



The association of lifetime physical inactivity with bladder and renal cancer risk: A hospital-based case-control analysis



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ABSTRACT

Objectives: Recreational physical inactivity has been gaining recognition as an independent epidemiological exposure of interest in relation to cancer endpoints due to evidence suggesting that it may associate with cancer independent of obesity. In the current analyses, we examined the associations of lifetime recreational physical inactivity with renal and bladder cancer risk.

Methods: In this hospital-based case-control study, we identified N = 160 renal cancer patients, N = 208 bladder cancer patients, and N = 766 age frequency-matched controls without cancer. Participants self-reporting never participating in any regular/weekly recreational physical activity throughout their lifetime were classified as physically inactive. Utilizing unconditional multivariable logistic regression analyses, we estimated odds ratios and 95% confidence intervals to represent the associations between lifetime physical inactivity and renal and bladder cancer risk.

Results: In multivariable logistic regression models, we observed significant positive associations between lifetime recreational physical inactivity and renal cancer and bladder cancer risk: odds ratio = 1.77 (95% CI: 1.10–2.85) and odds ratio = 1.73 (95% CI: 1.13–2.63), respectively. Similar associations also persisted among individuals who were not obese for both renal and bladder cancer: odds ratio = 1.75 (95% CI: 1.03–2.98) and odds ratio = 1.70 (95% CI: 1.08–2.69), respectively.

Conclusions: In this case-control study, we observed evidence of a positive association between renal and bladder cancer with lifetime recreational physical inactivity. These data add to the growing body of evidence suggesting that physical inactivity may be an important independent risk factor for cancer. However, additional studies using a larger sample and prospectively collected data are needed to substantiate the current findings.

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1. Introduction

In the United States, renal and bladder carcinomas are among the most common cancers diagnosed each year, with an estimated 61,560 and 74,000 newly diagnosed cases, respectively, in 2016 [1]. Well-established unmodifiable risk factors for bladder and renal cancer include age, a family history of bladder or renal cancer, and

sex, with men having a higher incidence of both cancers in comparison to women. Modifiable risk factors for bladder cancer include cigarette smoking, occupational exposures and low fluid intake, while the well-established modifiable risk factors for renal cancer include smoking, occupational exposures and obesity [2,3].

Currently, recreational physical activity is not recognized as a well-established protective factor for renal or bladder cancer [2–5]. In fact, despite the publication of several individual epidemiological studies examining the associations of bladder and renal cancer risk with incrementally higher levels of recreational physical activity exposure, the evidence remains inconclusive in terms of a public health physical activity recommendation specific to these

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cancers [4,5]. Furthermore, in the existing literature, the common approach of identifying physically inactive individuals as the referent group limits the ability to explicitly investigate and report the independent associations between physical inactivity and cancer endpoints. Importantly, despite calls for increasing investigations of the association of physical inactivity with cancer risk and prognosis [6], the independent associations of physical inactivity with renal and bladder cancer risk are not known.

Since the publication of The 2008 Physical Activity Guidelines, Americans have been encouraged to avoid recreational physical inactivity [7], yet the most recent national data suggest that 25% of American adults are completely physically inactive [8], and 50–79% are insufficiently active [9]. Given the high prevalence of recreational physical inactivity at the national level and the hypothesis that the greatest protective benefits can be achieved by increasing physical activity levels at the low end of the physical activity continuum [10], physically inactive individuals could be a particularly important group to study from a cancer prevention and public health perspective. Evidence also suggests that physical inactivity (i.e., the lowest end of the physical activity continuum) is assessed with less exposure misclassification in comparison to self-reported incremental levels of physical activity exposure in which individuals tend to over-report the amount of exercise or physical activity they perform [10,11]. Furthermore, emerging evidence suggests that physical inactivity is a behavioral construct that associates with disease independently from obesity [12,6]. Lastly, this approach may be particularly relevant for cancers that do not have a well-established dose-response association with physical activity (i.e., cancers other than breast, colorectal and endometrial). Thus, in the current analysis, we sought to investigate the association of lifetime recreational physical inactivity with renal and bladder cancer risk, hypothesizing that renal and bladder cancer patients would be more likely to report a history of physical inactivity in comparison to controls without cancer.

2. Methods

2.1. Study population

In this retrospective hospital-based case-control analysis, the study population was comprised of individuals who received medical services at Roswell Park Cancer Institute (RPCI) between 1989 and 1998 who also agreed to participate in the Patient Epidemiology Data System (PEDS), which involved completing a comprehensive epidemiological questionnaire. The RPCI Institutional Review Board approved the conduct of the study and all participants provided informed consent prior to study enrollment, which included consent for future data analyses.

Renal cancer cases were identified from the RPCI tumor registry and Diagnostic Index and included 160 individuals diagnosed with primary, incident renal cancer. Controls were age frequency-matched to cases (2 controls per case) on five-year age strata and included 318 individuals identified from a pool of 10,642 PEDS controls. PEDS control participants came to RPCI with a suspicion of malignant disease but were diagnosed with conditions that included non-malignant diseases of the circulatory system (27%), infectious and parasitic diseases (24%), diseases of the genitourinary system (23%), diseases of the gastrointestinal system (19%), diseases of the respiratory system (6%), and other conditions (1%). Bladder cancer cases included 208 individuals diagnosed with primary, incident bladder cancer, who were also identified from the RPCI tumor registry and Diagnostic Index. Controls were selected and matched as described above and included 448 individuals with infectious and parasitic disease (29%), diseases of

the circulatory system (29%), diseases of the genitourinary system (19%), diseases of the digestive system (18%), and diseases of the respiratory system (7%).

2.2. Epidemiological questionnaire

The PEDS questionnaire was a self-administered epidemiological survey offered to patients receiving medical service as part of the admission process at Roswell Park Cancer Institute. The PEDS questionnaire was offered to all new patients, independent of diagnosis or reason for seeking care, with an approximate 50% response rate [13]. Detailed methodology pertaining to the PEDS study and questionnaire has been previously described [13–16]. Briefly, the questionnaire was designed to assess a variety of health-related variables, including unmodifiable and modifiable factors such as age, race, reproductive factors, height, weight, and dietary patterns. Epidemiological variables pertinent to the current analyses included family history of renal or bladder cancer, cigarette smoking, alcohol consumption, and lifetime physical activity.

More specifically, regarding family history, patients were asked to indicate whether spouses or first-degree relatives (parents, children, and siblings) had ever been diagnosed with cancer. If yes, respondents were then queried to specify the person, the relationship and the type of cancer. Alcohol consumption was assessed by the average number of drinks of beer, wine or liquor consumed each week via rankings ranging from zero to more than 21 drinks per week. Cigarette smoking information was also collected with a series of items including smoking status (i.e., ever/never and former/current), and among current or former smokers, the age of onset of smoking and packs smoked per day were queried. Additionally, the recreational physical activity section of the questionnaire was comprised of a five-part item assessing whether the participant had “ever regularly exercised for health or pleasure (for example, jogging, walking, aerobics, etc.)”. If yes, participants were then probed about the age of initiation of physical activity, the total duration of the physical activity in years, and the frequency of the physical activity in times per week or month.

2.3. Lifetime recreational physical inactivity

The exposure of interest in the current analyses was lifetime recreational physical inactivity. We defined recreational physical inactivity in general accordance with The 2008 Physical Activity Guidelines for Americans, which suggests that individuals engaging in no regular, weekly recreational physical activity should be classified as “physically inactive” [7]. Thus, in the current analyses, individuals reporting no weekly recreational physical activity throughout their life (on average, less than one session per week or less than four sessions per month) were classified as physically inactive, the exposure of interest. Conversely, participants reporting at least some regular, weekly physical activity throughout their lifetime (i.e., at least one weekly session or four sessions per month) were classified as active.

Our primary exposure of interest was lifetime physical inactivity prior to study enrollment, in which participants were classified as physically inactive if they never engaged in any regular recreational physical activity throughout their lifetime. However, in exploratory analyses designed to examine a potentially more relevant exposure window closer to diagnosis of cancer, we also examined physical inactivity in the two decades prior to study enrollment. Importantly, participants were only classified as physically inactive if they reported no regular physical activity throughout their lifetime, or for a minimum of twenty years prior to study enrollment.

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