Leisure Time Physical Activity and Disease-Specific Mortality Among Men With Chronic Bronchitis: Evidence From the Whitehall Study

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Objectives. This study examined the association between leisure time physical activity and cause-specific mortality among male Whitehall Study participants with chronic bronchitis.

Methods. Rate ratios were calculated for 4 mortality outcomes, according to level of activity and baseline bronchitis status, in a 25-year follow-up of 6479 men.

Results. After multiple adjustment for potential confounding or mediating variables, activity was inversely related to all-cause, cardiovascular, coronary heart disease, and noncardiovascular mortality among men free of chronic bronchitis. Among men with bronchitis, weak, nonsignificant positive associations were observed between activity and these outcomes, with the exception of noncardiovascular mortality.

Conclusions. The suggestion of a positive activity–mortality association among individuals with chronic bronchitis—albeit weak and nonsignificant—requires further investigation. (*Am J Public Health.* 2003;93:817–821)

The frequently observed inverse association between leisure time physical activity and the incidence of coronary heart disease (CHD) in cohorts of healthy individuals[1,2] has been attributed, in part, to the normalizing effect of activity on a number of CHD risk factors, including body weight and blood pressure.[3] Similar acute beneficial effects of physical activity among individuals with chronic diseases, such as type 2 diabetes[4,5] and ischemia,[6,7] have been revealed and may likewise partially explain the cardioprotective impact of activity observed in long-term follow-ups of these groups.[8-17]

There is also evidence suggesting that, among individuals with pulmonary diseases such as bronchitis, exercise programs have a favorable effect on cardiorespiratory fitness, quality of life, and dyspnea.[18] The trials on which these findings are based are characterized by small sample sizes, brief follow-up intervals, and multifaceted interventions, which make it difficult to isolate exercise-attributable effects. However, given this apparent short-term beneficial effect of activity, it is plausible that, in keeping with observations involving other subgroups, activity may be associated with reduced longer-term CHD risk in individuals with bronchitis.

In the present study, we tested this hypothesis by following a group of British male civil servants who self-reported their chronic bronchitis status and leisure time physical activity patterns on their entry into the Whitehall Study. We compared associations between leisure time physical activity and mortality rates in men with and without bronchitis, allowing us to explore the possibility that this condition may modify the nature of these relationships. We are unaware of any other study reporting on these associations in this group.

METHODS

Study Participants

The Whitehall Study participants were London-based male civil servants who were aged 40 to 64 years when they were examined at study entry between September 1967 and January 1970. Data were collected for 18 403 men, representing a 74% response rate. Participants completed a study questionnaire and underwent a medical examination, both of which have been described in detail elsewhere.[19] In brief, the questionnaire included items focusing on civil service employment grade (a marker of socioeconomic position),[20] smoking habits,[21] intermittent claudication,[22,23] angina,[22,24] chronic bronchitis,[25] and physical activity.[26]

A calibrated sphygmomanometer (London School of Hygiene)[27] was used to record participants' blood pressure level via a single reading taken from the left arm. Standardized protocols were used to determine forced expiratory volume in 1 second,[28] presence of ischemia,[29] fasting plasma cholesterol levels,[30] fasting and 2-hour blood glucose levels,[26] height,[31] and weight.[32]

Assessment of Leisure Time Physical Activity

During the course of the study the baseline questionnaire was modified, and the leisure time physical activity data reported here were based on a question administered to 6702 of the study participants: "Do you have any hobbies or sports?" Individuals responding positively to this question were asked to specify the nature of their hobbies or sports. On this basis, respondents were classified as being typically inactive, moderately active, or active during leisure.[26] The active group included men who engaged in vigorous sports such as swimming, cycling, and athletics; the moderately active group comprised men who participated in energetic hobbies such as gardening, home maintenance, and woodworking; and the inactive group was made up of men who reported no physical exertion.

In a previous article, we reported on the association of this activity index with the mortality experiences of the Whitehall participants[33] and the experiences of a subset of the men with type 2 diabetes or impaired glucose tolerance.[9] We have also examined the activity–mortality relation among the study participants who were administered

the unmodified version of the questionnaire, which included an item regarding active travel to work.[34] Because the expected relationships between this marker of physical exertion and cause-specific mortality were not as strong as anticipated, and because no associations with known physical activity correlates were apparent, we were unconvinced of the validity of these data. We therefore elected a priori not to examine further the relation of travel activity to mortality among men with chronic bronchitis.

Assessment of Chronic Bronchitis Status

Two questions focused on chronic bronchitis: "Do you bring up any phlegm from your chest first thing in the morning in the winter?" and "Do you get short of breath walking with people of your own age on level ground?"[25] Men were classified as having chronic bronchitis if they responded positively to both questions; all other participants were categorized as free of this condition.

Ascertainment of Mortality

The records of 6648 men (99.2% of the study participants) were traced and flagged at the National Health Service Central Registry through January 1995. Death certificates were coded according to the eighth revision of the *International Classification of Diseases* (*ICD-8*). Cause-specific mortality was classified as attributable to cardiovascular disease (CVD; *ICD-8* codes 390–459), CHD (*ICD-8* codes 410–414), or noncardiovascular disease (deaths excluding *ICD-8* codes 390–459).

Data Analyses

Cox's proportional hazard regression model[35] was used to calculate rate ratios and accompanying confidence intervals for the association between physical activity and each mortality outcome. These models were initially adjusted for age and then for other potential confounding factors (e.g., employment grade, smoking). To address the issue of reverse causality—that is, physical inactivity is attributable to preexisting disease, and this factor is responsible for higher rates of mortality in the inactive group—we created a disease-at-entry variable for participants reporting the presence of 1 of the following: ischemia, intermittent claudication, unexplained weight loss in the preceding year, or physician-diagnosed heart problems or high blood pressure.

Because we were interested in identifying the independent effect of physical activity, we also adjusted for several mediating variables (e.g., blood pressure, body mass index) in our analyses. Models fitted with a Leisure Activity × Follow-Up Time interaction term confirmed that the proportional hazards assumption was not violated. To determine whether the linear trend across activity levels was the same for respondents with and without bronchitis, we used likelihood ratio statistics to compute tests for interactions that compared the goodness of fit of models that included and did not include interaction terms.

RESULTS

Our results were based on 6479 men with no missing data. During 25 years of follow-up, 140 (75.3%) of the 186 men identified as having chronic bronchitis at baseline died, whereas there were 2660 deaths (42.3%) among the 6293 men who were free of this condition. Associations between physical activity and the mortality end points, according to chronic bronchitis status at study entry, are presented in Table 1. In age-adjusted analyses, leisure time physical activity was inversely related to all mortality end points among men who were bronchitis-free when they entered the study (trend $P \leq .001$); in contrast, weak, nonsignificant positive associations were observed among the group of men with bronchitis. That the nature of the physical activity–mortality association differed markedly according to bronchitis status in this age-adjusted analysis was confirmed by the results of the tests assessing interactions involving all-cause ($P=.003$), CVD ($P=.01$), CHD ($P=.02$), and non-CVD ($P=.08$) mortality.

After adjustment for potentially confounding or mediating variables, the same pattern of association as that seen for the age-adjusted analysis was evident for all end-points with the exception of non-CVD mortality, in which the suggestion of a positive association with physical activity among men with bronchitis was no longer present. In this fully adjusted analysis, tests for interactions confirmed effect modification according to bronchitis status for all-cause ($P=.04$), CVD ($P=.08$), and CHD ($P=.09$) mortality in relation to physical activity.

In our analyses, we adjusted for the potential confounding effect of diagnosed disease; however, among the group of men without bronchitis, undiagnosed disease may be an alternative explanation for the inverse association observed between physical activity and mortality and, hence, the significant interaction statistics. To explore this possibility, we excluded men who died during the first 5 years of follow-up from our analyses, reasoning that most deaths due to undiagnosed disease at baseline would have occurred within this period. Whereas the strength of the association of physical activity with each mortality end point was essentially unchanged in a fully adjusted analysis involving men without bronchitis, the positive association observed among men with this condition was strengthened further, as were the interaction statistics (all-cause mortality, $P=.02$; CVD mortality, $P=.04$; CHD mortality, $P=.03$.

After baseline characteristics had been stratified according to chronic bronchitis status, there were noticeable differences in the prevalence of cigarette consumption and ischemia (in both cases, the differences were significant at $P<.001$), such that the highest prevalence of each was observed among men with this condition. We therefore conducted further analyses of the study sample to determine whether, rather than bronchitis modifying the activity–mortality relation, this disorder was acting as a proxy for these other mortality risk factors. When we assessed the relation of leisure time physical activity to all-cause and CHD mortality in a fully adjusted analysis, we found no difference in the association after we stratified the data according to smoking status (nonsmokers vs smokers; interaction P values were .41 for all-cause mortality and .43 for CHD mortality) and ischemia status (electrocardiogram evidence vs no evidence; P values were .88 for all-cause mortality and .27 for CHD mortality).

TABLE 1—Rate Ratios for the Association of Leisure Time Physical Activity With Selected Mortality Endpoints, by Chronic Bronchitis Status at Study Entry

		All Causes			Cardiovascular Disease			Coronary Heart Disease			Noncardiovascular Disease		
	No. of Participants[a]	No. of Deaths	Age-Adjusted Rate Ratio (95% CI)	Multiply-Adjusted[b] Rate Ratio (95% CI)	No. of Deaths	Age-Adjusted Rate Ratio (95% CI)	Multiply-Adjusted Rate Ratio (95% CI)	No. of Deaths	Age-Adjusted Rate Ratio (95% CI)	Multiply-Adjusted Rate Ratio (95% CI)	No. of Deaths	Age-Adjusted Rate Ratio (95% CI)	Multiply-Adjusted Rate Ratio (95% CI)
No chronic bronchitis													
Total	6293	2660	…	…	1350	…	…	889	…	…	1306	…	…
Leisure activity status													
Inactive	2149	1027	1.42 (1.3, 1.6)	1.21 (1.1, 1.3)	522	1.39 (1.2, 1.6)	1.22 (1.0, 1.4)	342	1.32 (1.1, 1.6)	1.15 (1.0, 1.4)	502	1.45 (1.3, 1.7)	1.18 (1.0, 1.4)
Moderate	2617	1085	1.12 (1.0, 1.2)	1.06 (1.0, 1.2)	544	1.08 (0.9, 1.2)	1.03 (0.9, 1.2)	351	1.01 (0.8, 1.2)	0.96 (0.8, 1.1)	541	1.16 (1.0, 1.3)	1.10 (0.9, 1.3)
Active	1527	548	1.0	1.0	284	1.0	1.0	196	1.0	1.0	263	1.0	1.0
P value for linear trend	…	…	.0001	.0003	…	.0001	.005	…	.0006	.07	…	.001	.03
Chronic bronchitis													
Total	186	140	…	…	64	…	…	48	…	…	76	…	…
Leisure activity status													
Inactive	119	87	0.60 (0.3, 1.2)	0.70 (0.3, 1.4)	37	0.54 (0.2, 1.6)	0.51 (0.2, 1.5)	26	0.51 (0.2, 1.7)	0.57 (0.2, 2.0)	50	0.65 (0.3, 1.7)	0.93 (0.3, 2.5)
Moderate	57	44	0.65 (0.3, 1.3)	0.73 (0.3, 1.6)	23	0.70 (0.2, 2.1)	0.52 (0.2, 1.6)	19	0.77 (0.2, 2.6)	0.72 (0.2, 2.7)	21	0.60 (0.2, 1.6)	0.91 (0.3, 2.6)
Active	19	9	1.0	1.0	4	1.0	1.0	3	1.0	1.0	5	1.0	1.0
P value for linear trend	…	…	.26	.45	…	.18	.45	…	.12	.31	…	.76	.94
P value for interaction[c]	…	…	.003	.04	…	.01	.08	…	.02	.09	…	.08	.61

Note. CI = confidence interval.
[a]For analyses featuring all-cause mortality as the endpoint of interest. In the cause-specific mortality analyses, 4 men in the no-chronic-bronchitis group with unknown information on cause of death were excluded.
[b]Adjusted for age, employment grade, cholesterol level, systolic blood pressure level, smoking status, body mass index, forced expiratory volume in 1 second, and presence of disease at study entry.
[c]*P* value for interaction tests to determinine whether the linear trend across activity levels was the same in the chronic-bronchitis and no-chronic-bronchitis groups.

DISCUSSION

The main findings of this study were an inverse relation between leisure time physical activity and all-cause, CVD, and CHD mortality among men free of chronic bronchitis and the suggestion of a weak positive association among men with bronchitis. Although the positive relations among the study respondents with bronchitis were not statistically significant at conventional levels, they were nonetheless markedly different from the relations observed among respondents free of the condition, as evidenced by the significance tests for interaction.

A number of alternative explanations for the apparent modifying effect of chronic bronchitis on the physical activity–mortality relation exist. These explanations include confounding, reverse causality, bronchitis as a proxy for other mortality risk factors; lack of validity of the physical activity data; measurement error; and chance.

Although there was some degree of attenuation of risk after adjustment for potentially confounding or mediating variables, most of the associations held, as they did when we excluded men who had died during the first 5 years of follow-up so as to explore the effect of undetected disease at study entry (i.e., reverse causality). In addition, when the baseline data were stratified according to bronchitis status, there were noticeable differences in prevalence of cigarette consumption and ischemia, with the least favorable levels seen in the bronchitis group. It is plausible that one of these characteristics, rather than bronchitis itself, was modifying the activity–mortality relationships. However, after stratification by both of these risk factors, there was no evidence that they modified the relation of physical activity to mortality experience.

The Whitehall Study assessed leisure time physical activity in the late 1960s, and thus the qualitative index used is simplistic by contemporary standards. However, these data have been shown to be inversely associated with all-cause and CHD mortality,[33] as well as mortality due to stroke,[36] among disease-free men included in the present analyses. Because these are frequently observed associations,[1,2,37,38] the implication is that the present data have a degree of predictive validity. Leisure time physical activity data also were related to age, socioeconomic status and resting heart rate (a physiological consequence of aerobic conditioning) in the expected directions,[39–41] suggesting a degree of concurrent validity. Accordingly, it is unlikely that the rather crude method used in this study to as-

sess physical activity could explain the suggestion of a positive association of activity with CHD among men with chronic bronchitis.

The present study almost certainly involved a degree of misclassification of exposure status, collateral data, and our effect modifier (bronchitis) over the follow-up period. Levels of leisure time physical activity and some of the covariate data (e.g., data on body mass index and smoking status) would have fluctuated over time, as evidenced by the low tracking coefficients reported in similar studies.[42,43] Furthermore, some of the men who were bronchitis-free at study entry would, in time, have undoubtedly gone on to develop the condition. It is likely, however, that these sources of misclassification would have been random, resulting in an underestimation of the true activity–mortality association.[44] Finally, in all of our analyses, the number of active men with bronchitis was low; the result was low statistical power, as evidenced by wide confidence intervals. Thus, the apparent deleterious effect of physical activity observed in the present study among men with chronic bronchitis is most likely a chance finding.

Although the relationship of physical activity to cause-specific mortality has been examined among individuals with preexisting disease such as type 2 diabetes, hypercholesterolemia, and ischemia, our study is the first, to our knowledge, to assess this relationship among persons with bronchitis. Studies involving people with type 2 diabetes or impaired glucose tolerance,[8,9] and most[14-17] but not all[45] studies featuring men with ischemia, have shown physical activity to be cardioprotective, whereas studies involving people with increased cholesterol levels have revealed no apparent association.[46] It is noteworthy that stratifying the physical activity–mortality association according to the condition of interest, as we did in the present study, is uncommon; most investigators prefer to focus exclusively on the disease under examination.[12,15]

In conclusion, leisure time physical activity was inversely related to all-cause, CVD, and CHD mortality among male government employees without chronic bronchitis, whereas there was a suggestion of a weak positive association in the group of men with bronchitis; however, the latter association did not attain statistical significance. Given the small number of cases examined in the present study, which resulted in a low level of statistical power, the positive relationship between physical activity and mortality among individuals with chronic bronchitis should be examined in other data sets. ■

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Contributors

G.D. Batty and G. Davey Smith generated the study hypotheses. M.J. Shipley conducted the data analyses and contributed to several revisions of the article. M.G. Marmot and G. Davey Smith also contributed to revisions of the article.

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Human Participant Protection

At the time the Whitehall Study was conducted, there was no requirement to obtain ethical approval for scientific studies of humans.

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