

Research Article

Change in Physical Activity and Colon Cancer Incidence and Mortality

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Abstract

Background: Although data on the association of physical activity and colon cancer risk is convincing, little research has examined whether change in physical activity alters risk of cancer incidence and mortality.

Methods: We examined the association of 10- and 15-year change in physical activity with risk of colon cancer incidence and mortality in the Cancer Prevention Study II. Endpoints were verified through medical record abstraction or registry or National Death Index linkage. Ten-year physical activity analysis included 1,863 incident and 826 fatal cases, whereas the longer-term exposure analysis included 1,386 incident and 602 fatal colon cancer cases. Age and multivariable-adjusted hazard ratios were estimated using Cox proportional hazards models.

Results: Neither measure of physical activity change was associated with colon cancer incidence. Fifteen-year change was not associated with colon cancer mortality. However, consistently high physical activity over 10 years was associated with a decreased risk of colon cancer mortality as compared with those with consistently low activity. The association attenuated to borderline significance with adjustment for body mass index. Those consistently at or above sample median physical activity levels over 15 years had half the risk of colon cancer death as those consistently below the median.

Conclusions: Regular long-term physical activity was associated with a lower risk of colon cancer mortality.

Impact: This study suggests that long-term participation in physical activity provides the greatest reduction in risk of colon cancer death. *Cancer Epidemiol Biomarkers Prev*; 19(12); 3000–4. ©2010 AACR.

Introduction

Consistent evidence indicates that physical activity across the lifecourse reduces colon cancer incidence (1–5). Change in physical activity is less well studied and results are inconsistent (6–8). Similarly, few studies have examined the association of physical activity with colon cancer mortality, with mixed results (9–11). Understanding whether changes in physical activity during adulthood are associated with changes in risk of developing or dying from colon cancer can aid in tailoring prevention messages. The American Cancer Society Cancer Prevention Study II (CPS II) Nutrition Cohort provides one of the few opportunities to prospectively examine change in physical activity during adulthood with colon cancer incidence and mortality.

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Materials and Methods

The men and women in this analysis were drawn from the CPS II Nutrition Cohort, a prospective study of cancer incidence and mortality established in 1992 as a subgroup of the larger 1982 mortality cohort (12–14). In 1982, physical activity was assessed using a single question: "How much exercise do you get (work or play)?" Possible responses were none, slight, moderate, or heavy. Physical activity in 1992 and 1997 were assessed in more detail, from self-reported questionnaires (15). Participants reported the average number of hours per week spent at 7 recreational activities (walking, jogging/running, lap swimming, tennis or racquetball, bicycling or stationary biking, aerobics/calisthenics, and dancing) in the previous year. Data were coded into metabolic equivalent (MET) hours per week (16).

Mortality follow-up is ongoing through automated linkage with the National Death Index for date and cause of death (17). Cancer diagnosis is self-reported and then verified through medical record abstraction or state cancer registry linkage (18). All aspects of the study protocol have been approved by the Emory University Institutional Review Board.

This analysis includes individuals enrolled in 1992 or 1993. The study observation period for each participant ended with the diagnosis of colon cancer, death, or the end of the follow-up period (June 30, 2005, for incident cancers, December 31, 2006, for colon cancer mortality). We excluded persons who a) were not known to be deceased but failed to respond to both 1997 and 1999 questionnaires, b) reported an unverified colon cancer, c) reported a history of cancer at baseline, or d) reported missing or uninterpretable data for physical activity in 1982 or 1992. After exclusions, 158,253 men and women remained for analysis (156,331 for incidence analyses), among whom 1,863 incident colon cancers were diagnosed and 846 fatal colon cancer cases were identified.

We examined 15-year change in physical activity (from 1982 to 1997) in relation to incident colon cancer from 1998 to 2005 and colon cancer mortality from 1998 to 2006. Because the physical activity question items changed over the 3 available measures of physical activity (1982, 1992, and 1997), we used change in z-score as the exposure variable for long-term change in physical activity (19). z-score is the difference of each person's activity level from the mean level, divided by the SD. We calculated change in z-score using a regression of the 3 time points. For the 1982 data, in which responses were qualitative, we assigned the 4 responses an ordinal number of increasing value corresponding to increasing intensity. We also examined the association of 10-year (shorter term) change in physical activity with colon cancer incidence and mortality from 1992 to end of follow-up, using a simpler 2-level cross-classification scheme (20), to group participants as consistently low (none or slight in 1982 and <17.5 MET hours per week in 1992), consistently high (moderate or heavy in 1982 and ≥ 17.5 MET hours per week in 1992), increasing (low in 1982 and high in 1992) or decreasing (high in 1982 and low in 1992) physical activity. As participants had to have at least 2 physical activity measures to be included in the analyses, the final number of cases included was slightly less, depending on time period examined (1,386 incident and 602 fatal colon cancer cases for long-term change, 1,863 incident and 826 fatal colon cases for 10-year change). Finally, we conducted an exploratory analysis comparing those who reported moderate or heavy activity in 1982 and were at or above the median for physical activity in 1992 (8 MET hours per week) and 1997 (9 MET hours per week) to those who reported none or slight in 1982 and were below the median in 1992 and 1997. By definition, the sample size of this analysis was considerably smaller ($n = 454$ incident and 216 fatal cases).

Age- and multivariate-adjusted colon cancer hazard ratios (HR) were estimated using Cox proportional hazards models. Analyses were conducted using SAS (Version 9.2). Multivariable analyses adjusted for age, gender, smoking, body mass index (BMI), education,

postmenopausal hormone use (among women), and intake of multivitamins, red meat, folate, alcohol, calcium, fiber, nonsteroidal anti-inflammatory drugs (NSAID), and total energy (18). Colorectal cancer screening history was not collected until 1997. We adjusted analyses of physical activity change from 1982 to 1997 for screening history but did not adjust the analyses of 1982 to 1992 change, as screening would then be an intermediate variable.

Results

Most (50%) participants reported declining physical activity levels over 10 years. Nearly one-quarter were consistently low (22%) or consistently high (23%), and few participants increased their physical activity level (4%).

Updating an earlier analysis in this cohort with additional follow-up (18), we found physical activity in 1992 was associated with a reduced risk of colon cancer. Individuals reporting 30 or more MET hours per week of physical activity were nearly 30% less likely (HR = 0.72, 95% CI: 0.58–0.89) to develop colon cancer than those who reported no physical activity (data not shown). Physical activity in 1982 was not associated with risk of colon cancer (HR comparing none/light to moderate/heavy = 1.07, 95% CI: 0.96–1.18).

Neither long-term physical activity change assessed using z-scores nor 10-year change in physical activity was associated with risk of incident colon cancer (Table 1). Results were unchanged when cases from the first 2 years of follow-up were excluded. Adjusting 15-year physical activity change for history of colon cancer screening did not change the result. Comparing those who were consistently active (at or above the sample median) to those who were consistently inactive (below the sample median) over 15 years, we found no association with colon cancer risk (HR = 0.87, 95% CI: 0.69–1.10) (data not shown).

There was no association between 15-year physical activity change and colon cancer mortality. However, when we compared those who had consistently high physical activity to those with consistently low physical activity over the 10 years from 1982 to 1992, those with consistently high physical activity had a significantly lower risk of colon cancer mortality (age adjusted HR = 0.81, 95% CI: 0.66–0.99). The association became borderline statistically significant in multivariable analysis. There was no difference in colon cancer mortality for those who increased or decreased activity from 1982 to 1992 as compared with those who were consistently low. In exploratory analyses, those who were consistently active (at or above the sample median over 15 years) were significantly less likely to die from colon cancer as those who were consistently inactive (multivariable HR = 0.45, 95% CI: 0.34–0.59), which held after adjusting for BMI (data not shown).

Table 1. Association of change in physical activity with colon cancer incidence and mortality, CPS II

Physical activity	Colon cancer incidence			Colon cancer mortality			
	Number of cases	Age-adjusted HR (95% CI)	Multivariable ^a HR (95% CI)	Number of cases	Age-adjusted HR (95% CI)	Multivariable ^a HR (95% CI)	Multivariable ^b HR (95% CI)
Change from 1982 to 1997 based on z-score of activity	1,386	0.94 (0.86–1.02)	0.95 (0.87–1.03)	602	0.93 (0.81–1.05)	0.93 (0.81–1.05)	0.92 (0.81–1.05)
Change from 1982 to 1992							
Increasing	78	0.99 (0.78–1.28)	1.02 (0.80–1.30)	41	1.03 (0.74–1.45)	1.05 (0.74–1.47)	1.08 (0.77–1.51)
Decreasing	983	1.10 (0.97–1.24)	1.08 (0.96–1.22)	419	0.91 (0.76–1.08)	0.88 (0.74–1.05)	0.91 (0.77–1.09)
Consistently high	434	1.01 (0.88–1.16)	1.02 (0.89–1.17)	180	0.81 (0.66–0.99)	0.82 (0.66–1.00)	0.86 (0.69–1.06)
Consistently low	368	reference	reference	186	reference	reference	reference

^aAdjusted for sex, education, smoking, use of postmenopausal hormones (among women only), intake of multivitamin, red meat, folate, alcohol, NSAIDs, fiber, calcium, and total energy.

^bAdjusted for above plus BMI.

Discussion

Consistent with a previous study of U.S. female nurses (6), we found no association of change in physical activity with risk of incident colon cancer. However, regular participation in physical activity over 10 years was associated (with borderline statistical significance) with a lower risk of colon cancer mortality compared with inactivity over that period of time. Those who were consistently at or above sample median physical activity levels over 15 years had half the risk of dying from colon cancer as those consistently below the median. These results are consistent with reports from other prospective studies, which suggest long-term participation in physical activity provides the greatest risk reduction (7, 21). Other studies that rely on retrospective assessment of lifetime physical activity also support the association of an active lifestyle with colon cancer risk (4, 21–27).

Given previous data indicating a clear association of physical activity with colon cancer risk, the lack of a change in relative risk with changing physical activity in this large, well-characterized cohort suggest that physical activity might act earlier in the carcinogenic process. Alternatively, it may be that long-term physical activity rather than change, *per se*, is more relevant for colon cancer prevention. We found no association for an activity level at or above the sample population median over 15 years and colon cancer risk, though the median was lower than levels of activity typically seen as necessary to reduce cancer risk. This area of research deserves additional attention, specifically, prospective research examining when over the lifetime physical activity change might alter risk, the magnitude of the change needed to alter risk and how long the change needs to be sustained. We were unable to precisely examine the initiation of behavior change or the ultimate duration of change, specifically whether changes were long- or short-lived. We also were unable to discriminate between sufficiently high and sufficiently low levels of activity.

The lack of associations seen for change in activity despite consistent associations for lifetime and adult only activity may be attributable to several factors. First, these studies relied on the self-report of physical activity, which is known to be subject to measurement error. This error becomes compounded when the measures are combined into an indicator of change of physical activity over time. Adult physical activity levels may also undergo substantial fluctuations because of changing life circumstances and increasing risk of injury with age. Maintaining an increased physical activity level may be necessary to decrease colon cancer risk. The CPS II data used here relied on a maximum of 3 physical activity self-report measures spread over 15 years and therefore we could not precisely measure maintenance of physical activity change over adulthood or late adulthood. Finally, we do not know how long high physical activity levels

need to be maintained to decrease risk. Future research in this area is needed to address these questions of timing of physical activity over lifetime and its impact on colon cancer risk. This question is important for determining if adults can, during midlife, take up physical activity and significantly alter risk.

We found an association between a consistently active lifestyle and colon cancer mortality. Peel et al. found that high levels of cardiorespiratory fitness were associated with a reduced risk of colon cancer mortality in the Aerobics Center Longitudinal Study cohort (28), and Haydon et al. reported a significant reduction in colon cancer mortality among exercisers in Australia (9), perhaps indicating a role for physical activity earlier in the carcinogenic process, consistent with this study. However, Meyerhardt and colleagues found prediagnosis physical activity was not associated with mortality in a cohort of nurses (10). We were unable to examine the role of postdiagnosis physical activity in colon cancer mortality, which has been shown to have a significant role in reducing mortality (11).

Our analysis is subject to several limitations. The number of individuals who increased their physical activity was small (4% of the sample for 10-year change) and their increase may not have been large enough to induce a meaningful association. With so few participants increasing physical activity, we lacked power to conduct stratified analyses on factors such as age and BMI. In a previous analysis in this cohort (18), only physical activity at or above 30 MET hours per week in 1992 was associated with reduced risk of colon cancer. This level of activity is higher than the 17.5 MET hours per week cutpoint that is required to be included in the

increasing or consistently high group in this analysis. Yet, analyses in other cohorts reported risk reductions with as little as 30 minutes per day of walking (approximately 10 MET hours per week ref. 6).

The major strengths of this analysis are the prospective repeated measures of physical activity, detailed measurement of potential confounders, and confirmed diagnosis of colon cancer. However, self-reported physical activity is known to contain substantial error (29); such misclassification may mask true change in physical activity and bias the results toward the null. Furthermore, as the measure of physical activity was not identical across time, we were able to measure change in relative ranking of activity level, not absolute change.

In conclusion, in this large prospective study, there was no evidence that increasing or consistently high physical activity levels among older adults were associated with colon cancer incidence. Consistently high physical activity levels were associated with a reduced risk of colon cancer mortality as compared with consistently low levels of activity. These findings, together with previous reports, suggest a need for better understanding of the time in the lifecourse at which physical activity may be most beneficial in reducing colon cancer risk and mortality and may provide support for the notion that factors that reduce risk of cancer may not be equally associated with a reduced risk of cancer death (30).

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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