Physical Activity and Cancer Prevention—Data from Epidemiologic Studies

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ABSTRACT

LEE, I.-M. Physical Activity and Cancer Prevention: Data from Epidemiologic Studies. *Med. Sci. Sports Exerc.*, Vol. 35, No. 11, pp. 1823–1827, 2003. **Purpose:** The aim of this paper is to examine whether physical activity plays any role in the prevention of cancer. **Methods:** To accomplish this, data from published epidemiologic studies on the relation between physical activity and the risk of developing cancer were reviewed. **Results:** The data are clear in showing that physically active men and women have about a 30–40% reduction in the risk of developing colon cancer, compared with inactive persons. Although the data are sparse, it appears that 30–60 $min \cdot d^{-1}$ of moderate- to vigorous-intensity physical activity is needed to decrease risk. There is a dose-response relation, with risk declining further at higher levels of physical activity. It is also clear that physical activity is not associated with the risk of developing rectal cancer. With regard to breast cancer, there is reasonably clear evidence that physically active women have about a 20–30% reduction in risk, compared with inactive women. It also appears that 30–60 $min \cdot d^{-1}$ of moderate- to vigorous-intensity physical activity is needed to decrease the risk of breast cancer, and that there is likely a dose-response relation. For prostate cancer, the data are inconsistent regarding whether physical activity plays any role in the prevention of this cancer. There are relatively few studies on physical activity and lung cancer prevention. The available data suggest that physically active individuals have a lower risk of lung cancer; however, it is difficult to completely account for cigarette smoking. There is little information on the role of physical activity in preventing other cancers. **Conclusion:** Physical activity is associated with lower risk of developing certain site-specific cancers, in particular colon and breast cancers. **Key Words:** BREAST CANCER, COLON CANCER, EPIDEMIOLOGY, EXERCISE, LUNG CANCER, PHYSICAL ACTIVITY, PROSTATE CANCER, RECTAL CANCER

The idea that physical activity may be important in preventing cancer is not a new one. The earliest epidemiologic studies on this topic date back to 1922, when two studies were published (2,19). Both groups of investigators, working independently, examined mortality rates, including cancer mortality rates, among men with different occupations in Australia, England, and the United States. The investigators observed that the cancer mortality rates in these countries declined with increasing physical activity required for the occupation. They proposed a new hypothesis in the etiology of cancer, that "hard muscular work" was important for cancer prevention.

After these two early studies, the hypothesis languished until the 1980s. Subsequently, more than a hundred epidemiologic studies on the role of physical activity and cancer prevention have been published. In this paper, I would like to highlight some of the evidence regarding whether physical activity plays any role in the prevention of cancer, as well as discuss what data are available on the specific details of the physical activity required. This is not intended to be an exhaustive review of the subject; for a comprehensive review, the reader is directed to a recent publication on this topic (6). Instead, the studies cited in this paper are intended to be representative of the larger body of literature and are intended to illustrate the points being made.

The available studies of physical activity and cancer prevention clearly indicate that physical activity has a different association with different site-specific cancers. Therefore, in this paper, the different site-specific cancers will be reviewed separately. Not surprisingly, the most commonly studied cancers in relation to physical activity also are the most commonly occurring cancers in men and women. In 2002, the American Cancer Society estimated that the three most commonly occurring cancers (other than nonmelanoma skin cancer) in men were prostate, lung, and colorectal cancers (30%, 14%, and 11% of all new cases, respectively); for women, they were breast, lung, and colorectal cancers (31%, 12%, and 12% of all new cases, respectively) (5). The association of physical activity with each of these cancers will be discussed below.

PHYSICAL ACTIVITY AND RISK OF COLON CANCER

To date, at least 50 studies have examined the association between physical activity and the risk of developing colon cancer (6). (In addition, 17 studies have investigated the

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relation between physical activity and the risk of developing colorectal cancer. These 17 studies will not be discussed further because the available data indicate that physical activity has different associations with colon and rectal cancer. Thus, when combining the two site-specific cancers, the individual associations with physical activity may be obscured.) These studies have been conducted in many countries in North America, Europe, Asia, Australia, and New Zealand. Although the results from individual studies vary (ranging from 80% reduction in risk among active compared with sedentary subjects, to 60% increase in risk), the overall data show a clear pattern of lower risk among men and women who are physically active. The median relative risk over all studies comparing those most active with those least active is 0.7 for men and 0.6 for women, indicating a 30–40% reduction in risk. More than half the studies tested for a dose-response relation across levels of physical activity, and the data indicate that there is a dose-response. That is, at higher levels of physical activity, risk continues to decline.

Although it is clear that physical activity is associated with a decreased risk of developing this cancer, details of the relationship are less clear. Few studies have examined specific issues such as the amount, intensity, and duration of physical activity required. One study providing information on the amount of physical activity required is the Harvard Alumni Health Study (7). In this study of 17,148 men followed for up to 26 yr, during which 225 men developed colon cancer, men who expended $\geq$ 1000 kcal·wk^{-1} in walking, climbing stairs, and participating in sports or recreational activities experienced half the colon cancer rates of their less active counterparts. This amount of energy expenditure is equivalent to at least 30 min of moderate-intensity physical activity, 5 d·wk^{-1}, which is in line with current physical activity recommendations (16,17). In the Nurses' Health Study, which followed 67,802 women for 6 yr and observed 212 cases of colon cancer, women expending 11–21 MET·h·wk^{-1} in moderate and vigorous recreational activities had a 33% reduction in risk of colon cancer, of borderline significance, compared with those expending $<$2 MET·h·wk^{-1} (14). (The midpoint for this category, 16 MET·h·wk^{-1}, is equivalent to about 4 h·wk^{-1} of moderate-intensity physical activity.) At $>$21 MET·h·wk^{-1} (or approximately 5 h·wk^{-1} of moderate-intensity physical activity), a greater risk reduction that was statistically significant, 46%, was observed.

Little information is available regarding the intensity of physical activity necessary to reduce the risk of colon cancer. In the Diet, Activity, and Lifestyle Colon Cancer Study, a multicenter case-control study of men and women, participation in vigorous-intensity activities (amounting to at least 60 min·d^{-1}), was associated with decreased colon cancer risk, but not participation in moderate-intensity activities (20). With regard to the duration of physical activity required, current recommendations allow for the accumulation of several bouts of physical activity of $\geq$ 10 min daily (16,17). However, there currently are no studies directly examining whether several such short bouts of physical activity daily are comparable with a single, longer bout of physical activity as far as risk reduction for colon cancer is concerned.

Thus, although the data are sparse, it appears that 30–60 min·d^{-1} of moderate- to vigorous-intensity physical activity is sufficient to decrease the risk of colon cancer in men and women.

PHYSICAL ACTIVITY AND RISK OF RECTAL CANCER

At least 30 studies have investigated the relation between physical activity and the risk of developing rectal cancer (6). These studies have been carried out in North America, Europe, Asia, and Australia. Although the results from individual studies vary (ranging from 70% reduction in risk among active compared with sedentary subjects, to 150% increase in risk), the overall data show no association between physical activity and rectal cancer rates in men and women. The median relative risk over all studies comparing those most active with those least active is 1.0, indicating similar rates of this cancer among active and inactive subjects.

PHYSICAL ACTIVITY AND RISK OF BREAST CANCER

With regard to this cancer, the most commonly occurring cancer in U.S. women, at least 57 studies have examined its association with physical activity (6). These studies have been conducted in several countries in North America, Europe, Asia, and Australia. As with the other cancers discussed above, the findings from individual studies vary (ranging from 60% reduction in risk among active compared with sedentary subjects, to 90% increase in risk); however, the overall data show a reasonably clear pattern of lower breast cancer rates among active women. The median relative risk over all studies comparing most active with least active women is 0.8; among postmenopausal women this is 0.7 (i.e., indicating a 20–30% reduction in risk). Approximately half the studies tested for a dose-response relation over different levels of physical activity, with about two-thirds of them reporting a significant trend of declining risk with increasingly higher levels of physical activity.

As with the studies of colon cancer, little information is available regarding specific details of the relation between physical activity and breast cancer. It appears that at least 30–60 min·d^{-1} of moderate to vigorous intensity physical activity is required to decrease risk. For example, in a study of 25,624 Norwegian women followed for a median of 14 yr, 351 women developed breast cancer (21). Women who spent at least 4 h·wk^{-1} exercising to keep fit had 37% lower breast cancer rates than women whose leisure-time pursuits were sedentary (e.g., reading, watching television).

In the Norwegian study, the magnitude of risk reduction is somewhat larger than that seen in most other studies. In the large Nurses' Health Study, 3137 women developed breast cancer among 85,364 women followed for 16 yr (18). Nurses who spent 4–6.9 h·wk^{-1} in moderate or vigorous

recreational activities had a 15% lower risk of developing breast cancer during follow-up, compared with nurses who spent <1 h·wk^{-1} in these activities. Women who engaged in these activities for 7 or more hours per week had a somewhat larger risk reduction, or 18% lower risk, than those participating in moderate or vigorous recreational activities for <1 h·wk^{-1}. In the Women's Health Study, a similar magnitude of risk reduction was observed among 39,322 women followed for 4 yr, during which 411 developed breast cancer (9). Women who expended 1500 kcal·wk^{-1} or more in moderate and vigorous recreational activities (equivalent to approximately 3–4 h·wk^{-1}) experienced 20% lower rates of breast cancer than women who expended <200 kcal·wk^{-1}.

There are no studies directly examining what duration of exercise bouts (i.e., several short bouts vs a single long bout) is required to decrease the risk of developing breast cancer (6).

PHYSICAL ACTIVITY AND RISK OF PROSTATE CANCER

Currently, at least 36 studies have investigated the association of physical activity with the risk of developing prostate cancer, the most commonly diagnosed cancer in U.S. men (6,10). These investigations have been carried out in North America, Europe, and Asia. The findings from these studies have been inconsistent. Although individual studies have observed as much as a 70% reduction in risk among most active compared with least active men, several studies also have reported increased risks of twofold and greater (up to 287% increase). Overall, there is not strong support for the hypothesis that physical activity decreases the risk of this cancer. The median relative risk across all studies, comparing most with least active men, is 0.9, or almost similar rates of prostate cancer in these two groups.

In the Health Professionals' Follow-Up Study, where 47,542 men were followed for 8 yr, 1362 developed prostate cancer, 200 of which were metastatic at diagnosis (3). Total physical activity—assessed from walking, climbing stairs, and participating in moderate and vigorous recreational activities—was not associated with the risk of developing all prostate cancer or metastatic prostate cancer. However, vigorous physical activity requiring $\geq$ 6 METs predicted a lower incidence of metastatic prostate cancer. The most active men (expending a median of 41 MET·h·wk^{-1} in vigorous activity, or the equivalent to some 4–8 h·wk^{-1}) experienced a 54% lower incidence, compared with the least active men, who did not participate in vigorous activities.

In the Harvard Alumni Health Study, initial observations (8) concurred with the findings from the Health Professionals' Follow-Up Study. Among 17,719 alumni followed for up to 26 yr between 1962 and 1988, 419 men developed prostate cancer. Men who expended >4000 kcal·wk^{-1} (equivalent to perhaps 5 h·wk^{-1} or more of vigorous exercise) had a lower incidence of prostate cancer, compared with those expending <1000 kcal·wk^{-1}. This was especially true for prostate cancer occurring among men aged $\geq$ 70 yr, where a 47% reduction in incidence was observed. However, these findings could not be replicated in subsequent follow-up of these individuals between 1988 and 1993 (13).

One possible explanation for the inconsistent findings in the Harvard Alumni Health study could be due to differences in prostate cancer diagnosis over time. In the initial publication, the prostate cancer cases were diagnosed between the 1960s and 1980s, when testing for prostate-specific antigen (PSA) was not yet widely used. In the subsequent study, the prostate cancer cases were diagnosed in the late 1980s and 1990s, when PSA screening for prostate cancer became popular. If physically active men also were more likely to be health conscious and undergo health screening (including PSA screening), this could have led to increased diagnosis of early prostate cancers among the active men, obscuring the inverse relation between physical activity and the risk of prostate cancer that was previously observed.

Other epidemiologic studies of physical activity and the prevention of prostate cancer also have yielded inconsistent findings. Although it appears biologically plausible for physical activity to lower the risk of developing this cancer (discussed in a companion paper from this symposium), further research is needed to clarify the relation. At the moment, the available epidemiologic data do not support a role of physical activity in preventing prostate cancer.

PHYSICAL ACTIVITY AND RISK OF LUNG CANCER

Lung cancer has been less well studied than the other cancers described above. There have been at least 21 studies conducted in the United States and Europe investigating physical activity and the prevention of lung cancer (6). The majority of studies reported lower rates of lung cancer among physically active individuals (median relative risk comparing most with least active subjects, 0.8, or 20% reduction; range 0.4, or 60% reduction, to 1.4, or 40% increase). However, it is difficult to be certain that the effect of cigarette smoking was completely controlled for. Although the duration and amount of cigarette smoking can be adjusted for, there are several other factors which may be important, such as whether low-tar cigarettes or filter tips were used, the depth of inhalation when smoking, passive smoking, etc. Most of these issues can be eliminated by conducting studies among individuals who have never smoked; however, lung cancer occurs at a very low frequency in these individuals and so such studies would have very limited statistical power to detect an effect of physical activity.

Studies of physical activity and lung cancer include a Norwegian study of 81,516 men and women followed for up to 19 yr. During follow-up, 413 men and 51 women developed lung cancer (22). Investigators observed an inverse relation between the level of recreational physical activity and the risk of lung cancer. After adjusting for smoking habit and the number of cigarettes smoked, men who walked or bicycled for at least 4 h·wk^{-1} had a 25% reduction in risk

compared with men who had sedentary leisure-time hobbies. Men at the next higher level of physical activity (exercising for ≥ 4 h·wk^{-1} to keep fit, regular hard training, or competing in sports) had a somewhat larger risk reduction, or 29%.

Investigators also examined the association by histologic type of lung cancer. They found significant inverse associations for small cell and adenocarcinoma, but not for squamous cell cancers. This may lend some indirect evidence that the findings do not reflect residual confounding by cigarette smoking. Although cigarette smoking increases the risk of all lung cancers, this association is particularly strong for squamous cell and small cell lung cancers, but less marked for adenocarcinoma.

Among women, there were no significant associations observed between physical activity and lung cancer risk; however, the number of lung cancers developing among women in this Norwegian study was small.

A similar inverse, dose-response relation between physical activity and lung cancer was observed among men in the Harvard Alumni Health Study (12). In this analysis, 13,905 men were followed for up to 16 yr and 245 developed lung cancer. After accounting for cigarette smoking, men who expended 1000–1999, 2000–2999, and $\geq$ 3000 kcal·wk^{-1} in walking, climbing stairs, and participating in sports or recreational activities had 13%, 24%, and 39% reductions in lung cancer risk, respectively, compared with men who expended $<$1000 kcal·wk^{-1} in these activities (1000 kcal·wk^{-1} is approximately equivalent to 2.5 h·wk^{-1} of moderate-intensity physical activity).

PHYSICAL ACTIVITY AND RISK OF OTHER SITE-SPECIFIC CANCERS

Other site-specific cancers that have been studied in relation to physical activity include endometrial, ovarian, testicular, pancreatic, kidney, bladder, and hematopoietic cancers (6,11,15). The data for these cancers are limited and further research is needed. Based on these limited data, it is possible that regular participation in physical activity may play a role in preventing the occurrence of some of these cancers as well.

CONCLUSION

There currently is a large body of epidemiologic data examining whether physical activity can reduce the risk of cancer developing in men and women. The data are clearest in supporting a role of physical activity in reducing rates of colon cancer in men and women, and breast cancer in women, as acknowledged recently by the American Cancer Society (1), and the International Agency for Research on Cancer (4). Although physically active persons also are likely to have better health habits, the observed associations are unlikely to be due to these associated healthy behaviors. The inverse relation between physical activity and risk of colon cancer still persists after adjusting for many potential confounders including body mass index, smoking, diet (such as energy intake, intake of fiber, micronutrients, vegetables, and meat), use of NSAID, and screening (6). For breast cancer, the inverse association continues to be observed after controlling for potential confounders such as body mass index, alcohol intake, use of oral contraceptives and hormone therapy, reproductive variables (ages at menarche and menopause, menopausal status, parity, age at first birth, breast feeding), benign breast disease, and family history (6).

Although the overall relation between physical activity and the risk of colon and breast cancers is clear, details regarding the optimal amount, intensity, duration, and frequency are less clear, as is the shape of the dose-response curve. Further research also is needed to clarify the whether physical activity is associated with the risk of developing other site-specific cancers.

Many of the examples used to illustrate the inverse relation between physical activity and the risk of developing cancer have been drawn from large cohort studies, such as the Harvard Alumni Health Study and the Health Professionals' Follow-up Study in men, and the Nurses' Health Study and the Women's Health Study in women. There are several reasons for this. First, the large number of subjects followed for long periods of time results in sufficient numbers of cancer for meaningful statistical analyses. Second, these studies have collected details on the kinds of activities carried out, and the frequency and duration of these activities. This level of detail is available in few other studies. Moreover, the information is updated over time and prospective, updated information on physical activity is almost nonexistent in other studies. Finally, these studies also have collected information on many other health habits and medical history, also updated over time, that allows for control of confounding by other health characteristics associated with physical activity.

However, such studies also have several limitations. First, subjects are predominantly white, and so one may question whether the findings are applicable to minority populations. Although empirical data on such populations are sparse, the biological underpinnings of an inverse relation between physical activity and cancer risk (discussed in a companion paper from this symposium) are likely to hold for persons of different ethnicity and race. Second, subjects in these large cohort studies also tend to be well educated and of higher socioeconomic status and do not resemble the general population of the United States. Again, these differences are unlikely to influence the biologic effects of physical activity. Finally, the kinds of activities carried out by these subjects may differ from those undertaken by the general population (for example, economically disadvantaged persons may not have the leisure-time to "exercise" in the traditional sense). Nonetheless, the findings from these large cohort studies can be expressed in more general terms, such as minutes per day in physical activity, which can be counted from walking for transportation, occupation, and household chores, apart from leisure-time activity. Although these large cohort studies have provided useful information, it is important to observe empirical data as well. Future

studies conducted in broader population groups are needed to supplement the data currently available and strengthen the hypothesis that physical activity reduces the risk of certain cancers.

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