jerome GJ, Elavsky S, Marquez DX, Ramsey SN (2003) Predicting long-term maintenance of physical activity in older adults. *Prev Med* 37:110–118
- Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ et al (1993) The European organization for research and treatment of cancer qlq-c30: a quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst* 85(5):365–376
- Coates A, Porzsolt F, Osoba D (1997) Quality of life in oncology practice: prognostic value of eortc qlq-c30 scores in patients with advanced malignancy. *Eur J Cancer* 33(7):1025–1030
- Joly F, Brune D, Couette JE, Lesaunier F, Heron JF, Peny J et al (1998) Health-related quality of life and sequelae in patients

- treated with brachytherapy and external beam irradiation for localized prostate cancer. *Ann Oncol* 9(7):751–757
25. Stone P, Richards M, A'Hern R, Hardy J (2001) Fatigue in patients with cancers of the breast or prostate undergoing radical radiotherapy. *J Pain Symptom Manage* 22:1007–1015
 26. Wei JT, Dunn RL, Litwin MS, Sandler HM, Sanda MG (2000) Development and validation of the expanded prostate cancer index composite (EPIC) for comprehensive assessment of health-related quality of life in men with prostate cancer. *Urology* 56:899–905
 27. Litwin MS, Hays RD, Fink A, Ganz PA, Leake B, Brook RH (1998) The UCLA prostate cancer index: development, reliability and validity of a health-related quality of life measurement. *Med Care* 1998(36):1002–1012
 28. Stone P, Hardy R, Huddart R, A'Hern R, Richards M (2000) Fatigue in patients with prostate cancer receiving hormone therapy. *Eur J Cancer* 2000(36):1134–1141
 29. McDowell I, Newell C (1996) *Measuring health: a guide to rating scales and questionnaires*, 2nd edn. Oxford University Press, New York
 30. Rejeski WJ, Brawley LR, Shumaker SA (1996) Physical activity and health-related quality of life. *Exerc Sport Sci Rev* 24:71–108
 31. Godin G, Sheppard RJ (1985) A simple method to assess exercise behaviour in the community. *Can J Appl Sport Sci* 10:141–146
 32. Courneya KS, Friedenreich CM (1997) Relationship between exercise during cancer treatment and current quality of life in survivors of breast cancer. *J Psychosoc Oncol* 15(3/4):35–37
 33. Courneya KS, Friedenreich CM (1997) Relationship between exercise pattern across the cancer experience and current quality of life in colorectal cancer survivors. *J Altern Complement Med* 3(3):215–226
 34. Jacobs DR, Ainsworth BE, Hartman TJ, Leon AS (1993) A simultaneous evaluation of ten commonly used physical activity questionnaires. *Med Sci Sports Exerc* 25:81–91
 35. Canadian Society for Exercise Physiology (1998) *The Canadian physical activity, fitness and lifestyle appraisal: CSEP's guide to healthy active living*. Health Canada, Ontario
 36. Schmitz KH, Holtzman J, Courneya KS, Masse LC, Duval S, Kane R (2005) Controlled PA trials in cancer survivors: a systematic review and meta-analysis. *Cancer Epidemiol Biomarkers Prev* 14(7):1588–1595
 37. Oldervoll LM, Kaasa S, Hjermstad MJ, Lund JA, Loge JH (2003) Physical exercise results in the improved subjective well-being of a few or is effective rehabilitation for all cancer patients? *Eur J Cancer* 40:951–962
 38. World Health Organization (1995) *Physical status: the use and interpretation of anthropometry*. WHO Technical Report Series, Geneva, Switzerland
 39. Brown JK, Byers T, Doyle C, Courneya K, Demark-Wahnefried W, Kushi LH et al (2003) *Nutrition and physical activity during and after cancer treatment: an American Cancer Society guide for informed choices*. *CA Cancer J Clin* 53:268–291
 40. Courneya KS (2003) Exercise in cancer survivors: an overview of research. *Med Sci Sports Exerc* 35(11):1846–1852
 41. Dimeo F, Rumberger BG, Keul J (1998) Aerobic exercise as therapy for cancer fatigue. *Med Sci Sports Exerc* 30(4):475–478
 42. Schwartz A (2004) Physical activity after cancer diagnosis: psychosocial outcomes. *Cancer Invest* 22(1):82–92
 43. Kristal AR, Chi C, Tangen CM, Goodman PJ, Etzioni R, Thompson IM (2006) Associations of demographic and lifestyle characteristics with prostate-specific antigen (PSA) concentration and rate of PSA increase. *Cancer* 106:320–328
 44. Penson D, Moul J, Gandhi S, Newling D (2006) Use of prostate-specific antigen in the follow-up of patients with localized prostate cancer: results of a nationwide survey of urologists. *Urology* 68(1):80–84
 45. Ulman C, Buyukyazi G, Taneli F, Uyanik BS (2004) Recreational and master athletic activity does not affect free and total prostate-specific antigen levels but lowers the free-to-total prostate-specific antigen ratio. *J Int Med Res* 32(6):583–589
 46. Courneya KS, Friedenreich CM, Quinney HA, Fields AL, Jones LW, Fairey AS (2004) Predictors of adherence and contamination in a randomized trial of exercise in colorectal cancer survivors. *Psycho-oncology* 13(12):857–866
 47. Courneya KS, Segal RJ, Reid RD, Jones LW, Malone SC, Venner PM et al (2004) Three independent factors predicted adherence in a randomized controlled trial of resistance exercise training among prostate cancer survivors. *J Clin Epidemiol* 57:571–579
 48. Knols R, Aaronson NK, Uebelhart D, Fransen J, Aufdemkampe G (2005) Physical exercise in cancer patients during and after medical treatment: a systematic review of randomized and controlled clinical trials. *J Clin Oncol* 23(16):3830–3842
 49. Wing RR (2000) Cross-cutting themes in maintenance of behaviour change. *Health Psychol* 19(Suppl):84–88
 50. Alibhai SMH, Gogov S, Allibhai Z (2006) Long-term side effects of androgen deprivation therapy in men with non-metastatic prostate cancer: a systematic literature review. *Crit Rev Oncol Hematol* 60:201–215