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Physical Activity and Survival after Cancer Diagnosis in Men

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Abstract

Background—The number of cancer survivors is increasing rapidly; however, little is known about whether engaging in physical activity after a cancer diagnosis is associated with lower mortality rates in men.

Methods—We conducted a prospective cohort study of 1,021 men (mean age, 71.3 years) who were diagnosed with cancer (other than non-melanoma skin cancer). Men reported their physical activities (walking, stair climbing, and participation in sports and recreational activities) on questionnaires in 1988, a median of 6 years after their cancer diagnosis. Physical activity was updated in 1993 and men were followed until 2008, with mortality follow-up >99% complete, during which 777 men died (337 from cancer, 190 from cardiovascular disease).

Results—In multivariate analyses, the relative risks for all-cause mortality associated with expending <2100, 2100–4199, 4200–8399, 8400–12,599, and 12,600 kJ/week in physical activity were 1.00 (referent), 0.77, 0.74, 0.76, and 0.52, respectively; *p*, trend <0.0001. Higher levels of physical activity also were associated with lower rates of death from cancer and cardiovascular disease; *p*, trend = 0.01 and 0.002, respectively.

Conclusions—Engaging in physical activity after cancer diagnosis is associated with better survival among men.

Keywords

epidemiology; exercise; mortality

With improvements in the early detection and treatment of cancer, as well as an aging population structure in high income countries, the number of cancer survivors has increased rapidly in recent years. For example, the number of cancer survivors almost quadrupled between 1971 and 2007 in the United States, from 3.0 to 11.7 million.¹ In the United Kingdom, there were more than 2 million cancer survivors in 2008, with this number rising by >3% annually.²

A large number of patients with cancer live for an extended period: an estimated 63–65% have survived for at least 5 years.^{1,3} After their diagnosis, many cancer survivors are highly motivated to seek information about whether lifestyle changes, such as physical activity, can improve their quality of life and survival.⁴ Among generally healthy, cancer-free populations, physical activity delays premature mortality.⁵ However, there are few data on whether engaging in physical activity after a cancer diagnosis also is associated with

greater longevity, with specific data available in breast, prostate, and colorectal cancer survivors.^{6–11} To our knowledge, there have been no studies investigating whether physical activity can delay premature mortality among persons diagnosed with other site-specific cancers.

Thus, we conducted the present study to examine the association of physical activity with mortality in a cohort of men diagnosed with various site-specific cancers.

METHODS

Study Subjects

The Harvard Alumni Health Study, initiated in the 1960's, is an ongoing cohort study of men who entered Harvard University, United States, as undergraduates between 1916 and 1950.¹² This study and the consent process for enrollment are approved by the Office of Human Research Administration, Harvard School of Public Health. Health information, including physician-diagnosed cancer and diagnosis date, was first obtained from subjects via questionnaires in either 1962 or 1966, then updated in 1977, 1988, 1993, and 1998. For the present study, we used data from a health questionnaire mailed in 1988. The choice of 1988 as the baseline for this study allowed sufficient follow-up for a meaningful number of deaths to occur, yet was not too dated with regard to contemporaneous methods of cancer diagnosis and treatment. Of the 12,805 men responding to the 1988 questionnaire, 1,055 who reported physician-diagnosed cancer, other than non-melanoma skin cancer, were eligible. We excluded 31 men not providing information on physical activity, and 3 who died during follow-up with unknown dates of death, leaving 1,021 men in this study.

Assessment of Physical Activity

Physical activity was assessed using the Paffenbarger questionnaire.¹² On the 1988 questionnaire, men reported their daily walking and stair climbing, sports and recreational activities in the past week, and the frequency and duration of participation. Using these data, we estimated the weekly energy expended on physical activity in kJ/week. This assessment of physical activity has been shown to be reliable and valid, including validation against doubly-labeled water ($r=0.67$), a gold standard for measuring energy expenditure.^{13–16} Physical activity information was updated in 1993, using an identical questionnaire, and in 1998, but using a modified, abbreviated questionnaire. Thus, for the present analysis, we used information on physical activity collected in 1988 and updated this with 1993 data only.

Assessment of Other Characteristics

From the 1988 questionnaire, we also obtained information on potential confounders, including weight, height, cigarette smoking, alcohol intake, diet (using a modified Willett semi-quantitative food frequency questionnaire¹⁷), and early parental mortality.

In analyses, we classified men using the following categories—smoking: never, past, or current; body mass index: <22.5, 22.5–<25.0, 25.0–<27.5, or ≥27.5 kg/m²; alcohol intake: none, 1–3, 4–6, or ≥7 drinks/week; red meat intake: 3 servings/month, 1–2 servings/week, or ≥3 servings/week; vegetable intake: 6 servings/week, 1–2 servings/day, or ≥3 servings/day; use of vitamin or mineral supplements: no or yes; and early parental mortality: no or yes. Groups were chosen to be clinically meaningful and to obtain a reasonable distribution (smoking, body mass index, use of vitamins/minerals, parental mortality), or based on questionnaire response options as well as a reasonable distribution (alcohol, red meat, vegetable intakes).

Ascertainment of Mortality

We used the National Death Index, a computerized list of death records compiled by the National Center for Health Statistics, United States, with high sensitivity and specificity for ascertainment of deaths¹⁸ to ascertain deaths after return of the 1988 questionnaire through 2008. Mortality follow-up in the Harvard Alumni Health Study is >99% complete.¹²

Data Analyses

We used Cox proportional hazards models to estimate the relative risks and 95% confidence intervals for mortality from all causes, cancer, cardiovascular disease (CVD), or causes other than cancer/CVD associated with physical activity (<2100, 2100–4199, 4200–8399, 8400–12,599, or 15,600 kJ/week). Initially, we adjusted for age (in years) only; additional models further adjusted for these potential confounders: smoking, body mass index, alcohol intake, red meat intake, vegetable intake, use of vitamin or mineral supplements, and early parental mortality.

In additional analyses, to minimize potential bias from men with worsening cancer who may have decreased their activity levels, we repeated analyses including only men diagnosed 5, and 10, years prior to baseline.

RESULTS

At baseline in 1988, the mean age of men was 71.3 years. The median year of cancer diagnosis was 1982 (interquartile range, 1976–1986), when men had a median age of 66.0 years. The most commonly reported cancers were prostate cancer (30%), colon cancer (16%), bladder cancer (8%), melanoma (6%), and lymphoma (5%), followed by smaller numbers of other cancers. Most men reported only one type of cancer (89%); 108 (11%) reported more than one type of cancer. Table 1 shows the characteristics of men according to physical activity level. Men who were more active were younger and less likely to smoke (although this was not statistically significant, likely because of the small number of current smokers); they also ate a diet that comprised less meat and more vegetables.

During an average follow-up of 11.8 years, 777 men died; 337 from cancer, 190 from CVD, 228 from non-cancer, non-CVD causes, and 22 from unknown causes. Of the non-cancer, non-CVD deaths, the most common causes were respiratory diseases (n=56), Parkinson's disease (n=19), and diseases of the pulmonary circulation (n=15), followed by smaller numbers of deaths from other causes.

Physical activity was inversely related to risk of dying during follow-up. The relative risks, adjusted for age, smoking, body mass index, early parental mortality and dietary variables, for all-cause mortality associated with increasing physical activity levels were 1.00 (referent), 0.77, 0.74, 0.76, and 0.52, respectively; p, trend <0.0001 (Table 2). Significant inverse associations also were noted for deaths from cancer, CVD, and non-cancer, non-CVD causes (p, trend = 0.01, 0.002, and 0.0002, respectively).

Since cancer severity and its treatment may confound the associations, we attempted to obtain information for these variables. However, because cancer was diagnosed many years prior (the median year of self-reported cancer diagnosis was 1982), we were able to obtain data for only 70 men. In a sensitivity analysis where we additionally adjusted for cancer stage (in situ or localized, regional or distant metastasis, unknown); grade (well differentiated, moderately or poorly differentiated, unknown); and surgery, chemotherapy, and radiotherapy treatment (all no, yes, unknown), the results differed little. The corresponding relative risks for all-cause mortality were 1.00, 0.77, 0.72, 0.70, and 0.51, respectively; p, trend <0.0001.

In additional analyses, we analyzed only men diagnosed with cancer at least 5 years prior to baseline ($n=421$); corresponding results were 1.00, 0.90, 0.67, 0.67, and 0.48, respectively; p , trend <0.0001 . Among men diagnosed at least 10 years prior ($n=262$), they were 1.00, 0.75, 0.73, 0.68, and 0.37, respectively; p , trend <0.0001 .

DISCUSSION

In this cohort of male cancer survivors who were diagnosed a median of 6 years prior to the start of follow-up, higher levels of physical activity at baseline were associated with lower rates of all-cause and cancer mortality during follow-up. Physical activity also was related to lower rates of CVD and non-cancer, non-CVD mortality. The amount of physical activity currently recommended for adults – at least 150 min/week of moderate-intensity physical activity¹⁹ – was sufficient to lower mortality rates (4,200 kJ/week is the approximate amount expended by an 80 kg man walking briskly for half-an-hour, five days a week).

While there is a large body of literature investigating physical activity in the primary prevention of cancer, few data are available on whether physical activity among persons with cancer is associated with better survival.²⁰ In a study of almost 3,000 women with breast cancer, 9 MET-hr/week – approximately equivalent to current recommendations – or more of activity was associated with lower rates of all-cause and breast cancer mortality.⁶ This same level of physical activity also was associated with lower all-cause mortality rates among some 900 breast cancer survivors in another study.⁷ In a separate study of almost 2,400 women with breast cancer, physical activity that satisfied current guidelines was associated with a 35% lower mortality rate.²¹ Among approximately 2,700 men with prostate cancer, 9 MET-hr/week was again significantly related to lower all-cause mortality rates.¹¹ Finally, three studies of colorectal cancer survivors (with approximately 600–800 subjects in each study) reported significantly lower mortality rates from all causes and colorectal cancer among those with 18–27 MET-hr/week of physical activity (some 2–3 times current recommendations) or more.^{8–10} The present study extends knowledge on this topic by including data for men with other site-specific cancers.

Strengths of the present study included enrollment of men with different cancers, detailed assessment of physical activity, and a long follow-up period. However, a limitation of the study was our inability to obtain information on the severity and treatment of cancer in the majority of subjects. When we controlled for variables related to these factors and included an “unknown” category, findings changed little. We did not have information on the socioeconomic level or health insurance status of men, and differential access to health care may have led to residual confounding. However, since all subjects are well educated, they presumably had uniformly high socioeconomic status and good access to care. We also were unable to examine the associations of physical activity with survival separately among men with different cancers, since the numbers of site-specific cancers were small. Another limitation was that physical activity was self-reported in this study. While the questionnaire used has good reliability and validity for large cohort studies,¹² self-reports still are imprecise. However, any misclassification is likely to be random (since reporting occurred before the endpoints of interest), leading to a tendency towards diluted results. Physical activity was ascertained, on average, 6 years after a cancer diagnosis; this may limit the ability to generalize findings to all cancer survivors.

In conclusion, this study provides data showing that higher levels of physical activity in male cancer survivors are related to lower rates of mortality from all causes, cancer, and CVD. While physical activity clearly decreases premature mortality in the generally healthy population, this finding is not well established for cancer survivors. Because many cancer survivors do live extended lives nowadays due to early diagnosis and better treatment, their

numbers are increasing rapidly. Thus, physical activity should be actively promoted to such individuals to enhance longevity.

(This is report No. XCIV in a series on chronic disease in former college students.)

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Table 1

Characteristics of Subjects at Baseline, 1988, by Physical Activity Levels, Harvard Alumni Health Study

Characteristic	Physical Activity Level, ^a kJ/week						P-value
	<2100 n= 237	2100–4199 n= 151	4200–8399 n= 204	8400–12,599 n= 152	12,600 n= 277		
Mean age, years (SD)	73.7 (8.1)	72.2 (7.9)	70.8 (8.3)	70.1 (7.8)	69.8 (7.4)		<0.0001
Smoking status, %							0.21
Never	25.4	32.5	35.3	31.3	31.3		
Past	63.6	59.6	58.3	61.3	63.6		
Current	11.0	8.0	6.4	7.3	5.1		
Alcohol intake, %							0.15
Never	36.0	37.6	28.9	27.3	28.2		
1–3 drinks/wk	14.4	8.7	15.7	19.3	18.4		
4–6 drinks/wk	9.8	15.4	12.8	15.3	12.6		
7 drinks/wk	39.8	38.3	42.7	38.0	40.8		
Red meat intake, %							0.01
3 servings/mo	22.9	19.6	23.4	23.5	24.7		
1–2 servings/wk	39.4	48.3	56.2	44.1	45.4		
3 servings/wk	37.7	32.2	20.4	32.4	29.9		
Vegetable intake, %							0.04
6 servings/wk	34.2	20.8	23.3	24.7	24.0		
1–2 servings/d	53.3	59.7	58.4	55.4	61.6		
3 servings/d	12.6	19.5	18.3	21.0	14.4		
Vitamin/mineral supplements, %	55.3	49.7	50.0	47.4	51.6		0.60
Early parental mortality (<65 years), %	36.1	39.0	38.0	34.7	32.4		0.63
Body mass index, %							0.26
<22.5 kg/m ²	31.8	23.3	24.5	25.0	22.0		
22.5–<25.0 kg/m ²	31.4	32.7	39.2	36.8	23.9		
25.0–<27.5 kg/m ²	20.8	30.0	24.5	25.7	30.0		
≥27.5 kg/m ²	16.1	14.0	11.8	12.5	14.1		

^a estimated from walking, climbing stairs and participation in sports/recreational activities

Table 2

Relative Risks (RR) and 95% Confidence Intervals (CI) for Mortality, 1988–2008, by Physical Activity Level, Harvard Alumni Health Study

Physical Activity Level, ^a kJ/Week	No. of Deaths	Age-adjusted RR (95% CI)	Multivariable ^b RR (95% CI)
All-cause mortality:			
<2100	211	1.00 (referent)	1.00 (referent)
2100–4199	117	0.74 (0.59, 0.93)	0.77 (0.60, 0.97)
4200–8399	151	0.69 (0.57, 0.85)	0.74 (0.60, 0.91)
8400–12,599	115	0.71 (0.56, 0.90)	0.76 (0.60, 0.97)
12,600	183	0.50 (0.41, 0.62)	0.52 (0.42, 0.65)
P, trend		<0.0001	<0.0001
Cancer mortality: ^c			
<2100	88	1.00 (referent)	1.00 (referent)
2100–4199	42	0.86 (0.61, 1.20)	0.89 (0.62, 1.29)
4200–8399	64	0.69 (0.51, 0.95)	0.77 (0.55, 1.06)
8400–12,599	59	0.93 (0.67, 1.30)	1.03 (0.73, 1.47)
12,600	84	0.58 (0.42, 0.80)	0.62 (0.44, 0.87)
P, trend		0.003	0.01
Cardiovascular mortality: ^c			
<2100	48	1.00 (referent)	1.00 (referent)
2100–4199	34	0.69 (0.43, 1.10)	0.81 (0.50, 1.32)
4200–8399	44	0.83 (0.57, 1.21)	0.87 (0.58, 1.30)
8400–12,599	27	0.54 (0.32, 0.91)	0.58 (0.34, 1.00)
12,600	37	0.47 (0.31, 0.72)	0.51 (0.33, 0.79)
P, trend		0.0006	0.002
Non-cancer, non-cardiovascular mortality: ^c			
<2100	63	1.00 (referent)	1.00 (referent)
2100–4199	38	0.65 (0.43, 1.00)	0.61 (0.39, 0.95)
4200–8399	41	0.64 (0.45, 0.92)	0.65 (0.45, 0.96)
8400–12,599	28	0.64 (0.42, 0.99)	0.65 (0.41, 1.04)
12,600	58	0.42 (0.29, 0.63)	0.41 (0.27, 0.62)
P, trend		<0.0001	0.0002

^a estimated from walking, climbing stairs and participation in sports/recreational activities

^b adjusted for age; cigarette smoking; body mass index, intakes of alcohol, red meat, vegetables, and vitamin/mineral supplements; and early parental mortality

^c analyses exclude 22 men known to be deceased for whom cause of death was unknown