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Intensity of leisure-time physical activity and cancer mortality in men

J A Laukkanen,1,2 R Rauramaa,3,4 T H Mäkikallio,2,5 A T Toriola,6 S Kurl1

ABSTRACT

Objective: There is a lack of evidence to show the role of exercise intensity in the prevention of cancer mortality because no previous studies have shown this relation. The relationship of leisure-time physical activity with cancer mortality was therefore assessed.

Methods: Participants were from a population-based sample of 2560 men from eastern Finland with no history of cancer at baseline. Physical activity was assessed using the 12-month leisure-time physical activity questionnaire. During an average follow-up of 16.7 years, a total of 181 cancer related deaths occurred.

Results: An increase of 1.2 metabolic units (MET or metabolic equivalents of oxygen consumption; 1 SD in metabolic equivalents) in the mean intensity of leisure-time physical activity was related to a decrease (relative risk (RR) 0.85, 95% CI 0.72 to 0.99) in cancer mortality mainly due to lung and gastrointestinal cancers, after adjustment for age, examination year, alcohol consumption, smoking, body mass index and energy, fibre and fat intake. Men with leisure-time physical activity of more than 5.2 MET (highest quartile) had a lower RR (0.63, 95% CI 0.40 to 0.99) cancer mortality compared with men whose mean intensity of physical activity was less than 3.7 MET (lowest quartile). The mean intensity of physical activity was related to the risk of cancer death among men who exercised at least 30 minutes per day on average.

Conclusions: This prospective study indicates that the mean intensity of leisure-time physical activity is inversely associated with the risk of premature death from cancer in men.

Little is known about the intensity of physical activity needed to reduce premature mortality from cancer, although physical activity has been associated with a reduced risk of cancer in some population studies.1-3 The specific quantity and intensity of physical activity needed to reduce premature overall mortality is based on a few prospective population-based studies.2-5 On the basis of existing evidence, at least 30 minutes of moderate-intensity physical activity on most, preferably all, days of the week is recommended for health promotion and cardiovascular disease (CVD) prevention. However, the beneficial levels of physical activity are likely to depend on the cause of disease because diseases have different pathophysiological mechanisms or even a genetic predisposition. Therefore, it is possible that the recommendations for the level of intensity of physical activity needed in the prevention of cancer risk may differ from the physical activity needed in the prevention of CVD as a result of different underlying causes of mortality. However, there are no studies showing the intensity of leisure-time physical activity that may be necessary to reduce cancer mortality. The principal aim of this study was thus to define the intensity of leisure-time physical activity required to reduce cancer mortality in a population-based sample of men from eastern Finland.

SUBJECTS AND METHODS

The present analyses were carried out among participants in an eastern Finnish follow-up study, which was initially designed to investigate risk factors for CVD and related outcomes in a population-based sample of middle-aged men. Of the 3453 men aged 42, 48, 54 or 60 years who resided in the town of Kuopio and its surrounding rural communities, 198 were excluded because of death, serious disease or migration away from area, and of the remaining men, 2682 (78%) agreed to participate in the study. Baseline examinations were conducted between March 1984 and December 1989. Men who had a history of cancer (n = 93) were excluded. Complete data on the duration, frequency and mean intensity of physical activity were available for 2560 men.

Physical activity

Physical activity was assessed using the 12-month leisure-time physical activity questionnaire. The checklist included the most common physical activities of middle-aged Finnish men, selected on the basis of a previous population study in Finland. For each activity performed, the subject was asked to record the frequency (number of sessions per month), average duration (hours and minutes per session), and intensity (scored as 0 for recreational activity, 1 for conditioning activity, 2 for brisk conditioning activity, 3 for competitive, strenuous exercise). A trained nurse checked and completed the questionnaire in an interview. The intensity of physical activity was expressed in metabolic units (MET or metabolic equivalents of oxygen consumption). Leisure-time physical activity was categorised according to type: (1) conditioning physical activity—walking (mean intensity, 4.2 MET), jogging (10.1 MET), skiing (9.6 MET), bicycling (5.8 MET), swimming (5.4 MET), rowing (5.4 MET), ball games (6.7 MET) and gymnastics, dancing, or weight lifting (5.0 MET), (2) non-conditioning physical activity—crafts, repairs, or building (2.7 MET), yard work, gardening, farming, or snow shovelling (4.3 MET), hunting, picking berries, or gathering mushrooms (3.6 MET), fishing (2.4 MET) and forestry (7.6 MET); and (3) walking (3.5 MET) or bicycling (5.1 MET) to work.
Physical fitness was measured by a maximal symptom-limited exercise tolerance test, which was performed by using an electrically braked cycle ergometer. A maximal symptom-limited exercise tolerance test was performed between 08:00 and 10:00 hours using an electrically braked cycle ergometer. The standardised testing protocol consisted of an increase in the workload of 20 W per minute with the direct analyses of respiratory gases. Physical fitness was defined as the highest value for or the plateau of directly measured oxygen uptake. For safety reasons, and to obtain reliable information on exercise test variables, the tests were supervised by an experienced physician with the assistance of an experienced nurse.

Diet and body composition
Dietary energy intake was assessed using 4-day food recording. Instructions were given and completed food records were checked by a nutritionist. The intake of nutrients was estimated using the NUTRICA? software. The data bank of NUTRICA? is compiled using mainly Finnish value nutrient compositions that take into account possible food preparation losses. Body mass index (BMI) was computed as weight in kilograms divided by the square of height in metres. Waist circumference was calculated as the average of two measurements taken after inspiration and after expiration (mean difference between the two measurements =1.5 cm) at the midpoint between the lowest rib and the iliac crest. The waist-to-hip ratio was defined as waist girth/hip circumference measured at the trochanter major. Height and weight were measured and recorded by a study nurse.

Smoking and alcohol consumption
Cigarette smoking was assessed by self-report. Cigarette pack-years denotes the lifelong exposure to smoking that was estimated as the product of years smoked and the number of cigarette smoked daily at the time of examination. Alcohol consumption was assessed with a structured quantity–frequency method using the nordic alcohol consumption inventory compiled using mainly Finnish value nutrient compositions that take into account possible food preparation losses. Body mass index (BMI) was computed as weight in kilograms divided by the square of height in metres. Waist circumference was calculated as the average of two measurements taken after inspiration and after expiration (mean difference between the two measurements =1.5 cm) at the midpoint between the lowest rib and the iliac crest. The waist-to-hip ratio was defined as waist girth/hip circumference measured at the trochanter major. Height and weight were measured and recorded by a study nurse.

Outcome events and statistical analyses
Cancer deaths were ascertained by linkage to the National Death Registry using the Finnish personal identification code. There were no losses to follow-up. All cancer deaths that occurred between study entry (March 1984 to December 1989) and December 2005 were included. A total of 181 cancer related deaths occurred during an average follow-up time of 16.7 years (range 0.2–21.7 years). The most common types of cancer deaths were due to cancers in the gastrointestinal tract (n = 57), lung (n = 48), prostate or urinary tract (n = 25), brain (n = 9) and lymphoma (n = 6) cancer. The association of physical activity with cancer mortality was analysed by using Cox multivariable proportional hazards’ models (SPSS 14.0 for Windows). The mean intensity of leisure-time physical activity was entered as dummy variables into forced Cox proportional hazards models. In these models, the mean intensity of physical activity was categorised according to quartiles. If possible, covariates were entered uncategorised into the Cox models.

RESULTS
At the beginning of the follow-up, the mean age of the subjects was 53.0 years (range 42.0–61.3 years). The mean intensity of leisure-time physical activity was 4.5 MET (range 2.0–12.5 MET) and the mean duration of physical activity was 462 minutes per week (range 0–3087 minutes per week). A total of 27% of the men performed exercise for less than 30 minutes per day during leisure time. The baseline characteristics of the study population are shown in table 1.

Table 1 Baseline characteristics of the study population
In a Cox model adjusting for age, examination year, cigarette smoking, alcohol consumption, BMI and total caloric, fibre and fat intake, 1.2 MET (1 SD) increase in the mean intensity of leisure-time physical activity was related to a decrease (relative risk (RR) 0.85, 95% CI 0.72 to 0.99) in cancer mortality. Age-adjusted RR for cancer death was 0.58 among those with the highest mean intensity of leisure-time physical activity compared with the lowest mean intensity of physical activity (table 2). Men with more than 5.2 MET mean intensity leisure-time physical activity had a lower (RR 0.64, 95% CI 0.40 to 1.00) cancer mortality compared with men whose mean intensity of physical activity was less than 3.7 MET, after adjusting for confounders (table 5). After further adjustment for the energy expenditure of physical activity, the respective risk did not change markedly (RR 0.64, 95% CI 0.40 to 1.01) among those with a mean intensity of physical activity (>5.2 MET).

The adjusted RR of cancer death among men with the mean intensity (<3, 3–6 and >6 MET) of leisure-time physical activity are presented in fig 1. After further adjustment for the energy expenditure of physical activity, RR for cancer mortality in the highest mean intensity categories did not change significantly (RR 0.52 for 5–6 MET and RR 0.31 for >6 MET).

The mean intensity of physical activity was related to cancer death only among those who exercise more than 30 minutes per day on average (1853 men, 135 deaths; age-adjusted RR 0.73, 95% CI 0.60 to 0.89, multivariable-adjusted RR 0.76, 95% CI 0.62 to 0.92 per 1.2 MET change). Among those who exercise less than 50 minutes per day (707 men, 46 deaths), the mean intensity of physical activity was not related to the cancer risk (age-adjusted RR 1.01, 95% CI 0.77 to 1.32, multivariable-adjusted RR 1.02, 95% CI 0.78 to 1.35). Also, an additional adjustment for the duration did not change the results.

Among those who exercised at least 50 minutes per day, the risk of cancer death was clearly decreased according to the mean intensity categories (>3, 3–6, >6 MET) of physical activity. In this group of men (duration at least 30 minutes per day) whose mean intensity of physical activity was 3–6 MET, the age-adjusted risk was 0.46 (95% CI 0.26 to 0.82) and among those whose mean intensity of physical activity was over 6 MET, the respective risk was 0.25 (95% CI 0.10 to 0.64). After adjustment for confounders (age, examination year, cigarette smoking, alcohol consumption, BMI, caloric, fibre and fat intake), the respective risks were 0.51 (95% CI 0.29 to 0.92) and 0.31 (95% CI 0.31 to 0.78) according to 3–6 MET and over 6 MET mean intensity categories, respectively. On the other hand, among those who exercised less than 50 minutes per day, there was no significant association.

The total volume of physical activity (assessed as mean intensity in MET multiplied by duration in minutes per week) was associated with cancer risk. Men in the highest quartile of total volume of physical activity had the lowest risk of cancer death (RR 0.62, 95% CI 0.41 to 0.96), after adjustment for age, whereas after adjustment for all confounders the respective risk was 0.72 (95% CI 0.47 to 1.10), when compared with men in the lowest quartile of the total volume of physical activity. The total volume of certain intense physical activities was inversely associated with cancer death. For example, we found that the
total volume of cross-country skiing was related to the risk of cancer death. However, the duration of leisure-time physical activity had no independent relationship to the risk of cancer death as well as the duration of non-conditioning or other light physical activities were not associated with cancer risk.

Physical fitness, as an objective measure of exercise capacity, was inversely related to the risk of cancer death. An increase of 3.5 ml/kg per minute (1 MET) of physical fitness amounted to a 12% (RR 0.88, 95% CI 0.81 to 0.96) reduced risk of cancer death, after adjusting for age, examination year and other confounders. When we included both the intensity of physical activity and physical fitness in the multivariable-adjusted model, physical fitness was related to the risk of cancer death (RR 0.89, 95% CI 0.83 to 0.97 per 1 MET change), whereas the association between the intensity of physical activity and cancer risk weakened (RR 0.89, 95% CI 0.74 to 1.05 per 1.2 MET change). The exclusion of cancer deaths that occurred during the first 3 years of follow-up did not change the results (table 3), which makes self-selection bias unlikely.

**DISCUSSION**

On the basis of the present study, at least moderately intense physical activity is more beneficial than low intensity physical activity in the prevention of premature death from cancer in men. The mean intensity of physical activity was related to the risk of cancer death among men who exercised at least 30 minutes per day on average. This finding is consistent with US consensus statements suggesting that at least a moderate intensity level of physical activity is needed to prevent chronic diseases mainly caused by CVD, although higher intensities of physical activity may be more effective in individuals who already meet the recommended level. It is proposed that the total amount of physical activity is more important than the type, frequency, or duration of a single session or intensity of physical activity. Moderate to high amounts of physical activity have been found to protect against prostate, breast, colon and lung cancers, but evidence is inconclusive for reproductive system rectal, pancreatic and other site-specific cancers. An energy expenditure of total leisure-time physical activity of 1000–2500 kcal per week and the intensity of activities performed at least at a moderate level (>4.5 MET) have been found to be sufficient to reduce the risk of prostate, colon and lung cancers. In our study, the intensity of leisure-time physical activity had a strong and independent association with cancer mortality. Men with a mean intensity of leisure-time physical activity of over 5.2 MET had a greatly reduced risk of cancer death.

Physical inactivity during the life span may be a key factor in the initiation of cancer development, although little research on the effect of exercise as a treatment for cancer has been conducted. Mechanisms through which physical activity could protect against cancer are beneficial effects on energy balance and body mass, intestinal transit time, hormonal concentrations (eg, reduced testosterone), prostaglandin levels and antioxidant enzyme activities. It is speculated that endurance exercise could exert a suppressive effect on prostate cancer development by increasing the production of sex hormone and insulin-like growth factor binding globulins and decreasing free testosterone levels, although little is known about the intensity of exercise needed to suppress testosterone levels. The F-series prostaglandins are increased whereas the E2-prostaglandins are

### Table 1 Baseline characteristics of the study population

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean (SD)</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>53.0 (5.2)</td>
<td>42.0–61.1</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>26.9 (3.6)</td>
<td>18.8–48.6</td>
</tr>
<tr>
<td>Waist-to-hip ratio</td>
<td>0.95 (0.06)</td>
<td>0.71–1.73</td>
</tr>
<tr>
<td>Alcohol consumption, g/week</td>
<td>75 (135.4)</td>
<td>0–2853.0</td>
</tr>
<tr>
<td>Smokers, %</td>
<td>30.9</td>
<td></td>
</tr>
<tr>
<td>Cigarette smoking, pack-years*</td>
<td>7.8 (15.9)</td>
<td>0–144</td>
</tr>
</tbody>
</table>

*Pack-years denotes the lifelong exposure to smoking that was estimated as the product of years smoked and the number of cigarettes smoked daily at the time of examination.

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### Table 2 Crude and age-adjusted RR of cancer mortality according to the quartiles of the mean intensity of leisure-time physical activity in men without clinical cancer at baseline

<table>
<thead>
<tr>
<th>Cancer mortality</th>
<th>Mean intensity of LTPA</th>
<th>RR (95% CI)*</th>
<th>p Value</th>
<th>RR (95% CI)†</th>
<th>p Value</th>
<th>No of events</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st quartile, &lt;3.7 MET</td>
<td>1.00 (reference)</td>
<td>1.00 (reference)</td>
<td>53</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2nd quartile, 3.7–4.4 MET</td>
<td>0.98 (0.67 to 1.44)</td>
<td>1.00 (0.68 to 1.47)</td>
<td>0.997</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3rd quartile, 4.5–5.2 MET</td>
<td>0.90 (0.61 to 1.32)</td>
<td>0.95 (0.65 to 1.41)</td>
<td>0.811</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4th quartile, &gt;5.2 MET</td>
<td>0.54 (0.34 to 0.84)</td>
<td>0.58 (0.37 to 0.91)</td>
<td>0.018</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Crude relative risks (RR); †Age-adjusted relative risks. LTPA, leisure-time physical activity; MET, metabolic units (or metabolic equivalents of oxygen consumption).
decreased with exercise, and these physiologic events have been shown to increase gut motility and decrease colonic cell division. Furthermore, other mechanisms by which physical activity has been proposed to prevent cancer are via immunologic mechanisms, effects on insulin regulation and oxygen-free radicals. It is possible that exercise training can improve the non-specific immune systems including monocytes, macrophages and natural killer cells, which are thought to be the primary line of defense against the development of malignancies. Exercise may also enhance the immune defence by affecting T cells, B cells and interleukin levels. Finally, physical exercise has been found to improve the decreased antioxidant defence that occurs normally with aging.12151618 It is possible that exercise training can improve gut motility and decrease colonic cell division and proliferation.21417214 It may decrease gastrointestinal cancer risk by allowing less opportunity for the initiation of colon carcinogenesis and colonic cell division and proliferation.218 In addition, it has been observed that exercise may decrease colon cancer risk through its impact on insulin metabolism.25 Inhibition of the growth factor by increasing the utilisation of free fatty acids and decreasing binding globulins may lead to an increase in colon cancer risk.25 It is thus possible that aerobic exercise alters the metabolism of fat by increasing the utilisation of free fatty acids and decreasing hyperinsulinemia. 

The most important limitation in studies on physical activity and cancer is the lag time between preclinical cancer and cancer death. The presence of undiagnosed cancer for a long period of time may decrease physical activity. On the other hand, it is possible that physical activity even has a protective effect on cancer by prolonging this lag time from preclinical tumour to cancer death. However, the importance of the lag period diminishes with longer follow-up, because any bias will be diluted by the increasing weight of the unbiased cases. We excluded men who died during the first 5 years of follow-up, but the results did not change markedly because of the few deaths occurring within the first 5 years (table 2). Furthermore, heritability in baseline level of physical fitness and its responses to exercise training were also characterised by a significant familial resemblance reflecting genetic and shared familial environmental factors. Therefore, it is possible that one additional reason for the observed association is partly due to the genetic predisposition on physical fitness and trainability of individuals. The promising point is that with the level of exercise capacity that we need for reducing the risk of some diseases, the vast majority of people may not be limited by their heredity. More studies are thus needed to identify groups of individuals such as the sedentary, overweight or obese who might be at high risk of developing cancer and who would be likely to benefit from adopting an exercise programme as well as dietary and behavioural changes. The strengths of the our study include our adjustment for dietary habits, alcohol consumption, smoking and body composition to avoid confounding problems seen in many previous observational studies showing an association between physical activity and cancer risk. Furthermore, our quantitative detailed questionnaire that includes the classification of the intensity of each physical activity enabled us to assess different components of physical activity, eg, energy expenditure, duration, frequency and intensity. The self-classification of the intensity of each physical activity is a reasonably accurate method for evaluating the quantity and intensity of leisure-time physical activity; although a single assessment of physical activity cannot accurately reflect physical exercise patterns throughout an individual’s life.

Our study has some limitations. The first is the fact that several lifestyle factors including physical activity and genetic factors might interact in the aetiology of different cancers, which makes it difficult to show that one factor can...
independently contribute to the risk reduction. Second, our measure of physical activity is based on an individual’s self-report, which may be subject to misclassification. Third, the study subjects are men and we cannot conclude whether our findings would apply to women or other ethnic groups. Fourth, it is possible that the influence of a healthy lifestyle cannot be fully controlled for in the multivariate models. One additional explanation for our current results may be that the intensity of physical activity is a more accurate measure than the duration of physical activity.

In conclusion, this prospective study indicates that the mean intensity of leisure-time physical activity is inversely and independently associated with the risk of premature death from cancer, mainly due to lung and gastrointestinal cancers in men. The intensity of leisure-time physical activity should be at least moderate so that beneficial effect of physical activity for reducing overall cancer mortality can be achieved.

Competing interests: None.

Ethics approval: None.

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