Short Communication

Physical Activity in Relation to Cancer of the Colon and Rectum in a Cohort of Male Smokers[1]

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Abstract

We examined the association between occupational and leisure physical activity and colorectal cancer in a cohort of male smokers. Among the 29,133 men aged 50–69 years in the Alpha-Tocopherol, Beta-Carotene Cancer Prevention study, 152 colon and 104 rectal cancers were documented during up to 12 years of follow-up. For colon cancer, compared with sedentary workers, men in light occupational activity had a relative risk (RR) of 0.60 [95% confidence interval (CI), 0.34–1.04], whereas those in moderate/heavy activity had an RR of 0.45 (CI, 0.26–0.78; *P* for trend, 0.003). Subsite analysis revealed a significant association for moderate/heavy occupational activity in the distal colon (RR, 0.21; CI, 0.09–0.51) but not in the proximal colon (RR, 0.87; CI, 0.40–1.92). There was no significant association between leisure activity and colon cancer (active *versus* sedentary; RR, 0.82; CI, 0.59–1.13); however, the strongest inverse association was found among those most active in both work and leisure (RR, 0.33; CI, 0.16–0.71). For rectal cancer, there were risk reductions for those in light (RR, 0.71; CI, 0.36–1.37) and moderate/heavy occupational activity (RR, 0.50; CI, 0.26–0.97; *P* for trend, 0.04), and no association for leisure activity. These data provide evidence for a protective role of physical activity in colon and rectal cancer.

Introduction

Higher levels of physical activity have been consistently associated with a lower risk of colon cancer in epidemiological studies (1). However, despite a strikingly consistent inverse association overall, the subsite-specific risk associations between increased physical activity and colon cancer remain controversial. Most investigations that have examined activity and rectal cancer have not seen inverse associations (2–8), although there are some exceptions (9, 10).

One potential problem identified in the epidemiological literature is that persons categorized as physically active may also exhibit other healthy behaviors that could account for the observed relationships (11, 12). Although control for potentially confounding variables may partially alleviate this concern, many studies have not had adequate dietary and life-style data to perform the necessary adjusted analyses.

In this large, prospective study of middle-aged Finnish male smokers, we examined the relationship between both occupational and leisure activity and cancer of the colon and rectum. Given concerns regarding the clustering of healthy behaviors in physically active individuals, the fact that this is a cohort of long-term smokers and that detailed prospective dietary information is available to address confounding makes this a unique group in which to address the association between physical activity and colorectal cancer.

Materials and Methods

Study Population. The Alpha-Tocopherol Beta-Carotene Cancer Prevention study was a randomized placebo-controlled trial designed to evaluate the effect of α-tocopherol and β-carotene on the incidence and mortality related to lung and other cancers. The cohort consisted of 29,133 white males, ages 50–69 years, who smoked five or more cigarettes per day and lived in southwestern Finland. Subjects were recruited between 1985 and 1988, and randomized to one of four intervention groups: 50 mg/d α-tocopherol, 20 mg/d β-carotene, both α-tocopherol and β-carotene, or placebo. The intervention ended on 30 April 1993, but postintervention follow-up continues. Men who had been diagnosed previously with cancer or other serious disease, as well as those taking supplements of vitamins E or A or β-carotene in excess of defined amounts also were not eligible to participate. Additional details of the study have been described previously (13).

Case Identification. Incident cases of colon (ICD-9 code 153) and rectal (ICD-9 code 154) cancer diagnosed between randomization and 30 April 1997 were identified through the Finnish Cancer Registry. Medical records and histopathological material were centrally reviewed for 98% of the cases. Malignant carcinoids ($n = 7$) and anal cancers ($n = 3$) were excluded from the analysis. When persons had more than one cancer of a single type (colon or rectum), the cancer used in the analysis was the first diagnosed ($n = 3$), or with simultaneously diagnosed colon cancers ($n = 2$), the ICD-9 code for colon cancer (location not specified) was used. In total, 152 colon and 104 rectal cancer cases were included in the final analysis. For subsite-specific analysis in the colon, cases were further categorized as proximal (cecum, ascending, and transverse colon) or distal (splenic flexure, descending, and sigmoid colon) colon cancer.

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Table 1 Selected baseline characteristics for colon cancer cases, rectal cancer cases, and noncases[a]

Characteristic	Colon cancer (n = 152)	Rectal cancer (n = 104)	Noncases (n = 28,879)
Age (yr)	59.4 ± 5.2	59.4 ± 5.2	57.2 ± 5.1
BMI (kg/m^2)	26.8 ± 3.9	26.2 ± 3.7	26.3 ± 3.8
Dietary intake[b]			
Energy (kcal)	2839 ± 742	2781 ± 798	2815 ± 787
Fruit (g)	93.9 ± 74.1	91.3 ± 88.2	88.7 ± 81.5
Vegetables (g)	153.6 ± 94.6	157.0 ± 99.3	153.1 ± 111.3
Fat (g)	123.9 ± 39.0	121.4 ± 38.6	122.9 ± 41.0
Fiber (g)	25.9 ± 10.0	25.1 ± 9.5	25.7 ± 10.3
Alcohol (g)	19.6 ± 23.0	17.3 ± 20.6	18.0 ± 21.6
Calcium (mg)	1342 ± 481	1414 ± 702	1398 ± 559
Years of smoking	37.8 ± 8.3	36.6 ± 9.4	35.9 ± 8.5
Cigarettes smoked per day	18.8 ± 8.8	19.3 ± 9.1	20.4 ± 8.8
Occupational activity (%)			
Nonworking	52.0	50.0	42.2
Sedentary	18.4	17.3	13.7
Walking	14.5	16.4	18.2
Lifting/walking	7.9	10.6	16.6
Heavy labor	7.2	5.8	9.2
Leisure-time activity (%)			
Sedentary	45.4	42.3	41.8
Moderate	49.3	50.0	52.2
Heavy	5.2	7.7	6.0

[a] Mean ± SD; some percentages may not add to 100% because of rounding error.
[b] Dietary variables available for 93% of the cohort (n = 27,111); values expressed on a per-day basis.

Data Collection. At baseline, subjects completed a general medical history questionnaire and provided a blood sample. Usual occupational and leisure-time physical activity was assessed based on two questions. The first question asked the respondent to describe their activity during their work in the past year as: (*a*) not working; (*b*) mainly sitting; (*c*) walking quite a lot, but not lifting or carrying; (*d*) walking and lifting; or (*e*) heavy physical work, with examples provided. The second question asked the respondents to describe their usual leisure-time activity in the past year as: (*a*) sedentary (*e.g.*, reading, watching television); (*b*) moderate (*e.g.*, walking, hunting, gardening) fairly regularly; or (*c*) heavy (*e.g.*, running, skiing, swimming) fairly regularly. Most of the participants (n = 27,111; 93%) also completed a self-administered food-use questionnaire.

Statistical Analysis. In all analyses, sedentary men were used as the reference group, and the nonworkers were kept as a separate occupational activity category with the understanding that "nonworking" is not well defined in terms of physical activity. Because of the small number of subjects reporting heavy physical work and the similarity in risk estimates for the two heaviest occupational categories, these two categories were combined into one "moderate/heavy" occupational category to provide more stable estimates of risk. Similarly, few subjects (~6%) reported regular, heavy leisure-time physical activity, and, therefore, the moderate and heavy categories were collapsed to create an "active" leisure category. To evaluate the effect of total physical activity on colon cancer, individuals were also categorized based on combined occupational and leisure-time activity, with those sedentary in both activity types serving as the referent group.

Statistical analyses were performed using Statistical Analysis Systems (SAS) software (SAS Institute, Cary, NC). Cox proportional hazards models were used to estimate the RR[5] and 95% CIs of colon and rectal cancers (separately) associated with level of physical activity. All of the models adjusted for intervention group and any other variable that produced significant changes in the log likelihoods or produced a greater than 10% change in the β-coefficients for the physical activity variables. Colon cancer models included age, intervention group, BMI, and smoking (cigarettes/day), and rectal cancer models included age and intervention group. Dietary factors including energy intake, fat, calcium, and fiber did not confound the observed associations. Effect modification of the association between colon cancer and occupational activity was assessed by including factors and their cross-product terms in separate models, and also through subgroup analysis based on median splits of the factors. Elimination of the first two years of follow-up did not substantially alter any of the results (data not shown). There were no departures from the proportional hazards assumptions for any covariate in the final models.

Results

Selected subject characteristics are depicted in Table 1 by case status. Both colon and rectal cancer cases were older than noncases, and colon cases had also smoked longer than noncases. Both rectal and colon cases were more likely than noncases to not be working, and those who were working were more likely to be in sedentary jobs. Fewer cancer cases reported being in the highest categories of occupational activity than did noncases, and for leisure activity, more colon cases reported being sedentary than noncases.

The association between occupational and leisure-time activities and both colon and rectal cancers is depicted in Table 2. For colon cancer, there was a highly significant, dose-response inverse relationship for occupational physical activity. A similar and significant association was observed for rectal cancer, with more active workers having lower risk. For both sites, nonworkers had a lower risk compared with sedentary workers. Regular leisure-time activity did not appear to be associated with either colon or rectal cancer.

[5] The abbreviations used are: RR, relative risk; CI, confidence interval; BMI, body mass index.

Table 2 Associations between occupational and leisure-time physical activity and colon and rectal cancers[a]

	No. of cases	Person-years[b]	RR[c] (95% CI)	*P* for trend[d]
Colon cancer				
Occupational activity				
Nonworker	79	105,034	0.61 (0.39–0.98)	
Sedentary	28	38,010	1.0	Reference
Light	22	50,662	0.60 (0.34–1.04)	
Moderate/Heavy	23	70,361	0.45 (0.26–0.78)	0.003
Leisure-time activity				
Sedentary	69	108,387	1.0	Reference
Active	83	155,626	0.82 (0.59–1.13)	
Rectal cancer				
Occupational activity				
Nonworker	52	104,985	0.62 (0.34–1.11)	
Sedentary	18	37,985	1.0	Reference
Light	17	50,639	0.71 (0.36–1.37)	
Moderate/Heavy	17	70,337	0.50 (0.26–0.97)	0.04
Leisure-time activity				
Sedentary	45	108,344	1.0	
Active	60	155,546	0.93 (0.63–1.37)	

[a] Relative risk (RR) and 95% confidence interval (CI).
[b] Total person-years for cases and noncases in category of activity.
[c] RR for colon cancer is adjusted for age, supplement group, BMI, and smoking (cigarettes/day). RR for rectal cancer is adjusted for age and supplement group.
[d] The tests for trend use the sedentary group as the reference category. Nonworkers are not included in the trend test in the occupational activity analysis.

We further explored the physical activity and colon cancer relationship through an analysis of combined occupational and leisure-time activity categories. Regardless of leisure-time activity, nonworkers and those reporting light or moderate/heavy occupational activity had a significantly lower risk of colon cancer compared with those sedentary at both work and leisure. Among those reporting light occupational activity, however, colon cancer risk was lower for those who were also active in their leisure time (RR, 0.38; CI, 0.18–0.82) than in those who were sedentary (RR, 0.61; CI, 0.28–1.32). The lowest risk was seen among those who reported regular moderate/heavy activity at work and regular activity in their leisure time (RR, 0.34; CI, 0.16–0.71).

We examined potential effect modification of the physical activity/colon cancer association by age, BMI, years of smoking, and dietary intakes of energy, fat, fiber, calcium, folate, fruit, and vegetables. None of the interactions tested was statistically significant (*i.e.*, all had $P > 0.05$); however, there was a suggestion of lower risk among the most active men who ate more dietary fat or fiber. These findings should be interpreted cautiously given a limited power to detect interactions in this study.

Significant differences in the physical activity association according to anatomical subsite within the colon were observed. There was no association for occupational or leisure-time activity for proximal colon cancers. In the distal colon, however, both nonworkers (RR, 0.39; CI, 0.20–0.77) and those in moderate/heavy work (RR, 0.21; CI, 0.09–0.51) had reduced risks of cancer compared with sedentary workers, with a significant dose-response relationship among the workers (*P* for trend <0.001). There was no relationship between leisure-time activity and cancer of the distal colon.

Discussion

This study suggests that occupational physical activity is protective against colon cancer in a dose-dependent manner. Additionally, although leisure-time activity itself did not appear to be associated with a reduced risk of colon cancer, persons reporting light occupational activity who also reported leisure activity had greater risk reductions than did those who were sedentary in their leisure time. Subsite analysis within the colon further revealed that the inverse relationship for occupational activity was more pronounced for distal *versus* proximal tumors, a finding consistent with the observed dose-dependent inverse association for rectal cancer.

The observed inverse association between occupational and total physical activity and colon cancer is consistent with the majority of published studies (1). The lack of a relationship for recreational activity may be attributable to the low levels of vigorous leisure-time activity in this older cohort, as well as the ability to accurately respond to a single question querying leisure-time activity. Our activity questions did not allow for the assessment of the duration or frequency of these activities, and consequently, activity could be overestimated. Despite these limitations, there did appear to be some additional benefit of leisure activity among men who were engaged in light activity at work. This finding may indicate that those engaged in heavier activity for a large portion of their day (*i.e.*, at work) may not gain additional benefit by increased leisure activity.

We observed significant associations with occupational activity and distal colon cancer, which is consistent with the majority of previous studies that have examined anatomical subsites (4, 6, 14–16), whereas others have noted greater associations proximally (3, 17), or no difference by subsite (18, 19). Some of these discrepancies may be attributable to variation in the methods used to define anatomical subsites or measure physical activity. In contrast to a majority of studies (2–8), we also saw an inverse association between occupational activity and cancer of the rectum, which seems consistent with the stronger association in the distal colon. Three previous studies have observed 20–50% lower risk of rectal cancer among those engaged in higher levels of activity (9, 10, 20).

Nonworkers represent a unique subgroup within our study cohort who experienced reduced rates of colon cancer compared with sedentary workers. Although we don't know specifically why these men reported not working, many of these older men may be retired, and given the low proportion of sedentary workers in the cohort as a whole, their lower risk may be related to earlier occupational activity. Indeed, previous studies have shown an inverse association between occupational activity at younger ages and later colon cancer risk (6, 10, 19). Increased leisure-time activity among the nonworkers does not seem to explain their reduced risk, because both nonworkers sedentary in their leisure, and those active in their leisure had similar risk estimates (RR, 0.49; CI, 0.26–0.94 *versus* RR, 0.47; CI, 0.25–0.86).

Age, BMI, and specific dietary variables have previously been examined as effect modifiers of the association between activity and colorectal cancer (3, 4, 6, 18, 20–23) with inconsistent findings, possibly attributable to variation in population characteristics, cofactor categorization, or chance. In our study, some of the lowest risks were seen among active men in the higher categories of fat and fiber intake, although risk was generally reduced among active men across all levels of the cofactors.

Certain limitations and strengths of our study should be considered. Our cohort is unique in that it was comprised of

male smokers in Finland who agreed to enroll in a cancer prevention trial. We used single questions to measure both occupational and leisure-time activity performed in the last 12 months. Although the relative intensity of the activity was incorporated into the response choices, we have no information on the frequency or duration of the activities performed, or how well the responses represent activity performed during other periods of life. Particular strengths of the study include its prospective nature and size. Additionally, we had detailed information on dietary intakes and smoking history that we used both for adjustment and evaluation of effect modification. Although the fact that the cohort consisted of all smokers is in some respects a limitation, it is also a unique strength. Because smoking was an exposure common to all of the participants, it allowed us to evaluate associations of physical activity and cancer in a group that does not practice optimal health behaviors, and should have reduced the possibility that physical activity acted as a surrogate marker of an overall healthy life-style. Additionally, smokers are believed to be at an increased risk for colorectal cancer (24), and despite this, we found that activity was protective even in those who had smoked for more than 36 years on average.

In summary, our findings provide further evidence of an inverse association between physical activity and colon cancer, consistent with previous studies. The lower risk among active men was consistently present across levels of the multiple cofactors examined here. The relationship appeared to be stronger in the distal colon, rather than the proximal colon, and in contrast to most prior studies, a similar association was seen for rectal cancer. Definitive investigations of the mechanisms responsible for this apparent protective relationship are needed.

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