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ORIGINAL ARTICLE

Physical activity and associations with treatment-induced adverse effects among prostate cancer patients

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Abstract

Purpose The present study aimed to determine the level of physical activity (PA) among prostate cancer (PCa) patients across treatment modalities and explore the association between PA and treatment-induced adverse effects (AEs).

Methods The present study was based on a cross-sectional postal survey among members of the Norwegian Prostate Cancer Association. Patients were eligible for the present study if they had either (1) completed radical prostatectomy, (2) completed radiotherapy and (neo)-adjuvant androgen deprivation therapy (ADT), or (3) were undergoing lifelong ADT. Adverse effects were measured by the Expanded Prostate Cancer Index Composite for Clinical Practice.

Results In total, 696 patients were included. There was no statistically significant difference in level of PA across treatment modalities. Bowel symptoms mainly related to radiotherapy decreased the odds of exercising ≥ 2 times per week, along with age ≥ 70 years, participation in the workforce, and BMI ≥ 25 kg/m^2. Among patients who were undergoing ADT, 5 years or more since diagnosis reduced the odds of exercising ≥ 2 times per week by almost 60%.

Conclusion The level of PA did not differ across PCa patients treated with different modalities. Increasing bowel symptoms reduced the likelihood of exercising ≥ 2 times per week. PCa patients should be educated about possible treatment-induced AEs affecting PA level, enabling them to counteract the development of physical inactivity.

Keywords Prostate cancer · Physical activity · Treatment-induced adverse effects · Radiotherapy · Androgen deprivation therapy · Prostatectomy

Introduction

Prostate cancer (PCa) is the most common cancer among men in Western countries [1]. In Norway, more than 5000 men are diagnosed with PCa each year, and the relative 5-year survival rate has exceeded 90% [2]. The standard curative treatment for patients with localized PCa and a life expectancy of at least 10 years involve either radical prostatectomy (RP) or radiation therapy (RAD) with or without (neo)-adjuvant androgen deprivation therapy (ADT). Among patients with metastatic PCa, life-long ADT is the primary treatment [3]. All these treatments are associated with specific treatment-induced adverse effects (AEs). Typical AEs after RP are urinary incontinence and erectile dysfunction [4, 5], while RAD also may be followed by bowel symptoms and urinary irritation [4, 6]. During long-lasting ADT, patients often experience several systemic AEs, such as sexual dysfunction, fatigue, increased fat mass and decline in physical function, muscle mass, and bone density [7–9], as well as increased risk of diabetes and cardiovascular morbidity [10]. Lack of energy and sexual problems may persist for several months and even years after discontinuation of ADT [6].

Physical activity (PA) has beneficial effects on several health aspects during and after cancer treatment [11].

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Therefore, adult cancer survivors should avoid physical inactivity, and as far as possible follow the oncology exercise guidelines, including 150 min of moderate intensity or 75 min of vigorous intensity (or an equivalent combination) aerobic exercise per week, and resistance training on 2 days or more per week [12].

PCa patients, particularly when undergoing ADT, are likely to benefit from PA by preserving and even improving physical performance and lean body mass and reducing fatigue [13]. Despite the potential to achieve these health benefits, the majority of PCa patients are not meeting the PA recommendations mentioned above [14–18]. There is evidence indicating that PCa patients treated with ADT are less physically active compared to men who have received other types of PCa treatments [18, 19]. However, more research regarding level of PA and treatment-related factors is needed to identify PCa patients in particular need of attention aiming to increase their activity level [18].

In order to assist PCa patients to increase their PA participation, health professionals have to understand the barriers these men meet. A limited number of qualitative and quantitative studies have reported local AEs such as urinary incontinence and bowel problems following PCa treatment as barriers to PA [20–23]. However, large-scale studies in relatively unselected populations of PCa patients documenting the statistical relationship between local and systemic treatment-induced AEs and level of PA are lacking.

Therefore, the aims of the present study were to compare the level of PA among PCa patients across different treatment modalities and explore the association between PA and treatment-induced AEs. We hypothesized that (1) the level of PA would be higher among those who had completed RP or RAD + ADT than patients undergoing ADT for metastatic disease and (2) treatment-induced AEs would be negatively associated with PA.

Material and methods

The Norwegian Prostate Cancer Patients Association (PROFO) is a patient organization founded in 2003, including PCa patients at all stages of the disease. In May 2013, all PCa patients who were members of PROFO were invited to participate in a questionnaire-based cross-sectional survey including assessment of PA, treatment-induced AEs, and global quality of life [24]. Members received an information letter, a questionnaire, and a postage-paid return envelope by mail. In April 2014, a follow-up e-mail was sent out, asking members who had not responded to the mailed version to complete the questionnaire electronically.

Questionnaire variables

Physical activity

Level of PA was assessed by asking how frequently they were exercising each week. The question used was a PA item (frequency) extracted from the 3 PA items (frequency, intensity, and duration) included in the Nord-Trøndelag Health Study: HUNT 1 [25]. The wording of this item was as follows: "By exercise we mean, for example, skiing, swimming, or training/sports leading to breathlessness or sweating. How frequently do you exercise?" The response categories were "never," "less than once per week," "once per week," "2–3 times per week," and "almost every day."

Treatment-induced adverse effects

Treatment-induced AEs were assessed by the Expanded Prostate Cancer Index Composite for Clinical Practice (EPIC-CP) [26]. EPIC-CP is a 16-item questionnaire for self-rating of urinary incontinence, urinary irritation/obstruction, bowel-related symptoms, sexual dysfunction, and vitality/hormonal symptoms in men with PCa. Each of the 5 EPIC-CP domains contains 3 items with 4 or 5 response alternatives scored on a Likert scale ranging from 0 to 4, with increasing score reflecting worse symptom severity/bother [26]. Studies have shown that EPIC-CP correlates highly with previous EPIC versions [27], has good internal consistency, reliability, and discriminative validity, and is responsive to changes in treatment-induced AEs after PCa treatment [26, 28]. For the present study, complete EPIC-CP domains of urinary incontinence, urinary irritation/obstruction, bowel-related symptoms, and sexual dysfunction were included. We extracted the "Lack of energy" item from the vitality/hormonal domain and used it as a stand-alone item dichotomized into no problem/very small problem/small problem versus moderate problem/big problem (no/yes), based on Sanda et al. [6].

Treatment groups

Patients were categorized into 3 groups based on self-reported treatment modalities: (1) completed open or robotic RP and denial of new/other cancer treatment (RP-group), (2) completed RAD and (neo)-adjuvant hormone treatment (ADT) and denial of new/other cancer treatment (RAD+ADT-group), or (3) undergoing ADT or completed orchiectomy, without RP or RAD (ADT-group). Patients not eligible for one of these groups were excluded.

Background variables

Demographic variables were age (< 70/≥ 70 years), basic education level (≤ 12 years/> 12 years), and work force participation, which was dichotomized into retired, sick-leave, work assessment allowance, or disability benefits versus working fulltime or part-time (no/yes). Medical variables included year of diagnosis, time since diagnosis, time since start of treatment, treatment modality (as described previously), and presence of comorbidity affecting general health (no/yes). Lifestyle−/health variables were BMI (calculated into < 25 kg/m^2/≥ 25 kg/m^2 from reported height and weight), daily smoking (no/yes), and perceived general health, which was dichotomized into not so good/poor versus good/excellent (poor/good).

Statistics

Data were analyzed using IBM SPSS Statistics version 21.0 for Windows (SPSS Inc. Chicago, IL, USA).

Continuous variables were displayed by medians and ranges or means and standard deviations (SDs), and categorical variables by frequencies and proportions. To assess differences in level of PA, AEs and background variables between treatment groups, chi-square tests were applied on categorical variables and one-way ANOVA with Tukey post hoc test continuous variables. Two-tailed p values of less than 0.05 were considered statistically significant.

Logistic regression analyses were applied to identify factors associated with level of PA (dependent variable). For these analyses, the level of PA variable was dichotomized into "< 2 times per week" and "≥ 2 times per week". Treatment-induced AEs and background variables (age, education, work-force participation, time since diagnosis, comorbidity, and BMI) represented the independent variables.

Statistically significant variables and variables considered clinically relevant with p values ≈ 0.1 from the univariable logistic regression analyses were included in the multivariable logistic regression analyses. The variables were reduced until only statistically significant variables remained. The strengths of associations were expressed as crude and adjusted odds ratios (cOR and aOR) with 95% confidence intervals (95% CI).

Ethics

The present study was based on an anonymous survey through PROFO, providing the authors with completely anonymous data. Therefore, the present study did not require approval from the regulatory ethics in Norway.

Results

Among 2700 invited patients in PROFO, 1343 returned the questionnaire (response rate ≈ 50%). Of these, 696 patients were eligible for the present study as they reported their primary treatment as completed RP or RAD + ADT, or ongoing ADT.

Characteristics of patients

At the time of survey, the median age was 69.8 years (range from 47 to 105 years) and the median time since diagnosis was 4.7 years (range from < 1 to 23 years) (Table 1). Median time since start of treatment was 45 months (range from < 1 to 241 months). The majority of the included patients were treated with RP (56%, $n = 393$), followed by RAD+ADT (29%, $n = 204$) and ADT alone (14%, $n = 99$) (Table 1).

Treatment-induced AEs

The mean EPIC-CP domain scores are shown in Table 2. Patients treated with RP had significantly higher symptoms of urinary incontinence than patients in the RAD+ADT and ADT-group ($p < .001$). Bowel symptoms were statistically significant higher among patients treated with RAD+ADT than patients in the RP and ADT group ($p < .001$), while those undergoing ADT had the highest sexual symptoms ($p < .001$). Lack of energy was statistically significant less prevalent among patients who had undergone RP (15%) than among those who had completed RAD+ADT (29%) or were undergoing ADT (34%) ($p < .001$).

Distribution of responses to all items in the EPIC-CP urinary incontinence score, urinary irritation/obstruction score, bowel symptom score, sexual symptom score, and lack of energy are given in Online Resource, Fig. 1a-5.

Level of PA

The overall level of PA did not differ between treatment groups ($p = .131$) (Fig. 1). The proportion of men who reported to exercise ≥ 2 times per week was 57% with a minimal non-significant intergroup difference (RP 56%, RAD+ADT 58%, and ADT alone 56%, $p = .892$). Due to the large difference in never exercisers between ADT (10%) and RP (3%), we performed a post-hoc chi-square test which gave a p value of 0.004 (data not shown).

Association between PA and treatment-induced AEs

Among all patients, multivariable logistic regression analyses showed that exercising ≥ 2 times per week was inversely

Table 1 Demographic and medical characteristics of prostate cancer patients treated with radical prostatectomy (RP), radiation therapy with (neo)-adjuvant androgen deprivation therapy (RAD+ADT), and androgen deprivation therapy alone (ADT)

	RP ($n = 393$)	RAD+ADT ($n = 204$)	ADT ($n = 99$)	P	Total ($n = 696$)
Demographic variables					
Age in years, median (min.-max.)	66.8 (47.0–82.8)	73.0 (55.0–105.0)	78.0 (52.1–88.0)		69.8 (47.0–105.0)
< 70 years, *n* (%)	286 (73)	58 (28)	23 (23)	< .001* [ac]	367 (53)
≥ 70 years, *n* (%)	107 (27)	146 (72)	76 (77)		329 (47)
Basic education, *n* (%)					
≤ 12 years	177 (45)	113 (56)	48 (49)	.044* [a]	338 (49)
> 12 years	213 (55)	88 (44)	51 (52)		352 (51)
Missing (*n*)	3	3	0		6
Workforce participation [1], *n* (%)					
No	224 (59)	169 (87)	85 (89)	< .001* [ac]	478 (72)
Yes	154 (41)	25 (13)	11 (12)		190 (28)
Missing (*n*)	15	10	3		28
Medical variables					
Year of diagnosis, *n (%)*					
Before 2010	192 (49)	129 (63)	61 (62)	.001* [ac]	382 (55)
2010 or later	201 (51)	75 (37)	38 (38)		314 (45)
Years since diagnosis, median (min.-max)	4.0 (< 1–23)	5.4 (< 1–15)	5.9 (< 1–16)		4.7 (< 1–23)
< 5 years, *n* (%)	268 (68)	98 (48)	46 (47)	< .001*[ac]	412 (59)
≥ 5 years, *n* (%)	125 (32)	106 (52)	53 (54)		284 (41)
Time since treatment start in months, median (min-max)	38 (< 1–241)	52 (< 1–171)	55 (1–188)	.010*[c]	45 (< 1–241)
Comorbidity affecting health, *n* (%)					
No	230 (60)	122 (60)	52 (54)	.564	404 (59)
Yes	156 (40)	80 (40)	44 (46)		280 (41)
Missing (*n*)	7	2	3		12
Lifestyle−/health variables					
BMI, *n* (%)					
< 25 kg/m^2	128 (33)	57 (28)	35 (35)	.354	220 (32)
≥ 25 kg/m^2	265 (67)	147 (72)	64 (65)		476 (68)
Daily smoker, *n* (%)					
No	357 (93)	188 (94)	87 (91)	.573	632 (93)
Yes	28 (7)	12 (6)	9 (9)		49 (7)
Missing (*n*)	8	4	3		15
General health, *n* (%)					
Poor	63 (16)	50 (25)	36 (37)	< .001* [abc]	149 (22)
Good	326 (84)	151 (75)	61 (63)		538 (78)
Missing (*n*)	4	3	2		9

SD standard deviation, *Min* minimum, *Max* maximum, *BMI* body mass index.*$p < 0.05$ [a] RP vs RAD+ADT; [b] RAD+ADT vs ADT; [c] RP vs ADT. Percentage may not add up to 100% because of rounding. [1] Retired: $n = 433$. Disability benefits: $n = 30$. Sick-leave: $n = 4$. Work assessment allowance: $n = 7$. Other: $n = 433$. *P* values obtained by chi-square-test and one-way ANOVA

associated with worsening (increasing score) of bowel symptoms (aOR .91, 95% CI .85–.97, $p = .003$) (Table 3). In addition, patients aged ≥ 70 years, participating in the workforce and reporting a BMI ≥ 25 kg/m^2 were statistically significant less likely to exercise ≥ 2 times per week than patients aged < 70 years, not participating in the workforce and reporting a BMI < 25 kg/m^2 (Table 3).

In the RP-group, patients aged ≥ 70 years and with a BMI ≥ 25 kg/m^2 were statistically significant less likely to exercise ≥ 2 times per week compared to patients aged < 70 years and with BMI < 25 kg/m^2 (Table 4). In the RAD+ADT-group, worse bowel symptoms decreased the likelihood of exercising ≥ 2 times per week (Table 5). In the ADT-group, time since diagnosis ≥ 5 years reduced the odds of exercising ≥ 2 times per week by approximately 60% (Table 6).

Discussion

Main findings

In the present study, there was no statistically significant difference in overall level of PA between the treatment groups. Worsening of bowel symptoms related to radiotherapy was inversely associated with exercising ≥ 2 times per week. Moreover, patients aged ≥ 70 years, those who participated in the workforce and men who were overweight, were less likely to exercise ≥ 2 times per week.

Level of PA

We hypothesized that patients undergoing ADT would report a lower level of PA than patients treated with RP and RAD+

Table 2 EPIC-CP scores and presence of lack of energy among prostate cancer patients treated with radical prostatectomy (RP), radiation therapy with (neo)-adjuvant androgen deprivation therapy (RAD+ADT), and androgen deprivation therapy alone (ADT)

	RP ($n = 393$)	RAD+ADT ($n = 204$)	ADT ($n = 99$)	P	Total ($n = 696$)
EPIC-CP domain score, mean (SD) (score out of 12^)					
Urinary Incontinence	3.1 (2.8)	1.4 (1.9)	1.4 (1.9)	< .001* ac	2.4 (2.6)
Urinary irritation/obstruction	1.9 (1.9)	3.0 (2.5)	2.9 (2.5)	< .001* ac	2.4 (2.2)
Bowel symptoms	1.0 (1.9)	2.7 (3.1)	1.6 (2.4)	< .001* ab	1.6 (2.5)
Sexual symptoms	7.1 (3.1)	7.3 (2.9)	9.1 (2.5)	< .001* bc	7.4 (3.0)
Lack of energy, *n* (%)					
No	335 (85)	145 (71)	65 (66)	< .001* ac	545 (78)
Yes	58 (15)	59 (29)	34 (34)		151 (22)

^Higher score = worse symptoms. *SD* standard deviation. *$p < 0.05$. [a] RP vs RAD+ADT; [b] RAD+ADT vs ADT; [c] RP vs ADT. *P* values obtained by chi-square-test and one-way ANOVA

ADT, due to the systemic AEs from ADT (e.g., fatigue and decreased muscle mass). Chipperfield et al. [19] found that patients treated with ADT were less physically active than patients treated with RAD only, and Forbes et al. [18] reported that patients who had undergone prostatectomy were more active than those who had received other PCa treatments. In contrast to our hypothesis and findings from previous studies, the overall level of PA in the present study was similar across treatment modalities. A possible explanation for this finding might be that patients in the ADT-group primarily have been more encouraged by health professionals to be physically active when starting ADT than patients treated with RP, due to the known benefits of PA on ADT-induced AEs. Also, patients in the ADT-group might have allocated more of their time to be physically active, as only 12% were active in the workforce (versus 41% in the RP-group). However, a post-hoc chi-square test comparing the prevalence of those reporting to never exercise indicated a significant difference between ADT and RP. This indicates that AEs associated with ADT, advanced cancer, and lower general health [9] can limit the ability to conduct PA leading to breathlessness and sweating, and that special attention should be paid towards PCa patients undergoing ADT to maintain or increase level of PA.

Interestingly, patients who had completed RAD+ADT were not more physically active than patients undergoing ADT. This might in part be explained by delayed recovery of testosterone production after discontinuation of adjuvant ADT, which is particularly frequent among older patients [29]. Consequently, these patients continue to suffer from AEs usually associated with undergoing ADT such as fatigue [6], a common exercise barrier among cancer survivors [30, 31].

Studies have reported that approximately 45% of PCa patients are meeting exercise guidelines of at least 150 min moderate or 75 min vigorous PA weekly [15, 17–19]. Among Norwegian men in the general population aged above 60 years,

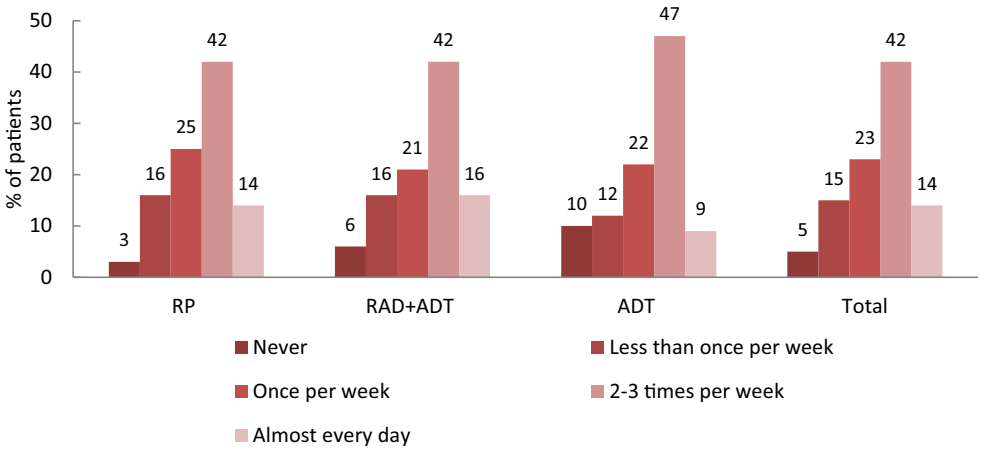

Fig. 1 Reported exercise frequency in per cent among prostate cancer patients treated with radical prostatectomy (RP), radiotherapy + androgen deprivation therapy (RAD+ADT) and ADT. There was no difference in overall exercise frequency between treatment groups ($p = .131$, obtained by chi-square test)

Table 3 All patients ($n = 696$): factors associated with exercising ≥ 2 times per week versus less

	Exercise frequency		Unadjusted analyses			Adjusted analyses		
	< 2 times/ week	≥ 2 times/ week	cOR	95% CI	*P*	aOR	95% CI	*P*
EPIC-CP domain score, mean (SD)(score out of 12[1])								
Urinary incontinence	2.5 (2.6)	2.3 (2.6)	.97	.92–1.03	.283			
Urinary irritation/obstruction	2.3 (2.2)	2.4 (2.2)	1.02	.96–1.09	.545			
Bowel symptoms	1.9 (2.6)	1.4 (2.3)	.91	.86–.97	*.003**	.91	.85–.97	.003*
Sexual symptoms	7.7 (3.0)	7.2 (3.1)	.95	.90–.99	*.027**			
Lack of energy, *n* (%)								
No (reference)	227 (42)	318 (58)	1.0					
Yes	76 (50)	75 (50)	.70	.49–1.01	*.058*			
Demographic variables								
Age, *n* (%)								
< 70 years (reference)	148 (40)	219 (60)	1.0			1.0		
≥ 70 years	155 (47)	174 (53)	.76	.56–1.03	*.072*	.56	.39–.82	.002*
Basic education, *n* (%)								
≤ 12 years (reference)	154 (46)	184 (54)	1.0					
> 12 years	144 (41)	208 (59)	1.21	.89–1.64	.218			
Work force participation, *n* (%)								
No (reference)	198 (41)	280 (59)	1.0			1.0		
Yes	91 (48)	99 (52)	.77	.55–1.08	*.128*	.52	.35–.79	.002*
Medical variables								
Time since diagnosis, *n* (%)								
< 5 years (reference)	170 (41)	242 (59)	1.0					
≥ 5 years	133 (47)	151 (53)	.80	.59–1.08	.146			
Comorbidity affecting health, *n* (%)								
No (reference)	170 (42)	234 (58)	1.0					
Yes	126 (45)	154 (55)	.89	.65–1.21	.448			
Health variables								
BMI, *n* (%)								
< 25 kg/m^2 (reference)	81 (37)	139 (63)	1.0			1.0		
≥ 25 kg/m^2	222 (47)	254 (53)	.67	.48–.93	*.015**	.66	.47–.93	.016*

[1] Higher score = worse symptoms. *SD* standard deviation, *cOR* crude odds ratio, *aOR* adjusted odds ratio, *95% CI* 95% confidence interval.*$p < 0.05$. *BMI* body mass index (kg/m^2). Numbers may not add up to 696 because of missing values. Percentage may not add up to 100% because of rounding. In adjusted analyses, bowel symptoms, sexual symptoms, lack of energy, age, work force participation and BMI were included (italic). [2] Number included in adjusted analyses: $n = 668$. Variables were reduced until only statistically significant variables were remaining

less than 40% meet these exercise guidelines, measured by accelerometer [32]. It is not possible to directly compare our findings with other studies, nor state whether the patients meet the exercise guidelines or not, as the PA question in the present study did not take into account duration or more detailed intensity. Still, our findings indicate that a considerable proportion of PCa patients are exercising once per week or less. Galvão et al. [14] found that only 12.3% of PCa survivors met the exercise guidelines of both aerobic and strength training; however, ≈ 53% reported to be physically active in some way. This finding is comparable with the prevalence of 57% reporting to exercise 2–3 times or more per week in the present study.

Level of PA and associated factors

Treatment-induced AEs

In agreement with our hypothesis, PCa patients who reported increasing bowel symptoms related to radiotherapy were less likely to exercise ≥ 2 times per week. Our finding is in line with Henriksson et al. [20], who conducted focus-group interviews with PCa patients and reported bowel symptoms after radiotherapy as a barrier to exercise. To our knowledge, this is the first cross-sectional study demonstrating that bowel symptoms may decrease the likelihood of exercising ≥ 2 times per week among irradiated PCa patients.

Table 4 Patients treated with radical prostatectomy (RP) (n = 393): factors associated with exercising ≥ 2 times per week versus less

	Exercise frequency		Unadjusted analyses			Adjusted analyses[2]		
	< 2 times/ week	≥ 2 times/ week	cOR	95% CI	P	aOR	95% CI	*P*
EPIC-CP domain score, mean (SD)(score out of 12[1])								
Urinary incontinence	3.2 (2.8)	3.0 (2.8)	.98	.91–1.05	.494			
Urinary irritation/obstruction	1.8 (2.0)	1.9 (1.8)	1.02	.92–1.13	.719			
Bowel symptoms	1.1 (1.9)	1.0 (1.9)	.96	.87–1.07	.471			
Sexual symptoms	7.3 (3.0)	6.9 (3.2)	.96	.90–1.02	.160			
Lack of energy, *n* (%)								
No (reference)	147 (44)	188 (56)	1.0					
Yes	26 (45)	32 (55)	.96	.55–1.69	.893			
Demographic variables								
Age, *n* (%)								
< 70 years (reference)	114 (40)	172 (60)	1.0			1.0		
≥ 70 years	59 (55)	48 (45)	.54	.34–.84	*.007**	.51	.33–.81	.004*
Basic education, *n* (%)								
≤ 12 years (reference)	84 (48)	93 (53)	1.0					
> 12 years	87 (41)	126 (59)	1.31	.88–1.96	.190			
Work force participation, *n* (%)								
No (reference)	94 (42)	130 (58)	1.0					
Yes	71 (46)	83 (54)	.85	.56–1.28	.425			
Medical variables								
Time since diagnosis, *n* (%)								
< 5 years (reference)	110 (41)	158 (59)	1.0					
≥ 5 years	63 (50)	62 (50)	.69	.45–1.05	*.083*			
Comorbidity affecting health, *n* (%)								
No (reference)	100 (44)	130 (57)	1.0					
Yes	67 (43)	89 (57)	1.02	.68–1.54	.918			
Health variables								
BMI, *n* (%)								
< 25 kg/m^2 (reference)	47 (37)	81 (63)	1.0			1.0		
≥ 25 kg/m^2	126 (48)	139 (53)	.64	.42–.99	*.043**	.60	.39–.94	.025*

[1] Higher score = worse symptoms. *cOR* crude odds ratio, *aOR* adjusted odds ratio, *95% CI* 95% confidence interval, *SD* standard deviation.*$p < 0.05$. *BM* body mass index (kg/m^2). Numbers may not add up to 393 because of missing values. Percentage may not add up to 100% because of rounding. [2] Numbers included in adjusted analyses: n = 393. Variables included in multivariable analyses were age, time from diagnosis to survey, and BMI (italic). Variables were reduced until only statistically significant variables were remaining

Contrary to our hypothesis, urinary incontinence did not influence PA in our study, which we expected to be particularly frequent among patients in the RP-group. According to Craike et al. [21], urinary incontinence is a barrier to PA the first weeks after surgery. Ottenbacher et al. [23] reported that recently diagnosed PCa patients who stated "problems with urination limit my activities," were less physically active in a PA intervention compared to those without urinary problems. Further, Geraerts et al. [22] found that the PA level among patients treated with RP was significantly lower 6 weeks after surgery, but returned to baseline levels shortly from that time. Most of the patients in our study only experienced urinary incontinence symptoms at a minor degree. Therefore, a reasonable explanation for our finding might be that long-term low-grade urinary incontinence is not a relevant PA barrier for most patients treated with prostatectomy.

In contrast to previous studies reporting lack of energy and fatigue as a PA barrier among PCa survivors [20, 31, 33], multivariable analyses among all patients showed no statistically significant association between PA level and lack of energy in the present study. However, patients in the ADT-group were significantly less likely of exercising ≥ 2 times per week if time since diagnosis was ≥ 5 years. In addition, lack of energy was borderline statistically significant negatively associated with exercising ≥ 2 times per week. This indicates that several factors associated with long-term ADT and aging might affect PA level, such as loss of muscle mass [34] and fatigue, which can worsen with time after initiation of ADT [35].

Table 5 Patients treated with radiotherapy and (neo)-adjuvant androgen deprivation therapy ($n = 204$): factors associated with exercising ≥ 2 times per week versus less

	Exercise frequency		Unadjusted analyses			Adjusted analyses[2]		
	< 2 times/ week	≥ 2 times/ week	cOR	95% CI	*P*	aOR	95% CI	*P*
EPIC-CP domain score, mean (SD)(score out of 12[1])								
Urinary incontinence	1.4 (2.0)	1.4 (1.9)	.99	.86–1.14	.853			
Urinary irritation/obstruction	3.0 (2.3)	3.1 (2.6)	1.02	.91–1.14	.762			
Bowel symptoms	3.6 (3.2)	2.0 (2.8)	.84	.76–.92	*< .001**	.84	.76–.92	< .001*
Sexual symptoms	7.7 (2.9)	7.1 (2.8)	.92	.83–1.02	*.101*			
Lack of energy, *n* (%)								
No (reference)	55 (38)	90 (62)	1.0					
Yes	31 (53)	28 (48)	.55	.30–1.02	*.057*			
Demographic variables								
Age, *n* (%)								
< 70 years (reference)	26 (45)	32 (55)	1.0					
≥ 70 years	60 (41)	86 (59)	1.17	.63–2.15	.626			
Basic education, *n* (%)								
≤ 12 years (reference)	51 (45)	62 (55)	1.0					
> 12 years	32 (36)	56 (64)	1.44	.81–2.55	.211			
Work force participation, *n* (%)								
No (reference)	69 (41)	100 (59)	1.0					
Yes	13 (52)	12 (48)	.64	.27–1.48	.294			
Medical variables								
Time since diagnosis, *n* (%)								
< 5 years (reference)	44 (45)	54 (55)	1.0					
≥ 5 years	42 (40)	64 (60)	1.24	.71–2.17	.446			
Comorbidity affecting health, *n* (%)								
No (reference)	46 (38)	76 (62)	1.0			1.0		
Yes	40 (50)	40 (40)	.61	.34–1.07	*.085*	.68	.37–1.21	.180
Health variables								
BMI, *n* (%)								
< 25 kg/m^2 (reference)	21 (37)	36 (63)	1.0					
≥ 25 kg/m^2	65 (44)	82 (56)	.74	.39–1.38	.339			

[1] Higher score = worse symptoms. *cOR* crude odds ratio, *aOR* adjusted odds ratio, *95% CI* 95% confidence interval, *SD* standard deviation. *$p < 0.05$. *BMI* body mass index (kg/m^2). Numbers may not add up to 204 because of missing values. Percentage may not add up to 100% because of rounding. [2] Numbers included in adjusted analyses: $n = 202$. In adjusted analyses, bowel symptoms, sexual symptoms, lack of energy, and comorbidity affecting health were included (italic). Variables were reduced until only statistically significant variables were remaining

Demographic and health variables

In the total sample and among patients treated with RP, we found that patients aged 70 years and older had nearly 50% lower odds of exercising ≥ 2 times per week compared to those younger than 70 years. It is well established that participation in PA declines with increasing age [36]. The inverse association between PA and advancing age is in line with previous studies both in healthy older adults and cancer patients [21, 30, 37].

Interestingly, workforce participation decreased the odds of exercising ≥ 2 times per week by almost 50%. This might be attributed to lack of time and energy for PA due to prioritizing being active in the workforce. Lack of time has been reported as a common PA barrier, both among PCa patients [21, 38], and among community dwelling older adults [39].

Among all patients and also in the subgroup of patients treated with RP, BMI ≥ 25 kg/m^2 was associated with lower odds of exercising ≥ 2 times per week. This is in line with previous findings among cancer patients [40, 41] and in the general population [37].

Limitations

Causal inferences between treatment-induced AEs and level of PA cannot be determined, due to the cross-sectional design of the present study.

Table 6 Patients treated with androgen deprivation therapy (ADT) ($n = 99$): factors associated with exercising ≥ 2 times per week versus less

	Exercise frequency		Unadjusted analyses			Adjusted analyses[2]		
	< 2 times/ week	≥ 2 times/ week	cOR	95% CI	*P*	aOR	95% CI	*P*
EPIC-CP domain score, mean (SD)(score out of 12[1])								
Urinary incontinence	1.7 (1.9)	1.2 (2.0)	.88	.71–1.08	.221			
Urinary irritation/obstruction	2.8 (2.5)	3.0 (2.4)	1.02	.87–1.21	.776			
Bowel symptoms	1.8 (2.6)	1.5 (2.3)	.95	.81–1.12	.560			
Sexual symptoms	9.3 (2.1)	8.9 (2.7)	.93	.79–1.10	.382			
Lack of energy, *n* (%)								
No (reference)	25 (39)	40 (62)	1.0			1.0		
Yes	19 (56)	15 (44)	.49	.21–1.15	*.100*	.42	.17–1.01	.053
Demographic variables								
Age, *n* (%)								
< 70 years (reference)	8 (35)	15 (65)	1.0					
≥ 70 years	36 (47)	40 (53)	.59	.23–1.56	.290			
Basic education, *n* (%)								
≤ 12 years (reference)	19 (40)	29 (60)	1.0					
> 12 years	25 (49)	26 (51)	.68	.31–1.51	.346			
Work force participation, *n* (%)								
No (reference)	35 (41)	50 (59)	1.0					
Yes	7 (64)	4 (36)	.40	.11–1.47	.168			
Medical variables								
Time since diagnosis, *n* (%)								
< 5 years (reference)	16 (35)	30 (65)	1.0					
≥ 5 years	28 (53)	25 (47)	.48	.21–1.07	*.073*	.41	.18–.96	.040*
Comorbidity affecting health, *n* (%)								
No (reference)	24 (46)	28 (54)	1.0					
Yes	19 (43)	25 (57)	1.13	.50–2.53	.770			
Health variables								
BMI, *n* (%)								
< 25 kg/m^2 (reference)	13 (37)	22 (63)	1.0					
≥ 25 kg/m^2	31 (48)	33 (52)	.63	.27–1.46	.281			

[1] Higher score = worse symptoms. *cOR* crude odds ratio, *95% CI* 95% confidence interval, *SD* standard deviation. *$p < 0.05$. *BMI* body mass index (kg/m^2). Numbers may not add up to 99 because of missing values. [2] Numbers included in adjusted analyses: $n = 99$. In adjusted analyses, lack of energy and time from diagnosis to survey were included (italic). Variables were reduced until only statistically significant variables were remaining

We acknowledge the shortcomings of our PA measure, not taking into account more details in terms of the reported exercise. In general, self-reported measures of PA are less accurate than objective measures of PA, such as accelerometers. By using self-report, there is a chance that the patients in the present study might have overestimated their level of PA [42]. In addition, as the patients in the present study might experience fatigue and reduced physical capacity due to their PCa trajectory resulting in more rapid breathlessness and sweating in daily activities not usually classified as "exercise," misclassification of a high PA level may have occurred. This may particularly apply for those undergoing or who recently completed ADT as these men can suffer from hot flashes causing spontaneous sweating due to hormonal changes [9]. Moreover, significantly worse physical performance among men undergoing ADT has been demonstrated compared to age-matched men from the general population [7]. However, there is also evidence that measuring PA with a single question can provide valid information about exercise participation [43]. For the present study, we believe our PA measure provide sufficient insight in PA for the aims of comparing engagement in PA across treatment groups, and explore the associations between PA and treatment-induced AEs.

As the response rate in the present study was 50% and only members of PROFO were invited to participate, our study might be limited by selection bias favoring PCa patients with relatively good general health and high education level. High education level has shown to influence level of PA positively [44]; thus, there is also chance that the patients in the present study represent PCa patients that are more likely to be physically active than PCa patients in general. Finally, as patients in the RAD+ADT-group were treated up to 14 years ago, these

patients might have experienced bowel problems at a larger scale due to outdated radiotherapy technologies compared to patients treated more recently.

Conclusion

In conclusion, the present study showed that more than 40% of PCa patients had a low level of PA after local curative treatment or during lifelong ADT. Bowel symptoms were inversely associated with exercising ≥ 2 times per week, and may represent a barrier to physical activity among irradiated PCa patients. In addition, PCa patients were less likely to exercise ≥ 2 times per week if aged 70 years or older, participating in the workforce or overweight. Health care professionals should educate patients undergoing treatment about possible treatment-induced AEs affecting PA level, enabling them to counteract the development of physical inactivity. PCa patients at risk of physical inactivity should be identified and offered support to engage in PA, e.g. by being motivated to allocate time for PA and guided in preserving or achieving a healthy body weight.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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