Research Article

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Physical Activity and Survival among Men Diagnosed with Prostate Cancer

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Abstract

Background: Few studies have investigated the association between post-diagnosis physical activity and mortality among men diagnosed with prostate cancer. The aim of this study was to investigate the effect of physical activity after a prostate cancer diagnosis on both overall and prostate cancer–specific mortality in a large cohort.

Methods: Data from 4,623 men diagnosed with localized prostate cancer 1997–2002 and followed-up until 2012 were analyzed. HRs with 95% confidence intervals (CI) were estimated using Cox proportional hazards models to examine the association between post-diagnosis recreational MET-h/d, time spent walking/bicycling, performing household work or exercising, and time to overall and prostate cancer–specific death. All models were adjusted for potential confounders.

Results: During the follow-up, 561 deaths of any cause and 194 deaths from prostate cancer occurred. Statistically significantly lower overall mortality rates were found among men engaged in $\geq$5 recreational MET-h/d (HR, 0.63; 95% CI, 0.52–0.77), walking/bicycling $\geq$20 min/d (HR, 0.70; 95% CI, 0.57–0.86), performing household work $\geq$1 h/d (HR, 0.71; 95% CI, 0.59–0.86), or exercising $\geq$1 h/wk (HR, 0.74; 95% CI, 0.61–0.90), compared with less active men within each activity type. For prostate cancer–specific mortality, statistically significantly lower mortality rates were seen among men walking/bicycling $\geq$20 min/d (HR, 0.61; 95% CI, 0.43–0.87) or exercising $\geq$1 h/wk (HR, 0.68; 95% CI, 0.48–0.94).

Conclusions: Higher levels of physical activity were associated with reduced rates of overall and prostate cancer–specific mortality.

Impact: Our study further strengthens previous results indicating beneficial effects of physical activity on survival among men with prostate cancer. *Cancer Epidemiol Biomarkers Prev; 24(1); 57–64.* *©2014 AACR.*

Introduction

Prostate cancer is the most common type of cancer among men in the Western world (1). The incidence is continuing to increase while mortality rates decrease (2). The vast majority of patients are diagnosed with localized disease (2) and have a good prognosis of survival. In Sweden, the 10-year survival rate for all stages combined is approximately 70% (3). Physical activity has previously been associated with increased muscular fitness, physical functioning and health-related quality of life among men with prostate cancer (4, 5) and could potentially complement existing treatments after diagnosis to improve survival.

There is consistent evidence linking increased physical activity to reduced all-cause mortality among cancer survivors, as well as reductions in breast and colon cancer–specific mortality (6). Among male cancer survivors, higher levels of physical activity have also been associated to both all-cause and cancer-specific mortality (7). Although increased physical activity was associated with a reduced risk of prostate cancer in a recent meta-analysis (8), very little is known about the association between post-diagnosis physical activity and survival among patients with prostate cancer.

Only 2 recent studies have previously investigated the effects of physical activity after diagnosis on prostate cancer progression and mortality. The first study published by Kenfield and colleagues (9) showed that among 2,705 men with nonmetastatic prostate cancer, those who were vigorously active post-diagnosis had a reduced risk of prostate cancer–specific mortality by 61% compared with less active men. The second study by Richman and colleagues (10), following 1,455 men, showed that men walking briskly during $\geq$3 h/wk had a 57% lower rate of progression than in men who walked at an easier pace for shorter duration. Also, a suggestive, but nonsignificant, inverse association between vigorous activity and prostate cancer progression was seen.

Using data from a cohort of 4,623 Swedish men diagnosed with localized prostate cancer, we aim to further investigate the effect of prostate cancer post-diagnosis physical activity on overall and prostate cancer–specific mortality in a larger study sample than previously used.

Materials and Methods

The Swedish National Cancer Register (NCR; ref. 11) holds information on all incident cancers in Sweden, whereas the National Prostate Cancer Register (NPCR; ref. 12) of Sweden includes 98% of prostate cancer cases in the NCR. The latter also holds information of tumor–node–metastasis (TNM) stage, serum prostate-specific antigen (PSA) levels, tumor differentiation at time of diagnosis, and primary treatment.

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Study participants in the present study (PROCAP, PROgression in CAncer of the Prostate) were derived from the NPCR of Sweden Follow-up Study (13), a retrospective nationwide cohort study of men with localized prostate cancer. In short, participants eligible for inclusion in this study were men registered with a localized prostate cancer in the NPCR between January 1, 1997 (January 1, 1998, in one region) and December 31, 2002. Further inclusion criteria were diagnostic serum PSA <20 ng/mL, local tumor stage T1-T2, no signs of lymph node metastasis (NX or N0), or bone metastasis (MX or M0), and being ≤70 years of age at diagnosis. In total, 8,304 patients fulfilled the criteria and 7,960 (96%) accepted inclusion to the NPCR of Sweden Follow-up Study.

All men in the NPCR of Sweden Follow-up Study who were still alive in 2007 ($n = 7{,}075$) were eligible for inclusion in PROCAP. In total, 5,779 (82%) of the invited men responded to a questionnaire assessing lifestyle factors and/or donated a blood sample for genetic analysis between January 2007 and June 2008. Participants responded to the questionnaire either in paper format (50%) or via the web (50%). Paper-based questionnaires were scanned into a digital format after being checked for completeness by study personnel, whereas data from the web-based questionnaires were directly saved in digital format. The PROCAP study has previously been described elsewhere (14). Men with missing clinical information ($n = 290$) or questionnaire data ($n = 301$) and men with incomplete data on physical activity ($n = 525$) were excluded. In total, 4,623 patients were included in the final analysis.

End points in the present study were prostate cancer–specific mortality and all-cause mortality. Cause of death and date of death were obtained from the Swedish Cause-of-Death Registry. Time to event was defined as time from prostate cancer diagnosis to date of death reported in the registry or censoring on December 31, 2012, whichever came first.

The study has been approved by the research ethics board at Karolinska Institutet (Stockholm, Sweden) and all patients included in PROCAP gave their written informed consent for participation at the time of inclusion.

Time spent walking/bicycling, performing household work, and exercising "after diagnosis" was estimated using a validated physical activity questionnaire (15). Participants were asked to report how much time they spent walking/bicycling, performing household work, or exercising "after diagnosis." Each activity was assigned a metabolic equivalent (MET) level based on MET values specified in *The Compendium of Physical Activities* (16). In the questionnaire, daily time spent walking and bicycling (MET = 3.6) had 7 time intervals specified: almost never, <20 min/d, 20–40 min/d, 40–60 min/d, 1–1.5 h/d, 1.5–2 h/d, and >2 h/d. Household work (MET = 2.5) was reported in 6 categories: <1 h/d, 1–2 h/d, 2–3 h/d, 3–4 h/d, 4–5 h/d, and >5 h/d. Exercise (MET = 5.5) was reported in 7 categories: almost never, <1 h/wk, 1–2 h/wk, 2–3 h/wk, 3–4 h/wk, 4–5 h/wk, and >5 h/wk. In the present study, the crude response alternatives were further combined into 2 categories based on the predefined response alternatives for each type of activity with walking/bicycling as <20 and ≥20 min/d, performing household work as <1 and ≥1 h/d, and exercising as <1 and ≥1 h/wk. Furthermore, the reported time spent walking/bicycling, performing household work, and exercising was multiplied by the MET-value for each activity. The resulting MET-hours (MET-h) were summarized into a continuous variable of total MET-h/d from recreational activities. A categorical variable with 2 levels (<5 MET-h/d and ≥5 MET-h/d) was thereafter created.

Total energy intake was assessed using a food frequency questionnaire similar to that previously validated (17). Body mass index (BMI; kg/m^2) at diagnosis was calculated on the basis of self-reported current height and weight and weight change since diagnosis. A categorical variable of weight change was also created and patients were categorized into 3 groups: no change or a change ≤5%, an increase >5%, or a decrease >5% since diagnosis. Furthermore, variables of smoking habits after diagnosis, education level, and occupation during the past year were assessed.

Statistical analysis

Distributions and means of demographic and clinical variables were studied across groups of total recreational MET-h after diagnosis. Statistically significant associations were tested for using one-way ANOVA for continuous variables and χ^2 test for categorical variables. Cutoff -points for categorical variables other than the physical activity categories which were defined as described above were based on established strata or arbitrarily defined before analysis. Overall and prostate cancer–specific survivals were analyzed using the Kaplan–Meier method, and time to event for the different activity categories was compared using log-rank test.

Cox proportional hazards models were used to estimate unadjusted, age-adjusted, and multivariable-adjusted HRs and 95% confidence intervals (95% CI) (18). Time since prostate cancer diagnosis was used as the underlying time scale. All patients were left truncated by study design at the date of inclusion to PROCAP. All exposure variables were included as categorical in the Cox proportional hazards models with the lowest level of total recreational MET-h or the shortest time interval reported used as reference.

To assess potential confounding factors to adjust for in the Cox proportional hazards models, we tested whether the covariates were statistically associated with both the physical activity exposures and the mortality outcomes. The association between covariates and the exposure was assessed using linear regression models, using the continuous variable of total recreational MET-h, and the association between the covariates and the outcome was assessed using Cox proportional hazards models. Covariates tested were age at diagnosis, weight change since diagnosis, BMI at diagnosis, total energy intake, education level, smoking habits, PSA level at diagnosis, T, N, and M stage, tumor grade and Gleason score at diagnosis, and primary treatment. A statistically significant association with both exposure and outcome was found for age at diagnosis (5-year categories), weight change since diagnosis (no change, >5% increase, >5% decrease), BMI at diagnosis (<25, 25–30, >30 kg/m^2), Gleason score at diagnosis (<6, 6, >6), PSA level at diagnosis (continuous), and primary treatment (curative intent, radical prostatectomy, radiation therapy, or hormone therapy) which were included in the final multivariable-adjusted models. In addition, to examine whether the reporting of physical activity was influenced by illness, we carried out sensitivity analysis with 18-month lag-time excluding men who died within 18 months of responding to the questionnaire.

The level of significance was set to $\alpha = 0.05$. All analyses were performed using STATA 12.1 (STATA Corporation).

Results

Characteristics of the 4,623 men included in analyses are presented in Table 1. The mean age at diagnosis was 63.1 (±5.1) years, and the majority of men had a BMI between 25 and 30 kg/m^2. Active men reporting ≥5 MET-h/d of recreational physical activity were statistically significantly older, weighed less, had a lower BMI, and reported having stable weight more often than men reporting <5 MET-h/d. The more active men also had higher total energy intake and were more often never smokers than the less active men. There was also a statistically significant difference between the groups with regards to tumor stage and primary treatment, but no clear direction of trends was seen.

During the follow-up, 561 deaths of any cause (12.1%) and 194 (4.2%) prostate cancer specific deaths occurred. The mortality rates in the whole cohort were 25.9 and 8.9 per 1,000 person-years for overall and prostate cancer–specific survival, respectively. The number of overall and prostate cancer–specific deaths and person-time for the whole group and categories of physical activity variables are displayed in Table 2. When excluding men who died within 18 months after inclusion to PROCAP, the total number of subjects was 4,500 with 438 (9.7%) deaths from any cause and 158 (3.5%) prostate cancer specific deaths.

Kaplan–Meier curves with log-rank test analysis (Figs. 1 and 2) showed a statistically significant difference between men in the different categories of total recreational MET-h/d, time spent walking/bicycling and exercising for both overall and prostate cancer–specific mortality. For time spent performing household work, a statistically significant difference was seen between men in different categories with regards to overall but not prostate cancer–specific mortality. For both overall and prostate cancer–specific mortality, there were clear trends of higher mortality among the less active men within each activity type, with the exception of household work and prostate cancer–specific mortality, compared with the more active men.

Results from unadjusted, age-adjusted, and multivariable-adjusted Cox proportional hazards models for overall and prostate cancer–specific mortality are shown in Tables 3 and 4, respectively. In crude and age-adjusted models, men with ≥5 MET-h/d, walking/bicycling ≥20 min/d, performing household work ≥1 h/d, or exercising ≥1 h/wk, had 31%–42% and 31%–41% statistically significantly lower rates, respectively, of overall mortality compared with the less active reference category within each activity type. In multivariable-adjusted models, results remained similar with statistically significantly lower mortality rates among men with ≥5 MET-h/d (HR, 0.63; 95% CI, 0.52–0.77), walking/bicycling ≥20 min/d (HR, 0.70; 95% CI, 0.57–0.86), performing household work ≥1 h/d (HR, 0.71; 95% CI, 0.59–0.86), or exercising ≥1 h/wk (HR, 0.74; 95% CI, 0.61–0.90) compared with the less active reference category. When introducing lag time of 18 months, the results were similar and remained statistically significant.

Prostate cancer–specific mortality rates were 29%–44% and 29%–43% lower in crude and age-adjusted models, respectively, among men in the higher categories of MET-h/d, walking/bicycling, and exercising than in the less active reference category within each type of activity. In multivariate-adjusted models, the results remained statistically significant for men walking/bicycling ≥20 min/d or exercising ≥1 h/wk compared with the less active men (HR, 0.61; 95% CI, 0.43–0.87 and HR, 0.68; 95% CI, 0.48–0.94, respectively). When introducing lag time, the results were similar and remained statistically significant for walking/bicycling while they were slightly attenuated for exercise.

Discussion

In this large cohort study of men with localized prostate cancer, we found that engaging in higher levels of MET-h/d from recreational physical activities, walking/bicycling ≥20 min/d, performing household work ≥1 h/d, or exercising ≥1 h/wk, statistically significantly decreased the overall mortality rates among men with prostate cancer. In addition, walking/bicycling ≥20 min/d and exercising ≥1 h/wk were also associated with statistically significantly lower rates of prostate cancer–specific mortality.

Physical activity has been investigated in relation to risk of prostate cancer with varying results. Recently, a meta-analysis (8) showed a statistically significantly reduced risk of prostate cancer by 10% when comparing the highest versus lowest of total physical activity. High levels of physical activity have also been linked to reduced overall mortality in the general population (19) as well as among cancer survivors (6). However, to our knowledge, only 2 studies examining the association between physical activity after a prostate cancer diagnosis and prostate cancer survival and progression have been published before our study (9, 10). Our results for walking/bicycling and exercise are in line with the previous studies, further strengthening the evidence of a potential link between physical activity and survival among patients with prostate cancer. The first study (9) showed that men who walked ≥90 min/wk at a normal to very brisk pace had a 46% lower risk of all-cause mortality (HR, 0.54; 95% CI, 0.41–0.71) than those walking for shorter durations at an easier pace. For prostate cancer–specific mortality, walking briskly for longer duration was suggestively, but not statistically significant, associated with a lower mortality rate. Men engaging in vigorous activity ≥3 h/wk had a 49% lower risk of all-cause mortality (HR, 0.51; 95% CI, 0.36–0.72) and a 61% lower risk of prostate cancer–specific death (HR, 0.39; 95% CI, 0.18–0.84) than men engaging in <1 h/wk of vigorous activity. In the second published study (10), men walking briskly for ≥3 h/wk had a 57% lower progression rate than men walking for shorter durations at an easier pace (HR, 0.43; 95% CI, 0.21–0.91). Independent of walking duration, the authors found that brisk walking pace was associated with a 48% decrease in progression rate compared with walking at an easy pace (HR, 0.52; 95% CI, 0.29–0.91).

Potential mechanisms for the effect of physical activity on cancer progression and mortality have been suggested to work through pathways of insulin and insulin-like growth factors (IGF), adipokine signaling, and inflammation (20). Regular exercise has been shown to affect the IGF axis resulting in lower levels of serum insulin and IGF1 and increased levels of IGF-binding protein-1 *in vivo* with reduced proliferation and increased apoptosis of prostate tumor cells *in vitro* (21, 22). A recent study also showed that serum extracted directly after strenuous exercise reduced the proliferation of prostate tumor cells *in vitro*, indicating an acute effect of physical activity on tumor growth (23). Altered levels of adipokines is an effect of obesity and also associated with tumor development (24). Favorable changes in body

Table 1. Characteristics of study participants included in analysis in the PROCAP study divided by total recreational MET-hours per day after diagnosis

	All ($n = 4,623$) Mean (SD)	Total MET-h/d <5 ($n = 1,206$) Mean (SD)	Total MET-h/d ≥5 ($n = 3,417$) Mean (SD)	P[a]
Height,[b] cm	177.4 (6.4)	177.5 (6.7)	177.4 (6.2)	0.589
Weight at diagnosis,[c] kg	82.5 (11.2)	84.0 (12.4)	82.0 (10.7)	<0.001
Total energy intake, kJ	9,536 (3,809)	9,190 (4,329)	9,658 (3,600)	<0.001
PSA,[d] ng/mL	8.5 (4.2)	8.5 (4.2)	8.4 (4.2)	0.626
	n (%)	*n* (%)	*n* (%)	
Age at diagnosis, y				<0.001
<55	328 (7.1)	126 (10.5)	202 (5.9)	
55–<60	946 (20.5)	234 (19.4)	712 (20.8)	
60–<65	1,465 (31.7)	319 (26.5)	1,146 (33.5)	
65–<70	1,617 (35.0)	445 (36.9)	1,172 (34.3)	
≥70	267 (5.8)	82 (6.8)	185 (5.4)	
BMI at diagnosis, kg/m^2				<0.001
<25	1,702 (36.8)	400 (33.2)	1,302 (38.1)	
25–30	2,369 (51.2)	604 (50.1)	1,765 (51.7)	
>30	509 (11.0)	186 (15.4)	323 (9.5)	
Missing data	43 (0.9)	16 (1.3)	27 (0.8)	
Walking or biking after diagnosis				<0.001
<20 min/d	1,105 (23.9)	671 (55.6)	434 (12.7)	
≥20 min/d	3,518 (76.1)	535 (44.4)	2,983 (87.3)	
Household work after diagnosis				<0.001
<1 h/d	1,612 (34.9)	1,079 (89.5)	533 (15.6)	
≥1 h/d	3,011 (65.1)	127 (10.5)	2,884 (84.4)	
Exercising after diagnosis				<0.001
<1 h/wk	1,914 (41.4)	820 (68.0)	1,094 (32.0)	
≥1 h/wk	2,709 (58.6)	386 (32.0)	2,323 (68.0)	
Weight change since diagnosis				<0.001
No change or <5% change	3,490 (75.5)	820 (68.0)	2,670 (78.1)	
>5% increase	724 (15.7)	265 (22.0)	459 (13.4)	
>5% decrease	409 (8.9)	121 (10.0)	288 (8.4)	
Education level				0.313
≤9 y	1,824 (39.5)	484 (40.1)	1,340 (39.2)	
>9–≤12 y	1,657 (35.8)	442 (36.7)	1,215 (35.6)	
>12 y	1,111 (24.0)	270 (22.4)	841 (24.6)	
Missing data	31 (0.7)	10 (0.8)	21 (0.6)	
Smoking				<0.001
Never smoker	1,980 (42.8)	452 (37.5)	1,528 (44.7)	
Past smoker	2,255 (48.8)	623 (51.7)	1,632 (47.8)	
Current smoker	360 (7.8)	123 (10.2)	237 (6.9)	
Missing data	28 (0.6)	8 (0.7)	20 (0.6)	
Tumor stage				0.001
T1a	200 (4.3)	68 (5.6)	132 (3.9)	
T1b	228 (4.9)	62 (5.1)	166 (4.9)	
T1c	2,262 (48.9)	555 (46.0)	1,707 (50.0)	
T2	1,775 (38.4)	481 (39.9)	1,294 (37.9)	
Missing data	158 (3.4)	40 (3.3)	118 (3.5)	
N-stage				0.479
N0	1,386 (30.0)	348 (28.9)	1,038 (30.4)	
N1	49 (1.1)	11 (0.9)	38 (1.1)	
NX	2,982 (64.5)	794 (65.8)	2,188 (64.0)	
Missing data	206 (4.5)	53 (4.4)	153 (4.5)	
M-stage				0.369
M0	2,278 (49.3)	581 (48.2)	1,697 (49.7)	
MX	2,162 (46.8)	577 (47.8)	1,585 (46.4)	
Missing data	183 (4.0)	48 (4.0)	135 (4.0)	
Gleason score				0.159
<6	1,107 (23.9)	282 (23.4)	825 (24.1)	
6	1,796 (38.8)	454 (37.6)	1,342 (39.3)	
>6	867 (18.8)	248 (20.6)	619 (18.1)	
Missing data	853 (18.5)	222 (18.4)	631 (18.5)	
Primary treatment				0.043
Surveillance	1,062 (23.0)	291 (24.1)	771 (22.6)	
Radical prostatectomy	2,328 (50.4)	571 (47.3)	1,757 (51.4)	
Radiation therapy	930 (20.1)	253 (21.0)	677 (19.8)	
Hormone therapy	115 (2.5)	39 (3.2)	76 (2.2)	
Missing data	188 (4.1)	52 (4.3)	136 (4.0)	

[a]P values from t test (continuous variables) and χ^2 test (categorical variables).
[b]Missing data: $n = 33$.
[c]Missing data: $n = 17$.
[d]Missing data: $n = 156$.

Table 2. Total number of subjects, survival time in person-years, and all-cause mortality and prostate cancer–specific deaths and events per 1,000 person-years by physical activity variables

	Total		Mortality			
			All-cause		Prostate cancer–specific	
	No. of subjects	Person-years	No. of events	Rate/1,000 person-years	No. of events	Rate/1,000 person-years
All study participants	4,623	21,697	561	25.9	194	8.9
Total recreational MET-h/d						
<5	1,206	5,499	207	37.6	63	11.5
≥5	3,417	16,198	354	21.9	131	8.1
Walking or biking after diagnosis						
<20 min/d	1,105	5,062	184	36.3	69	13.6
≥20 min/d	3,518	16,634	377	22.7	125	7.5
Household work after diagnosis						
<1 h/d	1,612	7,434	241	32.4	77	10.4
≥1 h/d	3,011	14,263	320	22.4	117	8.2
Exercising after diagnosis						
<1 h/wk	1,914	8,844	293	33.1	107	12.1
≥1 h/wk	2,709	12,852	268	20.9	87	6.8

composition and aerobic fitness as a result of physical activity have been correlated to beneficial effects on adipokine levels in men with prostate cancer (25). Inflammation has also been suggested to play a role in prostate cancer development and progression (26). Physical activity has been shown to reduce levels of C-reactive protein (27). In addition, exercise-induced decreases in oxidative stress have recently been suggested to delay prostate cancer development (28).

The present study has a number of strengths and limitations that need to be acknowledged. The population-based design, long

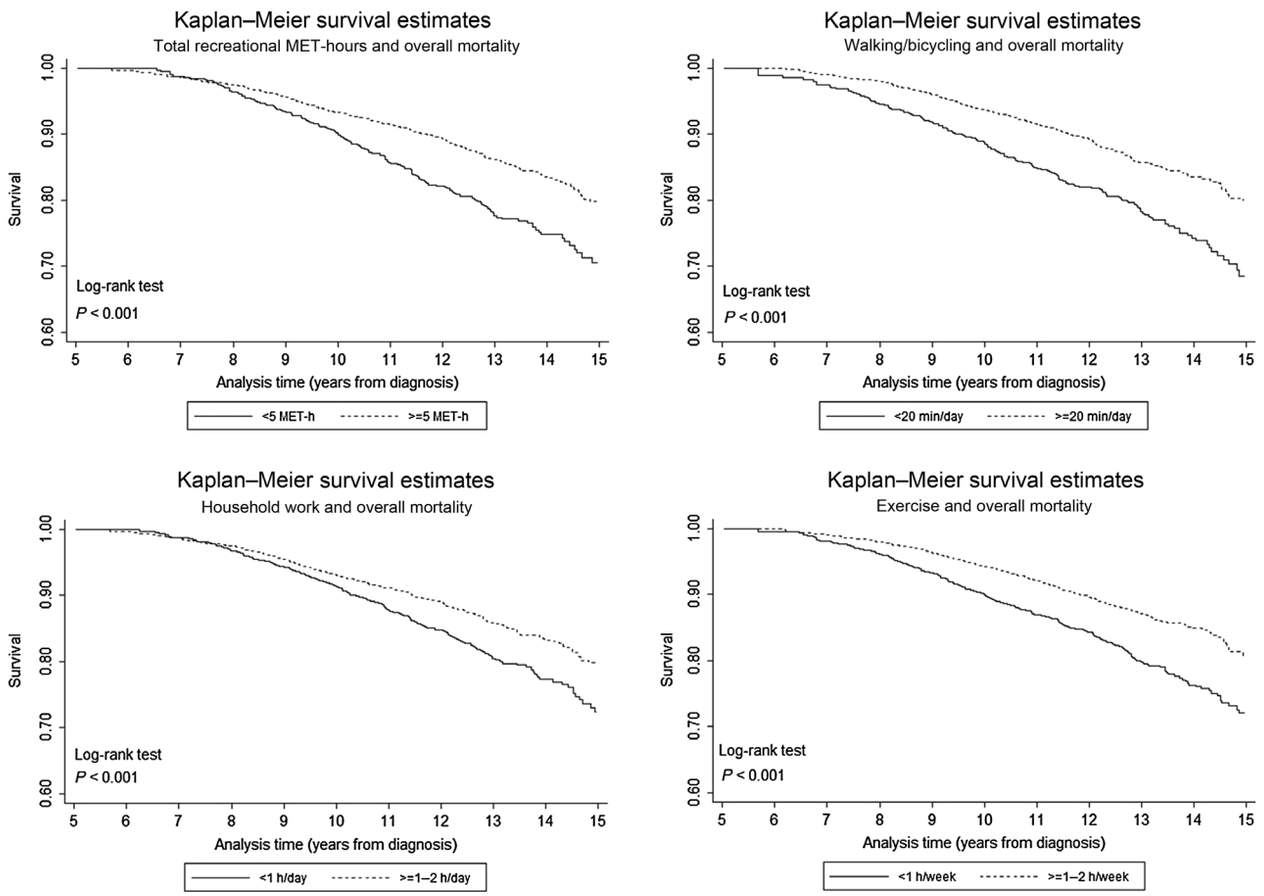

Figure 1.
Kaplan–Meier survival curves for overall mortality and total recreational MET-h, time spent walking/bicycling, time spent performing household work, and time spent exercising. On the *x*-axis, time from inclusion in PROCAP to death or censoring is shown; origin (time = 0) is the date of diagnosis in left-truncated Cox proportional hazards regressions.

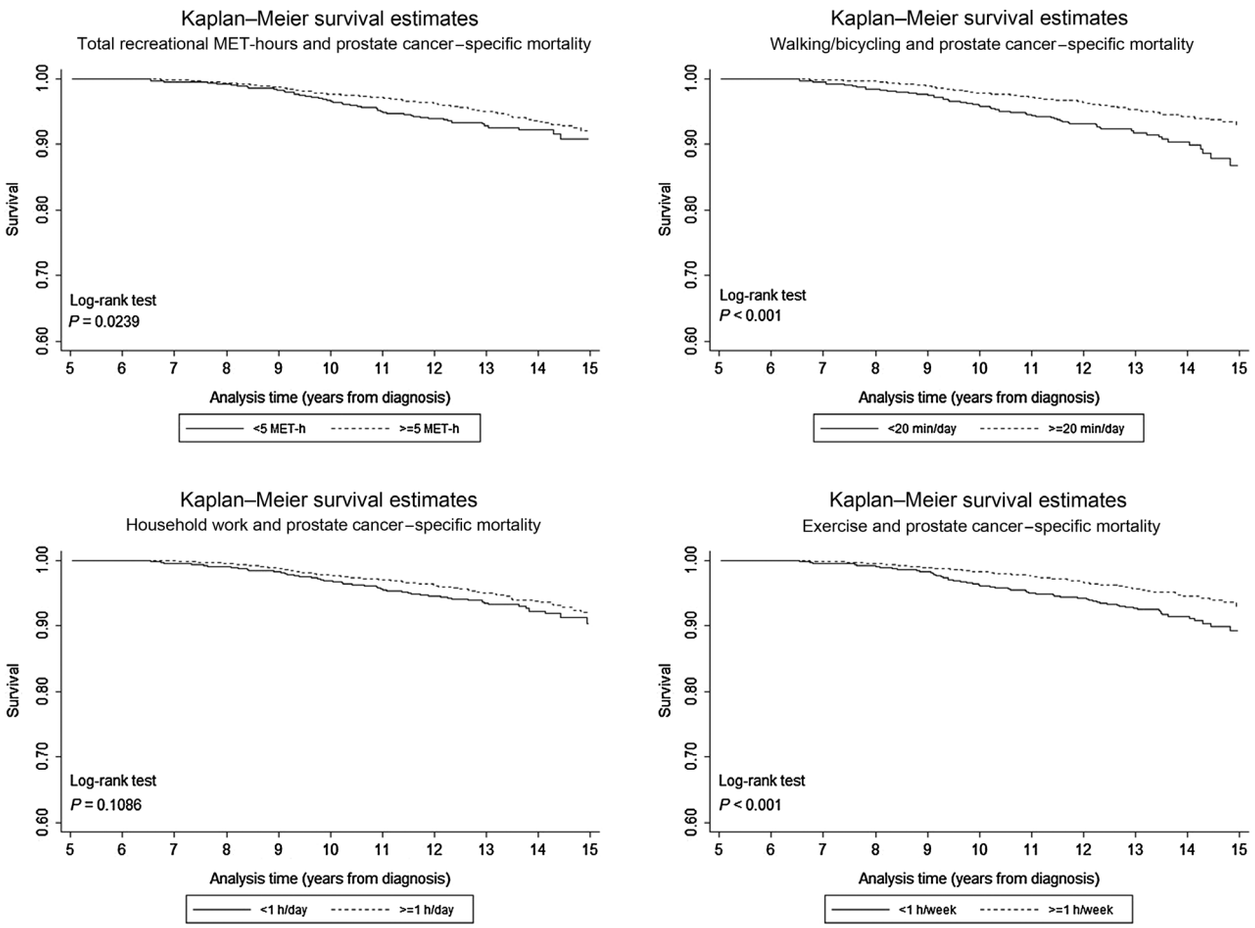

Figure 2.
Kaplan–Meier survival curves for prostate cancer–specific mortality and total recreational MET-h, time spent walking/bicycling, time spent performing household work, and time spent exercising. On the *x*-axis, time from inclusion in PROCAP to death or censoring is shown; origin (time = 0) is the date of diagnosis in left-truncated Cox proportional hazards regressions.

follow-up time, and large sample size are noteworthy strengths of the study. Compared with the previous study on physical activity and prostate cancer survival (9), our study had almost twice as many men diagnosed with prostate cancer as well as almost twice the number of prostate cancer–specific deaths during follow-up. A major limitation is, however, the study design with inclusion of men who were still alive at PROCAP study start 5 to 10 years after being diagnosed with prostate cancer.

Table 3. HRs with 95% CIs (crude, age-adjusted, and multivariable-adjusted with no lag-time and 18-month lag-time) for overall mortality by type of activity

Activity Total number of deaths (*n*)	HR crude (95% CI) 561	HR age-adjusted (95% CI) 561	HR adjusted[a] (95% CI) 430	HR-adjusted lag 18 mo (95% CI) 338
Total recreational MET-h/d				
<5	1.00	1.00	1.00	1.00
≥5	0.58 (0.49–0.69)	0.59 (0.50–0.70)	0.63 (0.52–0.77)	0.66 (0.53–0.83)
Walking/bicycling after diagnosis				
<20 min/d	1.00	1.00	1.00	1.00
≥20 min/d	0.63 (0.53–0.75)	0.64 (0.54–0.76)	0.70 (0.57–0.86)	0.64 (0.43–0.94)
Household work after diagnosis				
<1 h/d	1.00	1.00	1.00	1.00
≥1 h/d	0.69 (0.58–0.82)	0.69 (0.58–0.81)	0.71 (0.59–0.86)	0.78 (0.62–0.96)
Exercise after diagnosis				
<1 h/wk	1.00	1.00	1.00	1.00
≥1 h/wk	0.63 (0.53–0.74)	0.65 (0.55–0.77)	0.74 (0.61–0.90)	0.73 (0.59–0.90)

Abbreviation: CI, confidence interval.
[a]Adjusted for age at diagnosis (5-year intervals), Gleason score (<6, 6, >6), primary treatment, serum PSA (continuous), BMI at diagnosis (<25, 25–<30, ≥30 kg/m^2), and weight change (>5% increase, >5% decrease, no change).

Table 4. HRs with 95% CIs (crude, age-adjusted, and multivariable-adjusted with no lag-time and 18-month lag-time) for prostate cancer–specific mortality by type of activity

Activity Total number of deaths (*n*)	HR crude (95% CI) 194	HR age-adjusted (95% CI) 194	HR adjusted[a] (95% CI) 144	HR-adjusted lag 18 mo (95% CI) 118
Total recreational MET-h/d				
<5	1.00	1.00	1.00	1.00
≥5	0.71 (0.52–0.96)	0.71 (0.53–0.97)	0.78 (0.55–1.11)	0.90 (0.60–1.34)
Walking/bicycling after diagnosis				
<20 min/d	1.00	1.00	1.00	1.00
≥20 min/d	0.56 (0.42–0.75)	0.56 (0.42–0.76)	0.61 (0.43–0.87)	0.64 (0.43–0.94)
Household work after diagnosis				
<1 h/d	1.00	1.00	1.00	1.00
≥1 h/d	0.79 (0.52–1.05)	0.79 (0.59–1.05)	0.86 (0.61–1.20)	1.00 (0.68–1.45)
Exercise after diagnosis				
<1 h/wk	1.00	1.00	1.00	1.00
≥1 h/wk	0.56 (0.42–0.74)	0.57 (0.43–0.76)	0.68 (0.48–0.94)	0.73 (0.50–1.05)

Abbreviation: CI, confidence interval.

[a]Adjusted for age at diagnosis (5-year intervals), Gleason score (<6, 6, >6), primary treatment, serum PSA (continuous), BMI at diagnosis (<25, 25–<30, ≥30 kg/m^2), and weight change (>5% increase, >5% decrease, no change).

Results of survival in the present study are therefore conditioned on surviving long enough to be included. Although the survival rate during the first 10 years after diagnosis is close to 70% (3), men with the most aggressive disease were probably not included in the study, potentially limiting the generalizability of the results. However, any potential bias created by the left truncation of data is likely to result in conservative estimates rather than to induce a false-positive effect.

Another potential limitation is the self-reported assessment of physical activity. Although the physical activity questionnaire that we used has previously been shown to be valid (15), potential misclassification cannot be ruled out. Furthermore, reversed causation is a concern as men might reduce their physical activity due to a worse state of illness which could create a false association between lower levels of physical activity and shorter survival. To account for the possibility of reversed causation, we performed additional sensitive analysis using 18 months of lag-time, excluding men who died within 18 months after responding to the questionnaire. As our point estimates did not change notably, although the confidence intervals were attenuated due to loss of power in analysis of prostate cancer–specific mortality, we do not believe our results to be an artifact of reversed causality. In addition, adjustments for Gleason score and serum PSA, which also reduces the risk of reversed causation, were made in multivariable-adjusted models.

In conclusion, our study confirms and further strengthens the results from previous studies indicating positive effects of physical activity on survival after a prostate cancer diagnosis. We found that higher levels of total MET-h/d from recreational physical activities and longer time spent walking/bicycling, performing household activities, and exercising were associated with lower overall mortality rates. In addition, longer time spent walking/bicycling and exercising was also seen to decrease prostate cancer–specific mortality rates. This is of public health relevance, as the number of men surviving after a prostate cancer diagnosis is increasing worldwide.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Authors' Contributions

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Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis): S.E. Bonn, A. Sjölander, F. Wiklund, K. Bälter
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Administrative, technical, or material support (i.e., reporting or organizing data, constructing databases): E. Holmberg
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