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Original research

Cardiorespiratory fitness and lung cancer risk: A prospective population-based cohort study

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ABSTRACT

Objectives: Little is known about the role of cardiorespiratory fitness (CRF) and leisure-time physical activity (LTPA) with the risk of lung cancer. Previous research shows that maintaining a sufficient amount of physical activity may have a protective effect against cancer. The aim of this study is to examine the associations of CRF, LTPA and lung cancer among middle-aged Finnish men.
Design: Prospective cohort study.
Methods: In a population-based cohort study of 2305 men from Eastern Finland with no history of cancer at baseline. CRF and LTPA data was collected at baseline, 73 cases of lung cancer occurred during an average follow-up of 20-years.
Results: In a multivariate adjusted model, every 3.8 mL/kg/min (1 SD) increase of CRF was related to a 31% decrease in lung cancer risk across all VO_2max quartiles. Furthermore, a 2.8-fold (95% CI 1.14–7.22, $p = 0.024$) increased risk of lung cancer among men in the lowest quartile (≤20.3 mL/kg/min) of CRF as compared those in the highest quartile (>35.1 mL/kg/min). In a multivariate adjusted model LTPA was not associated to lung cancer.
Conclusions: In middle-aged men with no history of lung cancer, increasing levels of CRF serves as a protective factor against lung cancer. Increasing CRF may reduce the risk of lung cancer. Furthermore, CRF is a better predictor of lung cancer than LTPA.

1. Introduction

Lung cancer is the leading cause for cancer mortality worldwide.[1] According to the World Health Organization,[1] 30% of cancers could be avoided due to healthier lifestyles. Previous cohort studies have reported an inverse relationship between physical activity and lung cancer risk.[2] On the basis of existing evidence, 30 min of moderate physical activity on preferably all days of the week is recommended for the prevention of chronic diseases and disability.[3]

Regular physical activity has been associated with reduced risk in lung cancer.[4] However, the lack of association between physical activity and lung cancer has not been thoroughly investigated.[5,6] Inconsistent findings may be due to measurement errors associated with self-reported physical activity. The subjective nature of self-reported physical activity may exaggerate or understate physical activity and sedentary time.[7] In this study, we estimated energy expenditure (EE) of Finnish men during leisure-time physical activity (LTPA).

Little is known about the relationship of cardiorespiratory fitness (CRF) and lung cancer risk, although, there are previous reports on CRF and lung cancer mortality.[8,9] When comparing men with high and low CRF, Sui et al. reports a 57% reduction in lung cancer mortality.[8] Cardiorespiratory fitness is determined by the circulatory, respiratory and muscular systems ability to support the oxygen demands of physical activity. Maximal oxygen uptake (VO_2max) is considered to be the gold standard for measuring CRF.[10] Maximal oxygen uptake is dependent on physical activity exposure; however, age, gender, body size and genetics will influence CRF.[11] The aim of the present study is to investigate physical fitness versus physical activity in predicting lung cancer risk. Furthermore, we elucidate the predictability of CRF and LTPA.

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Table 1
Baseline characteristics of 2305 men from Eastern Finland whom were followed for an average of 20-years.

N	Without lung cancer, mean (SD) 2232	Lung cancer, mean (SD) 73	*p* Value
Age	52.78 (5.08)	54.58 (4.33)	0.003
VO_2max[a] (mL/kg/min)	30.32 (8.02)	27.09 (6.74)	0.001
LTPA[a] EE (kcal/day)	140.36 (173.14)	125.85 (214.52)	0.485
Total duration (h/year)	389.92 (349.02)	482.13 (582.55)	0.183
Total duration (h/week)	7.49 (6.71)	9.27 (11.20)	0.183
Smoking (cig/day)	5.01 (9.50)	17.69 (12.79)	<0.001
Alcohol (g/week)	71.5 (110.84)	135.04 (288.10)	<0.001
Years of education	8.72 (3.49)	7.82 (3.30)	0.030
Fruit and berries intake 4 days, g	164.31 (145.75)	108.75 (116.95)	0.001
Vegetable intake 4 days (g)	290.84 (125.72)	250.88 (96.58)	0.007
Body mass index (kg/m^2)	26.89 (3.47)	25.95 (3.49)	0.023
Cancer in family (%)	24	32	0.167

Data are means and standard deviations (SD).
p Value = *t*-test equality of means.
[a] VO_2max: maximal oxygen uptake; LTPA: leisure-time physical activity.

2. Materials and methods

The subjects were a part of the Kuopio Ischemic Heart Disease Risk Factor Study. This study was designed to examine several risk factors which include CRF, atherosclerotic CVD and cancers.[12] This population-based cohort was a randomly selected sample of 2305 men from eastern Finland with no history of cancer. These men resided in the town of Kuopio or the surrounding communities. Baseline examinations were conducted from March 20, 1984 to December 5, 1989.[13] The Research Ethics Committee of the University of Kuopio has previously approved for the study protocol in this research. Every participant gave written informed consent.

Cardiorespiratory fitness is described as the highest value or plateau of directly measured maximal oxygen consumption by a respiratory gas analyzer.[14] The Mijnhardt Oxycon 4 analyzer expressed the maximal oxygen uptake as the average of values recorded over a 30-s period, whereas the MGC 2001 analyzer expressed it as the average of values recorded over 8 s. The mean maximal oxygen uptake was 2.4 L/min when measured with the Mijnhardt Oxycon 4 analyzer and 2.6 L/min when measured with the MGC 2001 analyzer. Pearson's coefficient for the correlation between simultaneous Mijnhardt Oxycon 4 and MGC 2001 measurements in 13 men was 0.97, indicating a close correlation.[15] A maximal symptom-limited exercise tolerance test was performed between 8:00 a.m. and 10:00 a.m. using an electrically braked cycle ergometer. The standardized testing protocol comprised an increase in the workload of 20 W/min. The tests were supervised by an experienced physician with the assistance of an experienced nurse.[9]

The common reasons for stopping the exercise of (1838) men; included leg fatigue (1163 men), exhaustion (356), breathlessness (202), pain in the leg muscles, joints or back (117). The discontinuation of the test from cardiorespiratory symptoms or abnormalities of (361) men, included arrhythmias (69), dyspnea (108), systolic or diastolic blood pressure (51), dizziness (14), chest pain (84) and ischemic electrocardiographic changes (35).

Leisure-time physical activity was assessed using the 12-month physical activity questionnaire. This questionnaire included the most common physical activities (walking, jogging, swimming, skiing, etc.) of middle-aged Finnish men. For every physical activity, the subjects were required to indicate the frequency (sessions per month), average duration (hours and minutes per session) and intensity (0 no activity, 1 conditioning, 2 brisk, and 3 competitive). The subjects whom regularly smoked cigarettes, cigars or a pipe within the last 30 days were considered a smoker. The daily frequency and duration in years were recorded on a self-administered questionnaire which was checked by an interviewer. An estimation of lifelong exposure to smoking was determined by the number of smoking years and daily use of tobacco products.[16] The family history of cancer is determined whether the immediate family members including father, mother, sister or brother, have previously had, or currently have cancer. Alcohol consumption was determined by the quantity and frequency method for the Nordic alcohol consumption inventory. Frequency, quantity (dose), and type of drink recording onto a response form. This assessment alcohol intake and drinking patterns are then averaged into a weekly intake, based on the alcohol content of the drink and reported doses and frequencies.[14]

Food and nutrient assessment was taken at baseline by blood sampling the subjects. Dietary food and nutrient intake was calculated using the NUTRICA software, which used the quantitative recording of 4 days of data collection. NUTRICA is capable of determining the vitamins in fruits and vegetables.[14] Socioeconomic status was measured as a summary index, which includes education level, occupation, occupational prestige, material stand of living and housing conditions.[16] Education level was examined, which was determined on the basis of lifetime education. Participants were classified into four categories; less than elementary education, completion of elementary school, completion of middle school and completion of high school or above.[17]

Since 1953, all of the cancer cases diagnosed in Finland are reported to the Finnish Cancer Registry (FCR). Finnish personal identification number (PID) is given to all Finnish residents. FCR has access to virtually all follow-up data on cancer diagnosis. Therefore, cancer incidence over follow-up is automatically recorded through the participants PID. There was no loss to follow-up. Follow-up started at baseline and ended on 31 Dec 2011.

Cardiorespiratory fitness, measured as VO_2max was associated to the risk factors for lung cancer by covariate analyses and the risk for lung cancer by Cox proportional hazard modeling. The VO_2 max was entered as a continuous variable and classified into quartiles. Three sets of covariates were used: (1) age and examination year, (2) model 1 and cigarette smoking, alcohol consumption, and cancer in family and (3) model 1 + 2 and education, fruits and vegetables. In additional Cox models VO_2max were categorized into quartiles to predict risk. The association of conventional risk factors and the risk for lung cancer was analyzed using proportional hazards Cox model. Relative hazards which were adjusted for risk factors were estimated as antilogarithms of coefficients from multivariable models. All tests for statistical significance was defined as *p*-values of <0.05 were 2-sided. Statistical analysis was performed by using SPSS software, version 19.0 for Windows (SPSS, Inc, Chicago, Illinois).