Lung Cancer 95 (2016) 17–27

Contents lists available at ScienceDirect

Lung Cancer

journal homepage: www.elsevier.com/locate/lungcan

Leisure-time physical activity and lung cancer risk: A systematic review and meta-analysis

Darren R. Brenner[a,b,c,*], Demetra H. Yannitsos[a,b], Megan S. Farris[a,b], Mattias Johansson[d], Christine M. Friedenreich[a,b,c]

[a] Department of Cancer Epidemiology and Prevention Research, Cancer Control Alberta, Alberta Health Services, Canada
[b] Department of Community Health Sciences, Cumming School of Medicine, University of Calgary, Canada
[c] Department of Oncology, Cumming School of Medicine, University of Calgary, Canada
[d] Genetic Epidemiology Group, International Agency for Research on Cancer, Lyon, France

ARTICLE INFO

Article history:
Received 5 November 2015
Received in revised form 21 January 2016
Accepted 29 January 2016

ABSTRACT

Objectives: We conducted a systematic review and meta-analysis of the association between recreational physical activity and lung cancer risk to update previous analyses and to examine population subgroups of interest defined by smoking status and histology.
Materials and methods: We searched the PubMed database for studies up to May 2015. Individual study characteristics were abstracted including study design, number of cases, assessment of recreational physical activity and type and level of adjustment for confounding factors. Combined effect estimates were calculated for the overall associations and across subgroups of interest.
Results: We identified 28 studies that were eligible for inclusion in the meta-analysis. The overall analysis indicated an inverse association between recreational physical activity and lung cancer risk (Relative Risk (RR), 0.76; 95% Confidence Interval (CI), 0.69–0.85, p-value: <0.001). Similar inverse associations with risk were also noted for all evaluated histological subtypes, including adenocarcinoma (RR, 0.80; 95% CI, 0.72–0.88), squamous (RR, 0.80; 95% CI, 0.71–0.90) and small cell (RR, 0.79; 95% CI, 0.66–0.94). When we examined effects by smoking status, inverse associations between recreational physical activity and lung cancer risk were observed among former (RR, 0.77; 95% CI, 0.69–0.85) and current smokers (RR, 0.77; 95% CI, 0.72–0.83), but not among never smokers (RR, 0.96; 95% CI, 0.79–1.18).
Conclusion: Results from this meta-analysis suggest that regular recreational physical activity may be associated with reduced risk of lung cancer. Only four studies examining never smokers were identified, suggesting the need for additional research in this population.

1. Background

In 2014 lung cancer accounted for 14% of all new cancer cases [1] and was the leading cause of cancer-related mortality globally [1–4]. Smoking remains the predominant risk factor for developing lung cancer, with approximately 75–90% of lung cancer cases attributed to active tobacco smoking [2,4]. Several additional lifestyle and environmental factors have been associated with lung cancer risk, including radon exposure, exposure to asbestos, other chemicals and physical activity [2–13]. Physical activity has been associated with reduced lung cancer risk in three previous meta-analyses [5–7] with overall combined estimates suggesting a 20–50% decrease in the risk of developing lung cancer when comparing the least to the most physically active study participants [3]. These meta-analyses were limited in their focus on relevant subgroups; specifically, they did not include sub-group analyses stratified by smoking status and/or histology groups. Furthermore, previous analyses have not provided stratified analyses by assessment of recreational physical activity.

The association between physical activity and lung cancer risk may be confounded by tobacco. Study participants who partake in regular recreational physical activity may be less likely to be heavy smokers and may have had a lower lifetime exposure to active and passive smoking. Similarly it is possible that regular tobacco users may exercise less than non-smokers because of impaired lung function related to their smoking function [13]. Evaluating the relation between physical activity and lung cancer risk therefore requires

* Corresponding author at: Department of Cancer Epidemiology and Prevention Research, Cancer Control Alberta, Alberta Health Services, Holy Cross Centre, Room 514, Box ACB, 2210 2nd St. SW, Calgary, Alberta T2S 3C3, Canada.
E-mail address: Darren.Brenner@albertahealthservices.ca (D.R. Brenner).

http://dx.doi.org/10.1016/j.lungcan.2016.01.021
0169-5002/

a careful assessment of risk by smoking status and histological subtypes. Indeed, distinguishing a modifiable risk factor such as physical activity may identify avenues for primary prevention, in particular among former smokers who are motivated to find means of further reducing their lung cancer risk.

To address the identified gaps in and to update previous meta-analyses, we conducted a systematic literature review and meta-analyses of the association between recreational physical activity and lung cancer risk in epidemiologic studies. We focused this review on recreational physical activity rather than other types of activity, since knowledge translation into public health messages are more easily conveyed in this domain.

2. Methods

2.1. Study selection

We conducted a structured search of the PubMed database including studies up to May 1st 2015. The keywords and medical subject headings (MeSH) used were; physical activity, motor activity, exercise, cancer, neoplasm, carcinoma, tumor, lung, risk factor, risk factors and risk. Detailed search terms and sequences are given in Supplementary Table 1. There were no date, language, or geographical restrictions applied. No abstracts or unpublished results were included. Reference lists from included studies reference lists were also examined for potentially relevant studies.

Two reviewers (DHY and MSF) independently screened titles and abstracts. A combined list of identified studies was then examined for any discrepant inclusions. Any discrepancies between the two reviewers were examined by a third reviewer (DRB). Inclusion criteria for studies were: (1) having exposure measurement of recreational physical activity; and (2) an outcome of lung cancer risk. Exclusion criteria included, not providing a measure of statistical error or a definition of recreational physical activity.

Following the Meta-analysis of Observational Studies (MOOSE) Guidelines and PRISMA checklist [14,15] (Supplementary Fig. 1), we collected relevant data from the selected studies using a formalized abstraction form. The abstraction form included detailed information on the study characteristics, study design (case-control (population or hospital-based), cohort), type of smokers (never, ever, current, former), number of cases/controls, type/assessment of recreational physical activity, as well as relative risks (RRs), odds ratios (ORs), hazard ratios (HRs) and covariates used for adjustment in the studies. Location of study included the United States, Europe, Asia and Canada. The median year of data collection was dichotomized into before and after 2000 (derived to examine temporal trends related to methodological limitations in older studies and changes in reporting of recreational physical activity over time). Sex of the population in the included studies was categorized into combined, male or female. The median age of the populations were stratified into <50 years, between the ages of 50–60, and >60. The variables used for model adjustment were grouped and identified as: no adjustment, only age adjustment, basic model (adjusting for age, sex and smoking), basic model in addition to body mass index (kg/m^2) (BMI), or a detailed list of possible confounders (basic + BMI in addition to other factors such as dietary intake, alcohol consumption, or family history of cancer).

The volume of recreational physical activity was divided into four types of characterization that included: (1) meeting World Health Organization (WHO) Global Recommendations on Physical Activity for Health [16] (≥150 min of moderate physical activity per week, or ≥75 min of vigorous physical activity per week); (2) subjective measures provided by study participants, where levels of physical activity were classified as high versus low; (3) frequency of recreational physical activity estimated as the number of times per week they engaged in recreational physical activity; and (4) regular participation in sports. The time period in life that was assessed was separated into studies that examined activity for total lifetime, within the past year, or two or more years (but not lifetime).

The measures and characterization of recreational physical activity varied across studies. The comparisons of highest versus lowest measures of recreational physical activity were used to enable relative comparability and justify pooling across studies. If the reference group was the highest volume measure, the inverse of the study estimate was obtained. Furthermore, if there were multiple risk estimates presented within a single study, the risk estimates that were fully adjusted for confounding from a multivariable analysis were chosen.

Case confirmation of lung cancer in these studies was identified either through pathology reports, cancer registries, self-report, death certificates, or a combination of methods (including International Classification of Disease (ICD) codes, cancer registry and pathology reports). Quality of the articles was assessed by examining the following characteristics of the study design/methods: completeness of follow-up, measurement of recreational physical activity, case ascertainment methods, adjustment for confounding,

2.2. Statistical analysis

Individual study results were pooled overall and separately by design (cohort and case-controls) as well as by smoking subgroups and histology types. We used using random effects models to pool effect estimates across studies. Measures of heterogeneity were used to quantify the differences between studies and subgroups included in our meta-analysis [18], using the Cochrane Q statistic, the I^2 statistic, followed meta-regression analyses across subgroups and study characteristics of interest. Heterogeneity was examined by sex, study design, confounding adjustment, location, median age, median year of data collection, lung cancer case confirmation as well as the reporting period and parameters of recreational physical activity. The potential of publication bias was assessed using funnel plots and the Begg test [19]. Statistical analyses were performed in Stata version 13, R version 9.3 and assessed at a 5% significance level.

3. Results

3.1. Summary of search results

The literature search initially resulted in 507 articles (Supplementary Fig. 1). Of those articles, 121 were included based on titles and abstracts. After reviewing the abstracts, 80 studies were excluded. Forty-one full text articles were assessed for eligibility. Fourteen articles were excluded for failing to meet the inclusion criteria, eight of the 14 were excluded because they were repeated publications from the same populations. The remaining 28 studies were included in the systematic literature review. One study was excluded as it did not provide confidence intervals (Supplementary Fig. 1). Therefore, twenty-seven studies [20–37,39–47] were included in the meta-analysis. Six were case-control studies [18–22] and 21 were cohort studies [23–44]. Of the six case-control studies [20–25], three were population-based [23–25], three were hospital-based studies [20–22], and all involved frequency matching. All except one of the cohort studies were population-based [29]. There were six studies that reported men and women as separate effect estimates [20,28,31,39,44,45], as well as one study that reported never and current smokers separately [20], therefore, in total, there were 34 effect estimates included in the overall analysis.