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Physical Activity and the Risk of Community-Acquired Pneumonia in US Women

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Abstract

Background—Exercise bolsters the immune system, and can prevent various infections in certain populations. However, limited data exist regarding the role of physical activity and the risk of community-acquired pneumonia.

Methods—We prospectively examined, during a 12-year period, the association between physical activity and the risk of community-acquired pneumonia among 83,165 women in Nurses' Health Study (NHS) II who were between the ages of 27 and 44 years in 1991. We excluded women who had pneumonia prior to 1991, and those with a history of cancer, cardiovascular disease or asthma. Biennial self-administered mailed questionnaires were used to determine activity level. Cases of pneumonia required a diagnosis by a physician and confirmation with a chest radiograph.

Results—We identified 1265 new cases of community-acquired pneumonia during 965,168 person-years of follow up. After adjusting for age, women in the highest quintile of physical activity were less likely to develop pneumonia than women in the lowest quintile (relative risk [RR] =0.72; 95% confidence interval [CI], 0.60–0.86; p for trend < 0.001). However, the association was attenuated and only marginally significant after further adjusting for body-mass index (BMI), smoking and alcohol use (RR=0.84; 95% CI, 0.70–1.01; p for trend=0.06). Women in the highest quintile of walking were less likely to develop pneumonia compared to women who walked the least (multivariate adjusted RR=0.82; 95% CI, 0.69–0.98); however, the trend across quintiles was not significant (p for trend=0.25).

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Conclusions—Higher physical activity does not substantially reduce pneumonia risk in well-nourished women.

Introduction

Pneumonia and influenza combined rank as the seventh leading cause of death in the United States, accounting for over 65,000 deaths annually.¹ Additionally, pneumonia is a significant cause of outpatient visits and hospitalizations, particularly among individuals aged 65 years or older.^{2, 3} Despite advances in pharmacologic therapy for individuals with community-acquired pneumonia, hospitalization rates have increased over the past 15 years, and mortality rates have been rising.^{1, 2}

Physical inactivity along with poor diet account for over 15% of all deaths in the United States, and the rapid increase in the prevalence of overweight suggests that this figure is likely to increase over the next few years.¹ Exercise can bolster many components of the immune system, including antibody titers, T cell function, and macrophage response, all of which are integral to lung defenses in providing protection against pneumonia.⁴

Despite evidence that exercise improves immune function, few studies have investigated the role of physical activity on the development of infection in general, and pneumonia specifically. A cohort study conducted in three geographically distinct communities found an increased risk of pneumonia mortality among individuals with limitations in activities of daily living and cognitive impairment among both men and women.⁵ Inability to walk a half mile, climb stairs, or perform heavy housework was associated with increased risk of pneumonia mortality for women but not for men.⁵ Physical activity was inversely associated with pneumonia risk in a large prospective cohort of women; however, this risk was attenuated after further adjusting for body-mass index (BMI).⁶ The study had only 300 cases of pneumonia, and individuals were followed for only four years.

There are limited data regarding the role of physical activity and the risk of community-acquired pneumonia. We extend and expand upon prior studies by prospectively investigating the role of physical activity in the development of community-acquired pneumonia among a large cohort of well-nourished U.S. women.

Methods and Materials

Study Population

The Nurses' Health Study (NHS) II began in 1989 when 116,671 US female registered nurses aged 25 to 42 years returned a mailed questionnaire. Details of the study design and data collection used in the NHS II have been previously published.⁷ At the time of enrollment, participants provided a detailed medical history including diagnosed diseases, medications, and information on lifestyle factors including smoking, physical activity, and alcohol use. Information on dietary and supplemental vitamin intake was first ascertained in 1991 and updated every 4 years using a semi-quantitative food frequency questionnaire. Women were excluded from the analysis if they had incomplete questionnaires (12,360), had pneumonia prior to the baseline in 1991 (14,156), died prior to 1991 (37), or if they had a history of conditions known to affect pneumonia risk (6,953), including cancer, cardiovascular disease (myocardial infarction, stroke, or arterial surgery), or asthma diagnosed either prior to or during the study period.

Identification of Cases of Pneumonia

We considered a case to be self-reported physician-diagnosed pneumonia confirmed by chest radiography, and included only the first documented event of community-acquired pneumonia

occurring between June 1, 1991, and May 31, 2003. Women who reported pneumonia were sent a supplementary questionnaire asking whether the pneumonia diagnosis had been confirmed by x-ray. To examine the validity of self-reported pneumonia during the first two years of follow-up, a study physician blinded to exposure status examined the medical records of 76 women who had reported pneumonia. A radiology report of a pulmonary infiltrate confirmed the presence of pneumonia in 82% of the cases.⁶ After the first two years of follow-up, medical records were obtained from all women who reported physician diagnosed pneumonia that was confirmed with a chest radiograph. We reviewed medical records from a sample of 99 confirmed cases and found only one that was potentially hospital-acquired. Therefore, we considered all the cases to have community-acquired pneumonia.

Ascertainment of Physical Activity

Women were first asked about physical activity in 1989, and information was updated every two years. Women indicated the average time spent per week at various types of physical activity, such as walking, jogging, bicycling, and swimming, and also time spent performing leisure activity such as watching TV, driving, and sitting at home. We calculated a metabolic equivalents per hour score for recreational or leisure-time physical activity. One metabolic equivalent, the energy expended by sitting quietly, is equivalent to 3.5 milliliters of oxygen uptake per kilogram of body weight per minute, or to 1 kcal/kg of body weight per hour. For example, running (12 metabolic equivalents) requires 12 times the energy as sitting quietly. The metabolic equivalents per hour score was calculated for each participant by multiplying the reported average time spent at each activity per week by the typical energy expenditure requirements for the activity, expressed in metabolic equivalents per hour.^{6, 8} The validity of self-reported physical activity in this cohort has been described in detail elsewhere.⁹ Recall of physical activity within the previous year performed well when compared with previous week activity recalls ($r = 0.79$) in this cohort.^{9, 10}

Assessment of Other Covariates

Covariates considered in the multivariate model included age, body mass index, cigarette smoking and alcohol intake. BMI was calculated as weight in kilograms divided by height in meters squared using the reported height of the women at the start of the study and updated weight. Participants reported on the biennial questionnaire if they currently smoked and the number of cigarettes per day. Alcohol intake was assessed by the food frequency questionnaire.

Data Analysis

Person-time of follow-up was calculated as the time between the return of the 1991 questionnaire until the first report of community-acquired pneumonia, death, or the end of the study period (May 31, 2003). We first examined age-adjusted models for the association between physical activity and the risk of pneumonia. Cox proportional hazards multivariate models with updating of exposure variables were used to estimate multivariate relative risks (RR). The multivariate models adjusted for age, body mass index (<21 kg/m², 21–22.9, 23–24.9, 25–29.9, 30+), alcohol intake (0 gm/day, 0.1–5 gm, 5–9.9 gm, 10–14.9 gm, 15–29.9 gm, 30+ gm), and cigarette smoking (never, past, current smoker of 1–14 cigarettes per day, 15–24 per day, or 25+ per day). The adjusted relative risk of pneumonia was calculated per quintile of physical activity, with the referent group being the lowest quintile.

In additional analyses, we assessed the association between walking and pneumonia risk. We also assessed the relation between physical activity and pneumonia risk, stratifying by age (< 40 and ≥ 40 years of age).

We also assessed the relation between vigorous physical activity (running, jogging, biking, swimming, tennis, racquetball, squash, calisthenics, heavy outdoor work, and weight training)

and pneumonia risk. Vigorous physical activity was categorized into 5 groups, including a category of none, followed by quartiles.¹¹ Lastly, we assessed the relation between running and jogging (none, ≤ 1 hour per week, 1.0–1.9 hours per week, ≥ 2.0 hours per week) and pneumonia risk.¹²

We used the Mantel extension test to calculate tests for trends across quintiles of intake using the respective median values.¹³ SAS statistical software (version 9.1; SAS Institute; Cary, NC) was used for all analyses. Two-sided p-values <0.05 were considered significant.

This study was approved by the Human Subjects Committee of the Harvard School of Public Health.

Results

During 12 years of follow up (965,168 person-years), there were 1265 new cases of non-fatal community acquired pneumonia. At baseline in 1991, women who were more active were leaner, less likely to be current smokers, and consumed slightly more alcohol than women who were less active (Table 1).

After adjusting for age, women in the highest quintile of physical activity were 28% less likely to develop pneumonia than women in the lowest quintile (Table 2). This association was attenuated but remained significant after adjusting for BMI (RR=0.83; 95% confidence interval [CI], 0.69–1.00; p for trend=0.049); however, the association was no longer significant after further adjusting for smoking and alcohol use (RR=0.84; 95% CI, 0.70–1.01; p for trend=0.06).

Women in the highest quintile of metabolic equivalents per hour from walking were 18% less likely to develop community acquired pneumonia compared to women who walked the least, however, the trend across quintiles was not significant (p for trend=0.25). (Table 3)

Among women < 40 years of age, we observed an inverse relation between physical activity and pneumonia risk. After adjusting for age, women in the highest quintile of physical activity had a 32% lower risk of developing pneumonia (RR=0.68; 95% CI, 0.52–0.90; p for trend=0.004). This association was attenuated after multivariate adjustment (RR=0.78; 95% CI, 0.59–1.03; p for trend=0.06). Among women ≥ 40 years of age, we again observed an inverse relation between physical activity and pneumonia risk (age adjusted RR=0.74; 95% CI, 0.59–0.93; p for trend=0.02), which was no longer significant after adjusting for BMI (RR=0.88; 95% CI, 0.70–1.11; p for trend=0.34).

Women in the upper quartile of vigorous physical activity did not have a significantly lower risk of pneumonia than women who reported no vigorous physical activity (adjusted RR=0.86; 95% CI, 0.71–1.04; p for trend=0.09). Lastly, women who reported running or jogging ≥ 2.0 hours per week had a lower risk of pneumonia than women who spent no time running or jogging (adjusted RR=0.46; 95% CI, 0.29–0.72; p for trend=0.006). However, only 20 cases of pneumonia were reported in this group of women.

Discussion

We found that physical activity was not consistently associated with community-acquired pneumonia in well-nourished, young and middle-aged adult US women. Women who exercised more frequently, as well as those who walked more were less likely to develop pneumonia; however, these results were not significant after adjusting for BMI, smoking, and alcohol use. We observed that women who walked the most had an 18% lower risk of pneumonia compared to women who walked the least.

Prior studies have shown that immune function improves with exercise,^{14–16} and that exercise may slow an age related decline in immune function.⁴ An improvement in natural killer cell activity was observed in older women who participated in chronic resistance training compared to controls.¹⁷ Natural killer cell activity declines with age; however, this decline may be attenuated in individuals who exercise on a regular basis.¹⁸ Physical fitness improves the immune response to antigens in vivo. Another study demonstrated that adults who regularly performed aerobic exercise had greater amounts of anti-influenza IgG and IgM two weeks post immunization when compared to less active individuals.^{4, 19}

A population based study in China found pneumonia and influenza combined to be the fourth leading cause of mortality, accounting for 3.7% of all deaths in women.²⁰ In the same cohort, physical inactivity was associated with an increased risk of mortality (RR=1.20, 95% CI, 1.16–1.24) with a population attributable risk of death of 6.8%. An early prospective study among longshoremen in San Francisco found that lower physical activity was associated with an increase in all-cause mortality (RR=1.46), and an increased, but non-significant, risk of death due to pneumonia specifically (RR=3.86).²¹ In a study of male smokers 50–69 years of age, compared with those with light leisure physical activity, moderate and heavy activity were not associated with pneumonia risk.²² This study examined the first occurrence of hospital-treated pneumonia during a 3-year follow-up period as part of the Alpha-Tocopherol, Beta-Carotene Cancer Prevention (ATBC) Study.

Another prospective study investigating the relation between lifestyle factors and pneumonia risk found that physical activity was associated with a decreased risk of community-acquired pneumonia among women (RR comparing extreme quintiles = 0.66, 95% CI, 0.46–0.95) but not in men (RR comparing extreme quintiles = 0.96, 95% CI, 0.67–1.38).⁶ Physical activity was calculated for each participant by multiplying the reported average time spent for recreational or leisure-time physical activity per week by the typical energy expenditure requirements for the activity. This study included 300 cases of pneumonia in NHS II, during four years of follow-up.⁶ In the current study, we extended the follow-up and included nearly 1000 more cases and the results were attenuated.

We observed that women who reported running or jogging ≥ 2 hours per week had a significantly lower risk of pneumonia compared to women who spent no time running or jogging. While these results are interesting, there were only 20 cases of pneumonia in this active group of women.

Limitations of the study should be noted. Physical activity was self reported but has been demonstrated to be valid and the information was collected prospectively. Misclassification of the diagnosis of community-acquired pneumonia is certainly possible, however we included only participants with physician diagnosed and radiographically confirmed pneumonia. We were unable to distinguish between bacterial and viral pneumonia, but even in the best of circumstances the microbiological etiology of pneumonia is difficult to establish.^{23–25} Additionally, because some of the nurses were working in a hospital setting, it is possible that more than 1% of the cases may have been “hospital-acquired pneumonia”. We could not account for the impact of influenza and/or pneumococcal immunization, as we did not collect that information for a majority of the study period. Lastly, our results may not be generalizable to older women or men.

In conclusion, physical activity does not substantially alter community-acquired pneumonia risk in healthy young and middle-aged women.

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Dr Neuman had full access to the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Drs Neuman, Willett, and Curhan participated in all aspects of the study, including: study concept and design, acquisition of data, analysis and interpretation of data, drafting of the manuscript, statistical analysis, and critical revision of the manuscript for important intellectual content.

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Table 1
Baseline characteristics of women according to quintile of physical activity

Characteristic*	Quintile of Physical Activity (MET-hr/wk) †				
	1	2	3	4	5
Median MET-hr/wk	1.9	6.3	12.5	22.7	47.9
Range of MET-hr/wk	0.2–3.8	3.9–9.0	9.1–16.9	17.0–31.8	31.9–591
Walking MET-hr/wk (median)	0.6	2.7	3.8	5.0	10.0
Age (years)	37.0	36.0	36.0	36.0	35.0
Body Mass Index (kg/m ²)	25.8	25.0	24.4	24.0	23.3
Alcohol Intake (g/day)	2.6	2.8	3.0	3.4	3.8
Current Smoker (%)	13.9	12.9	11.2	10.2	11.1

* All values (except age) were standardized to the age distribution of the cohort. Values for age, body mass index and alcohol intake are means.

† MET denotes metabolic equivalent. The MET-hours represent the average amount of time per week spent in each of eight activities multiplied by the MET value of each activity. One MET is defined as the energy expended in sitting quietly, which is equivalent to an oxygen uptake of 3.5 ml per kilogram of body weight per minute for an average adult.

Table 2

Relative risk of community-acquired pneumonia by quintile of physical activity.

	Quintile of physical activity (MET-hr/wk)					P Value for Trend
	1	2	3	4	5	
No. of cases	294	276	237	239	219	
Person -years	186,701	188,367	196,616	195,765	197,719	
Age adjusted RR ¹	1.00	0.94	0.77	0.79	0.72	< 0.001
(95% CI)	Referent	(0.80–1.11)	(0.65–0.92)	(0.66–0.94)	(0.60–0.86)	
Multivariate RR ²	1.00	0.97	0.85	0.89	0.84	0.06
(95% CI)	Referent	(0.84–1.17)	(0.71–1.00)	(0.75–1.06)	(0.70–1.01)	

¹RR denotes Relative Risk (95% confidence interval [CI])²Adjusted for age, BMI, smoking, and alcohol use

Table 3

Relative risk of community-acquired pneumonia by quintile of walking.

	Quintile of physical activity spent walking (MET-hr/wk)					P Value for Trend
	1	2	3	4	5	
Median walking	0.1	2.0	3.0	5.6	11.2	
MET-hr/wk (range)	(0–0.6)	(0.7–2.5)	(2.7–3.8)	(4.0–7.5)	(10.0–56.2)	
No. of cases	281	274	268	191	251	
Person –years	190,540	183,491	207,053	154,079	228,005	
Age adjusted RR ¹	1.00	1.00	0.86	0.85	0.75	0.04
(95% CI)	Referent	(0.85–1.18)	(0.73–1.02)	(0.71–1.02)	(0.63–0.89)	
Multivariate RR ²	1.00	1.00	0.90	0.90	0.82	0.25
(95% CI)	Referent	(0.85–1.18)	(0.76–1.07)	(0.75–1.09)	(0.69–0.98)	

¹ RR denotes Relative Risk (95% confidence interval [CI])² Adjusted for age, BMI, smoking, and alcohol use