Relationship of Leisure-Time Physical Activity and Mortality

The Finnish Twin Cohort

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Context.—Physical activity and fitness are believed to reduce premature mortality, but whether genetic factors modify this effect is not known.

Objective.—To investigate leisure physical activity and mortality with respect to familial aggregation of health habits during childhood and factors that may enable some individuals to achieve higher levels of fitness.

Design.—Prospective twin cohort study.

Setting.—Finland.

Subjects.—In 1975, at baseline, 7925 healthy men and 7977 healthy women of the Finnish Twin Cohort aged 25 to 64 years who responded to a questionnaire on physical activity habits and known predictors of mortality. Those who reported exercising at least 6 times per month with an intensity corresponding to at least vigorous walking for a mean duration of 30 minutes were classified as conditioning exercisers, those who reported no leisure physical activity were classified as sedentary, and other subjects were classified as occasional exercisers.

Main Outcome Measures.—All-cause mortality and discordant deaths among same-sex twin pairs from 1977 through 1994.

Results.—Among the entire cohort, 1253 subjects died. The hazard ratio for death adjusted for age and sex was 0.71 (95% confidence interval [CI], 0.62-0.81) in occasional exercisers and 0.57 (95% CI, 0.45-0.74) in conditioning exercisers, compared with those who were sedentary (P for trend <.001). Among the twin pairs who were healthy at baseline and discordant for death (n=434), the odds ratio for death was 0.66 (95% CI, 0.46-0.94) in occasional exercisers and 0.44 (95% CI, 0.23-0.83) in conditioning exercisers compared with those who were sedentary (P for trend, .005). The beneficial effect of physical activity remained after controlling for other predictors of mortality.

Conclusion.—Leisure-time physical activity is associated with reduced mortality, even after genetic and other familial factors are taken into account.

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OBSERVATIONAL STUDIES have suggested that high physical activity or fitness reduces premature mortality. However, genetic selection or early childhood experiences may make it easier for some individuals to achieve high levels of physical activity or fitness and favor them with longevity. In the past few years, the importance of familial factors in longevity and mortality has been increasingly recognized. The identification of specific genes that increase susceptibility to major causes of death, such as coronary heart disease and cancer, has stimulated much research. The relative importance of factors over which the individual has little or no control, such as sex, intrauterine and childhood environment, or family history, compared with factors that can be modified, such as diet, smoking, and physical activity, needs further clarification. One method to distinguish between physical activity and genetic and other familial factors is to study family members, in particular, twins who share some or all of the same genes and nearly always the same childhood environment. In this study, we investigated leisure physical activity as a predisposing or preventive factor for premature mortality in the Finnish Twin Cohort.

METHODS

Selection of Subjects

The Finnish Twin Cohort was compiled from the Central Population Registry of Finland in Helsinki via procedures described elsewhere. In brief, the baseline sample comprised all same-sex twin pairs born in Finland before 1958 and with both cotwins alive in 1967. The original cohort also included other subjects who were not twins but who had the same family name and home parish and were born on the same day. The target group for the present study consisted of cohort subjects aged 25 to 64 years on January 1, 1976.

Subjects were mailed a questionnaire in autumn 1975 that included items on physical activity, occupation, body weight, height, alcohol use, smoking, and physician-diagnosed diseases. Among those whose addresses could be identified (93.5% of subjects), the response rate for twins was 87.6% and, for other subjects, 62.8% (as those found to be singletons were no longer sent a reminder). Zygosity (monozygotic, dizygotic, or unclassified) was defined on the basis of questions about strangers confusing the twins in childhood and similarity in childhood appearance, which have been used in other large twin samples. The 2-fold ratio of dizygotic monozygotic twins reflects the high frequency of fraternal twinning in Finland until the 1960s.
We included subjects who supplied complete questionnaire data and were alive on January 1, 1977. Because chronic disease may restrict the ability to exercise, we excluded at baseline subjects with certain chronic diseases. Based on the questionnaire, we excluded subjects who reported physician-diagnosed angina pectoris, myocardial infarction, stroke, or diabetes who had angina pectoris according to standard chest pain history items included in the questionnaire.\textsuperscript{15,16} Using the reliable nationwide hospital discharge register maintained by the National Board of Health,\textsuperscript{17} we also excluded subjects with inpatient admissions for diabetes (International Classification of Diseases, Revision 8\textsuperscript{th} [ICD-8] code 250), cardiovascular disease except for hypertension or venous diseases (ICD-8 codes 390-399 or 410-449), or chronic obstructive pulmonary diseases (ICD-8 codes 490-495) between 1972 and December 31, 1976. In addition, we eliminated all subjects who had been granted reimbursable medication for selected chronic diseases other than hypertension before December 31, 1976, based on data obtained from the Social Insurance Institution of Finland.\textsuperscript{18} We also excluded those who had had incident malignant cancer before 1977 according to the Finnish Cancer Registry.\textsuperscript{19}

**Assessment of Physical Activity**

At baseline we asked subjects about their leisure physical activity, including monthly frequency, mean duration, and mean intensity of physical activity sessions; their opinion of their overall physical activity level; and physical activity during the journey to and from work, using a series of structured questions (questionnaire available from authors).\textsuperscript{20} In the categorical classification of leisure physical activity, those who reported exercising at least 6 times per month for a mean duration of at least 30 minutes and with a mean intensity corresponding to at least vigorous walking to jogging were classified as conditioning exercisers. Those who reported not partaking in leisure physical activity were considered sedentary. As a check, sedentary subjects also had to report in other questions that the intensity of any activities did not exceed walking and that they participated in physical activities less than 6 times a month. Other subjects were classified as occasional exercisers.

We also classified subjects according to the intensity and total volume of leisure physical activity. For intensity, we classified physical activity according to their participation in vigorous leisure physical activities (yes/no) in which the intensity was greater than walking (ie, at least the equivalent of jogging or running), with or without any qualifications on frequency or duration. For volume of activity, we calculated an activity metabolic equivalent (MET) index by assigning a multiple of resting metabolic rate (MET score) to each activity and by calculating the product of intensity × duration × frequency of activity.\textsuperscript{21} In this calculation, we used the following MET values (work metabolic rate divided by resting metabolic rate): 4 (for exercise intensity corresponding to walking), 6 (vigorous walking to jogging), 10 (jogging), and 13 (running). We also used a MET value of 4 for physical activity during the work journey (usually walking). The activity MET index was expressed as the score of leisure MET hours per day. Only baseline physical activity data were used in the mortality analyses. To assess changes in physical activity patterns over time, a questionnaire with identical physical activity items was re-administered in 1981 to the twins, with a response rate of 91%.

**Risk Factor Assessment**

Using the subjects’ self-reports at baseline, we obtained information on other predictors of mortality: occupational group, body mass index (reported weight in kilograms divided by the square of reported height in meters), cigarette smoking, and alcohol consumption. Classification by occupational group was based on job title according to the Central Statistical Office of Finland in Helsinki.\textsuperscript{22} Smoking status was classified from responses to a detailed smoking history,\textsuperscript{23} and the lifelong dose of smoking was calculated as pack-years (equivalent to smoking 1 pack [20 cigarettes] per day for a year). Alcohol use was recorded in beverage-type specific items on frequency and quantity, converted into grams of absolute alcohol per day.\textsuperscript{24}

**Mortality Follow-up and Statistical Analyses**

To further minimize the effect of occult antecedent disease, we allowed a lag period of at least 1 year after physical activity assessment; the all-cause mortality follow-up began on January 1, 1977, and continued to December 31, 1994. During follow-up, causes of death were available from the Cause of Death Bureau files at the Central Statistical Office of Finland. Cause of death was recorded using ICD-8 codes. In 52% of cases, cause of death was clear based on forensic or medical autopsy; in other cases, the cause of death was clear based on clinical history. When studying natural-causes mortality (nonviolent causes: ICD-8 codes 000-649, mortality from external causes (including injuries, suicides, and homicides) was excluded. We first studied all-cause mortality in the entire study cohort by calculating hazard ratios (HRs) during follow-up by physical activity category and adjusting for age, smoking, occupational group, and use of alcohol at baseline using the Cox proportional hazards model.\textsuperscript{25} Our analyses of individuals were based on the statistical assumption of independent observations, which was not strictly true, as 36.8% of subjects were age-matched siblings of other study subjects. However, the correlations between twins for physical activity patterns were only very modest overall. The twin-cotwin intraclass correlation of activity MET index was 0.25 for male twin pairs (0.41 for monozygotic pairs and 0.20 for dizygotic pairs) and 0.20 for female twin pairs (0.38 for monozygotic pairs and 0.13 for dizygotic pairs).

Twin pairs discordant for death were examined to determine whether the mortality of physically active subjects differed from that of their sex- and age-matched sedentary siblings (either monozygotic or dizygotic). This study design does include adjustment for sex and age. These cotwins represent persons who have nearly always shared the same childhood environment and have part or all of their genes in common by descent. We calculated odds ratios (ORs) of death in discordant twin pairs using conditional logistic regression analysis.\textsuperscript{26} The twins were classified as discordant for death if one had died during the follow-up period and the cotwin was alive at the end of it. Zygosity by physical activity interaction was fitted after the main effects to test whether the risk of death by physical activity level differed by degree of genetic relatedness. Under the null hypothesis of no genetic selection, the ORs were not expected to differ. We first studied all-cause mortality, but we also studied twin pairs discordant for deaths from natural causes during follow-up.

All significance tests were 2-tailed. The analyses were performed with the SAS statistical package version 6.11 and the EPICURE program package.\textsuperscript{27}

**RESULTS**

Complete questionnaire data on leisure physical activity and all risk factors were obtained for 19,126 subjects (9400 men and 9726 women), 3224 of whom had chronic diseases (criteria above). Our final study cohort included 15,902 subjects (7925 men and 7977 women) who were presumably healthy at baseline (Table 1).

Among the study subjects, the majority were occasional exercisers; approximately 15% were sedentary, and 55% of men and 38% of women participated in vigorous activity. The Spearman correlation between the activity MET indexes and other risk factors is shown in Table 1.
in 1975 and 1981 was 0.48 for men and 0.41 for women. The means of activity MET index in 1975 and 1981 by leisure physical activity category in 1975. See Table 1 footnote for description of calculation of MET index.

Figure 1.—Leisure activity metabolic equivalent (MET) index as cumulative MET hours per day (mean and SEM) in 1975 and 1985 by leisure physical activity category in 1975. See Table 1 footnote for description of calculation of MET index.

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Of the entire study cohort, 1253 subjects (829 men and 424 women) who were healthy at baseline died during the follow-up period. Natural causes (ie, nonviolent causes) explained the death in 1035 subjects (82.6%, 659 men and 376 women). The most common specific causes of death were coronary heart disease in 319 subjects (237 men and 82 women) and cancer in 362 subjects (202 men and 160 women). No differences in all-cause mortality of individuals were observed by zygosity or twinship. The age-adjusted HR of death in women compared with men was 0.41 (95% confidence interval [CI], 0.36-0.46). After adjustment for age and sex, both occasional and conditioning exercisers had reduced risks of death compared with those who were sedentary (P for trend <.001). This finding persisted after further adjustment for smoking, occupational group, and use of alcohol (P for trend, .002) (Table 2) and was found when analyzed for men and women separately. After adjustment for all covariates, the all-cause mortality HR in those who participated in vigorous activity compared with the others was 0.74 (95% CI, 0.64-0.85; P<.001). After adjustment for all covariates, the decrease of HR of death by increasing MET index quintile was 5% (95% CI, 1%-9%: P for trend, .02).

Among the twin pairs, 434 same-sex twin pairs were discordant for death during follow-up, of which 173 also were discordant for categorical physical activity (Table 3). Occasional and conditioning exercisers had reduced risks of death compared with those who were sedentary among these twin pairs (P for trend,.005) (Table 4). Smoking habits explained some of the risk, but subsequent adjustment for other risk factors (including occupation, alcohol use, hypertension, and body mass index) changed the ORs only minimally (Table 4). The interactions between sex and physical activity category and zygosity and physical activity category were both nonsignificant in the pairwise analyses, thereby revealing that the risk of death declined with increasing physical activity category in both men and women (Figure 2). However, the statistical power to study differences by zygosity was low because, as expected, monozygotic twins had less extreme differences in their physical activity habits. Of the 120 death-discordant monozygotic twin pairs, only 1 time did it happen that 1 twin was sedentary and the cotwin was a conditioning exerciser at baseline; in this case, the conditioning exerciser survived.

In an analysis of the role of leisure physical activity in terms of intensity and total volume among twin pairs, the adjusted OR for mortality among those who participated in vigorous activity compared with the others was 0.79 (95% CI, 0.56-1.10). After adjustment for all covariates among twin pairs discordant for death and activity MET index, the OR of death compared with the lowest MET quintile decreased with increasing MET quintile (P for trend, .04) (Figure 3). There were 340 twin pairs who were healthy at baseline and discordant for death from natural causes during follow-up, among whom occasional exercisers (OR, 0.70; 95% CI, 0.47-1.04) and conditioning exercisers (OR, 0.38; 95% CI, 0.18-0.77) had reduced risks of death compared with sedentary cotwins (P for trend, .01). After adjustment for smoking, occupational group, and alcohol use, the OR was 0.79 (95% CI, 0.51-1.21) for occasional exercisers and 0.52 (95% CI, 0.24-1.13) for conditioning exercisers (P for trend, .04).
Table 2.—Risks of All-Cause Mortality, 1977-1994, Among Subjects of the Finnish Twin Cohort Healthy and Aged 25 to 64 Years in 1975 (N=15,902), According to Leisure Physical Activity Category

<table>
<thead>
<tr>
<th>Activity Category</th>
<th>N</th>
<th>No. of Deaths</th>
<th>Hazard Ratio† (95% CI)</th>
<th>Hazard Ratio‡ (95% CI)</th>
<th>Hazard Ratio§ (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sedentary</td>
<td>2516</td>
<td>302</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Occasional exercisers</td>
<td>1169</td>
<td>869</td>
<td>0.71 (0.62-0.81)</td>
<td>0.76 (0.67-0.87)</td>
<td>0.80 (0.69-0.91)</td>
</tr>
<tr>
<td>Conditioning exercisers</td>
<td>1692</td>
<td>82</td>
<td>0.57 (0.45-0.74)</td>
<td>0.68 (0.53-0.88)</td>
<td>0.76 (0.59-0.98)</td>
</tr>
</tbody>
</table>

P for trend <.001 <.001 .002

*The sedentary group is the reference group. CI denotes confidence interval. Adjustment for baseline body mass index and hypertension changed the hazard ratios only minimally.
†Adjusted for age and sex.
‡Adjusted for age, sex, and smoking (pack-years and smoking status).
§Adjusted for age, sex, smoking, occupational group, and use of alcohol (log-transformed).

Table 3.—Leisure Physical Activity Category in 1975 Among 434 Same-Sex Twin Pairs of the Finnish Twin Cohort Discordant for Death, 1977-1994

<table>
<thead>
<tr>
<th>Activity Category of Deceased Twin</th>
<th>Activity Category of Surviving Twin</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sedentary</td>
</tr>
<tr>
<td>Sedentary</td>
<td>29</td>
</tr>
<tr>
<td>Occasional exerciser</td>
<td>70</td>
</tr>
<tr>
<td>Conditioning exerciser</td>
<td>6</td>
</tr>
</tbody>
</table>

Table 4.—Risks of Death Among 434 Same-Sex Twin Pairs of the Finnish Twin Cohort Discordant for Death, 1977-1994, According to Leisure Physical Activity Category Compared With Sedentary Category in 1975*

<table>
<thead>
<tr>
<th>Activity Category</th>
<th>Nonadjusted Odds Ratio† (95% CI)</th>
<th>Adjusted Odds Ratio‡ (95% CI)</th>
<th>Adjusted Odds Ratio§ (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sedentary</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Occasional exercisers</td>
<td>0.66 (0.46-0.94)</td>
<td>0.70 (0.48-1.01)</td>
<td>0.73 (0.50-1.07)</td>
</tr>
<tr>
<td>Conditioning exercisers</td>
<td>0.44 (0.23-0.83)</td>
<td>0.56 (0.29-1.09)</td>
<td>0.56 (0.29-1.11)</td>
</tr>
</tbody>
</table>

P for trend .005 .04 .06

*The sedentary group is the reference group. CI denotes confidence interval. Adjustment for baseline body mass index and hypertension changed the odds ratios only minimally.
†Adjusted for smoking (pack-years and current smoking habit).
‡Adjusted for smoking, occupational group, and use of alcohol (log-transformed).

COMMENT

The results from the entire study cohort are consistent with earlier study findings1-13 that there is an inverse association between baseline physical activity and future premature mortality. In an earlier study of Danish twins born between 1870 and 1900, Herskind et al30 reported that longevity was moderately heritable. In our study, to evaluate the hypothesis that genetic or other familial selection explains the association between leisure physical activity and mortality, we studied baseline physical activity in twin pairs discordant for death during follow-up. Comparison of the physically active cotwins with their less active siblings produced further evidence that familial factors do not explain the mortality differences by physical activity found in individual-based analyses. In recent studies of the effects of longitudinal changes in physical activity and fitness, Paffenbarger et al31 found that increased physical activity and Blair et al32 that increased physical fitness were associated with reduced mortality. These findings support our conclusion.

We were unable to identify significant differences in mortality between monozygotic and dizygotic pairs by physical activity, but the relatively small number of discordant monozygotic pairs in the analysis reduced the power to detect possible differences by zygosity. The finding that leisure physical activity habits differ less among monozygotic than dizygotic twin pairs is in accordance with earlier findings.31 Because monozygotic twins usually have both similar genetic background and rather similar lifestyle habits, end points more sensitive than mortality should be studied to explore the effects of physical activity among monozygotic twin pairs. In choosing discordance in deaths as the main outcome of this study, our primary aim was not to study the differences by zygosity but rather to compare mortality in the population with mortality differences in siblings.

The categorization of baseline physical activity was based on our questionnaire items concerning frequency, intensity, and duration of exercise. All these factors are to some extent related to improved maximal oxygen uptake and prevention of diseases.32,33 Our analyses also revealed that both participation in vigorous activity and activity volume (MET index) contributed to the reduction in mortality. Despite similar relative risks, the statistical significance was reduced because of the lower number of observations in pairwise analyses compared with individual-based analyses. The dyspnea score (a hierarchical 5-category assessment of the degree of breathlessness associated with different levels of daily physical activity),17 which we found to be significantly associated (P<.001) with the leisure physical activity MET index among both sexes, was further evidence of the validity of the physical activity questions in our baseline questionnaire.

Although individuals who exercise also may differ in other lifestyle habits, the beneficial effect of physical activity remained after controlling for other predictors of mortality. Some of these covari-

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ates (eg, hypertension, smoking) have a role in the causal pathway between physical activity and premature mortality. Further adjustment for baseline body mass index and hypertension changed the relative risks only minimally.

Despite sex differences in mortality rates, it has been suspected that sedentary habits are probably as hazardous for women as for men and that inconsistent results in the literature regarding physical inactivity and morbidity in men probably are the result of misclassification because of inadequate assessment measures.\(^{14,15}\) In our study, the prevalence of physical inactivity was similar for men and women, but the statistical power for analyzing the associations among women was lower because of their smaller number of deaths. Even though the mean leisure physical activity MET index for those classified as conditioning exercisers was similar for both sexes, vigorous physical activity in 1975 was less common in women, which further weakened the possibility of studying the effects of physical activity in our female subjects. However, our findings from the pairwise analyses of the beneficial effect of high physical activity on mortality were similar for men and women.

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References