HHS Public Access

Author manuscript

Cancer Epidemiol. Author manuscript; available in PMC 2018 August 01.

Published in final edited form as:

Cancer Epidemiol. 2017 August ; 49: 24–29. doi:10.1016/j.canep.2017.04.017.

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

Rikki Cannioto[1], **John Lewis Etter**[1], **Lauren Beryl Guterman**[2], **Janine M. Joseph**[1], **Nicholas R. Gulati**[3], **Kristina L. Schmitt**[4], **Michael J. LaMonte**[5], **Ryan Nagy**[1], **Albina Minlikeeva**[1,5], **James Brian Szender**[6], and **Kirsten B. Moysich**[1]

[1]Department of Cancer Prevention and Control, Roswell Park Cancer Institute, NY 14263

[2]Department of Epidemiology, Emory University Rollins School of Public Health, Atlanta, GA 30322

[3]Department of Biomedical Engineering, Rochester Institute of Technology, Rochester, NY 14623

[4]College of Medicine, Lake Erie College of Osteopathic Medicine, Erie PA 16509

[5]Department of Epidemiology and Environmental Health, University at Buffalo, Buffalo, NY 14214

[6]Department of Gynecologic Oncology, Roswell Park Cancer Institute, Buffalo, NY, 14263

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

Corresponding Author: Dr. Kirsten B. Moysich, Department of Cancer Prevention and Control, Roswell Park Cancer Institute, 352 Carlton House, Elm and Carlton Streets, Buffalo, NY 14263, Phone: 716-845-8004, Fax: 716-845-1126, Kirsten.moysich@roswellpark.org.

Authorship Contribution:

- Rikki Cannioto - Concept & Design, Data Analysis, Drafting
- John Lewis Etter - Data Analysis, Drafting
- Lauren Beryl Guterman - Critical Review of Manuscript
- Janine M. Joseph - Critical Review of Manuscript, Administrative Support
- Nicholas R. Gulati - Critical Review of Manuscript
- Kristina L. Schmitt - Critical Review of Manuscript
- Michael J. LaMonte - Critical Review of Manuscript
- Ryan Nagy - Critical Review of Manuscript
- Albina Minlikeeva - Critical Review of Manuscript
- James Brian Szender - Critical Review of Manuscript
- Kirsten B. Moysich - Concept & Design, Critical Review of Manuscript

Conflicts Of Interest: Conflicts of interest: none

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 and 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.

Keywords

bladder cancer; kidney cancer; obesity; physical inactivity; renal cancer

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 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 physical activity and obesity[126]. 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.

2.4. Identification of Confounding Variables

Prior to analysis, we pre-specified age, sex, body mass index (BMI), family history of bladder or renal cancer, alcohol consumption, and smoking as important variables for adjustment. We also examined the potential confounding effects of additional epidemiological variables including education, race, and hypertension by applying the ten percent change-in-estimate method described by Maldonado et al.[17].

2.5. Statistical Analysis

In descriptive analyses, two-tailed t-tests and Pearson's Chi-square were conducted to evaluate differences between cases and controls for continuous and categorical variables, respectively. In multivariable analyses, we utilized unconditional logistic regression models to estimate the odds ratios (OR) and 95% confidence intervals (CI) for the association of physical inactivity with renal and bladder cancer risk; unconditional logistic regression was utilized because we did not use exact 1:1 age matching. Education, race, and hypertension were tested according to the ten percent change-in-estimate method as described above, but these variables did not appreciably change estimates of association and were excluded from further consideration in additional multivariable analyses. Thus, the final multivariable models for both renal and bladder cancer analyses were adjusted for age (continuous), sex (male or female), family history of cancer (yes/no; defined as first-degree family history of renal or bladder cancer, respectively), BMI (continuous), alcohol consumption (average drinks per week), and cigarette smoking (pack years 0, <30, 31-45, 46-64, >65). In exploratory analyses, we also examined associations stratified by sex and BMI classification. All statistical analyses were performed using SAS for Windows, version 9.4. All tests were two-sided and considered statistically significant at $p<0.05$.

3. Results

The descriptive characteristics of the renal and bladder cancer study populations are presented in Table 1. Briefly, renal cancer cases had a significantly higher BMI ($p<.001$) and were more likely to be physically inactive ($p=0.020$) than controls, but we observed no significant differences in age, smoking pack years, education level, and family history of cancer between groups (Table 1). Among the bladder cancer study population, cases were more likely to be ever smokers ($p<0.0001$) and were more likely to report a history of physical inactivity than controls ($p=0.016$). As expected, both renal and bladder cancer cases were more likely to be male ($p<0.0001$, Table 1).

In our primary analyses, we observed a significant positive association between lifetime recreational physical inactivity and renal cancer risk (OR=1.77, 95% CI: 1.10-2.85, $p=0.019$) and bladder cancer risk (OR=1.73, 95% CI: 1.13-2.63, $p=0.011$) (Table 2). In additional exploratory analyses designed to limit the physical inactivity exposure window to

the two decades prior to study enrollment, we observed similar relationships for both renal and bladder cancer risk: OR=1.48 (95% CI: 0.92-2.38) and OR=1.60 (95% CI: 1.04-2.45), respectively, but the association was shy of significance for renal cancer.

When analyses were stratified by sex (Table 3), we observed similar patterns in associations between physical inactivity and renal cancer as seen with the combined study sample; however the associations did not reach statistical significance among men. Among women, renal cancer cases were more than twice as likely as controls to report being physically inactive (OR=2.18, 95% CI: 1.08-4.40, p=0.031). When bladder cancer analyses were stratified by sex, we observed similarly elevated ORs in men and women, but the associations did not reach statistical significance: OR=1.62, 95% CI: 0.96-2.72, p=0.068 and OR=2.03, 95% CI: 0.94-4.39, p=0.072, respectively (Table 3). Lastly, in exploratory analyses stratified by obesity status (BMI<30 and BMI≥30), we observed significant associations between physical inactivity and bladder and renal cancer among non-obese participants: OR=1.70, 95% CI: 1.08-2.69, p=0.022 and OR=1.75, 95% CI: 1.03-2.98, p=0.040, respectively (Table 3). Among obese participants, the odds ratios were similarly elevated, but the associations did not reach statistical significance for bladder or renal cancer: OR=1.34, 95% CI: 0.40-4.44, p=0.635 and OR=1.33, 95% CI: 0.42-4.14, p=0.628, respectively.

4. Discussion

In this study, we observed consistent positive associations between recreational physical inactivity and renal and bladder cancer risk in participants who were physically inactive throughout their lifetime. To our knowledge, no previous studies have systematically examined recreational physical inactivity as an independent exposure of interest relative to renal and bladder cancer risk. Rather, the paradigm represented in the existing literature has been to identify physical inactivity as the referent group while examining the associations between incrementally higher quantities of physical activity exposure with cancer risk. While investigating the existence of a dose-response association between varying levels of physical activity and cancer risk is important, it should not preclude researchers from further examining the independent associations between physical inactivity and cancer endpoints when no clear dose-response association is detected.

Although the goal of the current study was to examine recreational physical inactivity as an independent exposure, it is worth noting that individual studies of the associations of recreational physical activity with bladder and renal cancer risk have yielded inconsistent findings. However, recent meta-analyses of these data suggest a protective role for physical activity for both renal (OR=0.88, 95% CI: 0.79-0.97)[18] and bladder cancer (OR=0.85, 95% CI: 0.74-0.98)[19] when comparing the highest physical activity group to the lowest. Despite these significant summary estimates, recreational physical activity is not currently recognized as a protective factor for renal or bladder cancer.

Several biological mechanisms have been proposed to account for an association between recreational physical inactivity and cancer. These include an increase in circulating levels of sex hormones, increased chronic inflammation, impaired insulin sensitivity, impaired

immune surveillance and responsiveness, increased adiposity, and a dysregulated adipokine milieu [20, 21]. Further mediators underlying a potential link between physical inactivity and renal cancer include hypertension, circulating levels of insulin-like growth factor 1, and lipid peroxidation [18]. Additional biologic pathways linking increased physical activity to decreased risk of bladder cancer may also include enhanced DNA repair and increased detoxification of carcinogens [19]. Interestingly, there has been an increasing recognition that obesity and physical (in)activity could be operating through independent pathways to exert an effect on carcinogenesis [6, 12, 22]. In the current analyses, we observed elevated odds ratios in both non-obese and obese participants, suggesting that physical inactivity may associate with cancer via pathways that are, at least in part, independent of obesity-driven pathways. While we only observed significant associations between physical inactivity and bladder and renal cancer risk among non-obese participants, we may have lacked statistical power to observe a significant association within the obese study population strata.

A strength of our study is that we were able to assess the potential confounding role of a number of established risk factors of both renal and bladder cancer, as well as other factors that tend to parallel physical activity (or inactivity) in lifestyle patterns. Importantly, our use of lifetime physical inactivity, spanning all of the years of adulthood prior to diagnosis, as the primary exposure of interest decreases the likelihood that the observed associations could be explained by a reverse causation bias.

Conversely, the potential measurement error associated with self-reported physical inactivity data categorized dichotomously is an important limitation of the current work. However, there is a body of literature suggesting that simplified physical activity questionnaires, including binary categorization of physical (in)activity behavior, is a valid method for identifying the most physically inactive individuals in a population [23-29]. Additionally, self-reported physical inactivity prevalence among controls (i.e., 45.3% and 52.5% among renal and bladder controls, respectively), was similar to population estimates suggesting that 50-79% of Americans are insufficiently physically active [9], thus enhancing our confidence in the characterization of recreational physical inactivity.

We also recognize that a referent group broadly defined as physically active could result in misclassification among individuals with lower compared to higher physical activity levels, and this approach precludes the ability to examine a dose-response association between bladder/renal cancer risk and physical activity exposure. However, the aim of the current analyses was to examine lifetime physical inactivity as an independent exposure, and any misclassification between the physically inactive-active groups would likely be non-differential to case and control status, given that controls were also seen at a hospital and diagnosed with health conditions that could affect physical activity level, or the recall of physical activity, in a manner similar to cases. Therefore, if a biased measure of association were to occur, it most likely would be conservative and non-differential based upon case-control status, resulting in an underestimation of the association between physical inactivity and cancer risk.

These findings are also limited because we do not account for other domains of physical activity and we cannot account for explicitly sedentary behavior (i.e., hours of sitting,

television viewing, or reading), a similar but distinct behavioral construct. We also cannot account for additional unmeasured variables that could be associated with bladder and renal cancer risk, such as occupational exposures, diabetes, and/or other comorbidities. While hypertension did not meet the criteria for a confounding variable in the current analyses, we may have been limited by the large percentage of missing hypertension data. It is also worth noting that we did not observe significant differences in self-reported smoking behavior between renal cancer cases and controls. However, this could be due to the fact that controls were seen at the hospital and diagnosed with non-neoplastic disease and thus may be more similar to cases in terms of lifestyle behaviors than would be expected in a population-based study.

Further, we were likely insufficiently powered to conduct subgroup analyses by obesity status, tumor stage, tumor histology or sex. For example, in the current analysis, we observed significant associations between physical inactivity and renal cancer risk in the combined study population, but in sex-stratified analyses, the association was no longer significant among men and was strengthened in women. These findings may be due to the relatively small number of physically inactive female cases in our analyses. In comparison, in a recent meta-analysis, Behrens & Leitzmann reported a significant association between physical activity and renal cancer risk in the combined study population, but the sex-stratified associations were shy of statistical significance[18]. Further, in the current bladder cancer analyses, we also observed a significant association between physical inactivity and bladder cancer risk in the combined study population, but the association was no longer significant in sex-stratified analyses. In contrast, a recent meta-analysis reported a significant association between physical activity and bladder cancer risk in the overall study population, but when analyses were stratified by sex, the association only remained significant in women[19].

Lastly, our findings may also be limited by the nature of the recruitment methods inherent in this hospital-based case-control study. Specifically, the accrual of participants with non-neoplastic diagnoses could have resulted in a higher prevalence of unhealthy individuals comprising the control group. However, if control participants reported a higher prevalence of recreational physical inactivity than the general population, our observed estimates would be attenuated toward the null.

In conclusion, the current analyses suggest that lifetime recreational physical inactivity is significantly and positively associated with renal and bladder cancer risk. Given that renal and bladder cancers are among the most common cancers in the United States, and given the persistence of recreational physical inactivity at the population level, replicating these findings with further investigations could be of significant public health importance. If the observed association between recreational physical inactivity and renal and bladder cancer is substantiated, additional work via targeted intervention studies should be pursued to characterize the dose of physical activity required to mitigate this risk.

Acknowledgments

Funding:

- K.B. Moysich was supported by New York State Department of Health (NYS DOH C019286)
- N.R. Gulati, R. Nagy and K.L Schmitt were supported by the Roswell Park Alliance Foundation
- J.B. Szender was supported by the National Institutes of Health (NIH 5T32CA108456)

References

1. ACS. Cancer Facts & Figures 2016. 2016. Available from URL: http://www.cancer.org/acs/groups/content/@research/documents/document/acspc-047079.pdf
2. ACS. Kidney Cancer Detailed Guide: American Cancer Society. 2014
3. ACS. Bladder Cancer Detailed Guide: American Cancer Society. 2014
4. WCRFI/AICR. Diet, nutrition, physical activity and kidney cancer. Continuous Update Project for the World Cancer Research Fund's Food, Nutrition, Physical Activity, and the Prevention of Cancer. World Cancer Research Fund International. 2015
5. WCRFI/AICR. Diet, nutrition, physical activity and bladder cancer. Continuous Update Project for the World Cancer Research Fund's Food, Nutrition, Physical Activity, and the Prevention of Cancer. World Cancer Research Fund International. 2015
6. Sanchis-Gomar F, Lucia A, Yvert T, et al. Physical inactivity and low fitness deserve more attention to alter cancer risk and prognosis. Cancer Prev Res (Phila). 2015; 8:105–110. [PubMed: 25416409]
7. USDHHS. Physical Activity Guidelines for Americans. Washington, D.C.: Office of Disease Prevention and Health Promotion; 2008. 2008
8. Moore LV, Harris CD, Carlson SA, Kruger J, Fulton JE. Trends in no leisure-time physical activity--United States, 1988-2010. Res Q Exerc Sport. 2012; 83:587–591. [PubMed: 23367822]
9. USDHHS. Prevalence and Trends Data: Nationwide Physical Activity - 2013. [accessed November 1, 2014, 2014]
10. Bull, FC., Armstrong, TP., Dixon, T., Ham, S., Neiman, A., Pratt, M. Physical Inactivity. Comparitive Quantification of Health Risks: Global and Regional Burden of Disease Attributable to selected Major Risk Factors. In: WHO. , editor. WHO. 2004. p. 729-881.
11. Celis-Morales CA, Perez-Bravo F, Ibanez L, Salas C, Bailey ME, Gill JM. Objective vs. self-reported physical activity and sedentary time: effects of measurement method on relationships with risk biomarkers. PLoS One. 2012; 7:e36345. [PubMed: 22590532]
12. Byers T. Physical activity and gastric cancer: so what? An epidemiologist's confession. Cancer Prev Res (Phila). 2014; 7:9–11. [PubMed: 24346343]
13. Baker JA, Odunuga OO, Rodabaugh KJ, Reid ME, Menezes RJ, Moysich KB. Active and passive smoking and risk of ovarian cancer. Int J Gynecol Cancer. 2006; 16(Suppl 1):211–218. [PubMed: 16515593]
14. Friel G, Liu CS, Kolomeyevskaya NV, et al. Aspirin and Acetaminophen Use and the Risk of Cervical Cancer. J Low Genit Tract Dis. 2015; 19:189–193. [PubMed: 25856123]
15. Kolomeyevskaya NV, Szender JB, Zirpoli G, et al. Oral Contraceptive Use and Reproductive Characteristics Affect Survival in Patients With Epithelial Ovarian Cancer: A Cohort Study. Int J Gynecol Cancer. 2015; 25:1587–1592. [PubMed: 26273932]
16. McCann SE, Moysich KB, Mettlin C. Intakes of selected nutrients and food groups and risk of ovarian cancer. Nutr Cancer. 2001; 39:19–28. [PubMed: 11588898]
17. Maldonado G, Greenland S. Simulation study of confounder-selection strategies. Am J Epidemiol. 1993; 138:923–936. [PubMed: 8256780]
18. Behrens G, Leitzmann MF. The association between physical activity and renal cancer: systematic review and meta-analysis. Br J Cancer. 2013; 108:798–811. [PubMed: 23412105]
19. Keimling M, Behrens G, Schmid D, Jochem C, Leitzmann MF. The association between physical activity and bladder cancer: systematic review and meta-analysis. Br J Cancer. 2014; 110:1862–1870. [PubMed: 24594995]
20. McTiernan A. Mechanisms linking physical activity with cancer. Nat Rev Cancer. 2008; 8:205–211. [PubMed: 18235448]
21. Walsh NP, Gleeson M, Shephard RJ, et al. Position statement. Part one: Immune function and exercise. Exerc Immunol Rev. 2011; 17:6–63. [PubMed: 21446352]

22. Hildebrand JS, Gapstur SM, Gaudet MM, Campbell PT, Patel AV. Moderate-to-vigorous physical activity and leisure-time sitting in relation to ovarian cancer risk in a large prospective US cohort. Cancer Causes Control. 2015

23. Li S, Carlson E, Holm K. Validation of a single-item measure of usual physical activity. Percept Mot Skills. 2000; 91:593–602. [PubMed: 11065323]

24. Milton K, Bull FC, Bauman A. Reliability and validity testing of a single-item physical activity measure. Br J Sports Med. 2011; 45:203–208. [PubMed: 20484314]

25. Rose S, Elley CR, Lawton BA, Dowell AC. A single question reliably identifies physically inactive women in primary care. The New Zealand Medical Journal. 2008; 121

26. Schechtman KB, Barzilai B, Rost K, Fisher EB Jr. Measuring physical activity with a single question. Am J Public Health. 1991; 81:771–773. [PubMed: 2029054]

27. Siconolfi SF, Lasater TM, Snow RC, Carleton RA. Self-reported physical activity compared with maximal oxygen uptake. Am J Epidemiol. 1985; 122:101–105. [PubMed: 4014188]

28. Smith BJ, Marshall AL, Huang N. Screening for physical activity in family practice: evaluation of two brief assessment tools. Am J Prev Med. 2005; 29:256–264. [PubMed: 16242587]

29. Weiss TW, Slater CH, Green LW, Kennedy VC, Albright DL, Wun CC. The validity of single-item, self-assessment questions as measures of adult physical activity. J Clin Epidemiol. 1990; 43:1123–1129. [PubMed: 2243250]

Highlights

- We observed an association between lifetime inactivity and bladder cancer.
- We observed an association between lifetime inactivity and renal cancer.
- Associations between inactivity and cancer persisted among individuals with a BMI <30kg/m^2.
- Lifetime inactivity may be an independent risk factor for renal and bladder cancer.

Table 1

Descriptive Characteristics of the Renal and Bladder Cancer Study Population

Epidemiological Variable	Renal Cancer Study Population			Bladder Cancer Study Population		
	Cases (N = 160)[a]	Controls (N = 318)[a]	p-value[b]	Cases (N = 208)[a]	Controls (N = 448)[a]	p-value[b]
Age	60.76 (13.53)	60.89 (13.77)	0.9216	65.01 (11.41)	65.65 (10.99)	0.4963
Sex			<.0001			<.0001
Male	100 (62.50%)	134 (42.14%)		154 (74.04%)	210 (46.88%)	
Female	60 (37.50%)	184 (57.86%)		54 (25.96%)	237 (52.90%)	
Missing	0 (0.00%)	0 (0.00%)		0 (0.00%)	1 (0.22%)	
BMI (kg/m^2; continuous)	27.51 (4.89)	25.79 (4.76)	0.0003	26.91 (5.09)	26.57 (5.14)	0.4277
BMI classification			0.0097			0.4342
Underweight (<18.5)	0 (0.00%)	4 (1.26%)		3 (1.44%)	5 (1.12%)	
Normal (18.5-24.9)	55 (34.38%)	148 (46.54%)		71 (34.13%)	181 (41.40%)	
Overweight (24.9-29.9)	66 (41.25%)	113 (35.53%)		92 (44.23%)	177 (39.51%)	
Obese (>=30)	38 (23.75%)	47 (14.78%)		41 (19.71%)	78 (17.41%)	
Missing	*1 (0.63%)*	*6 (1.89%)*		*1 (0.48%)*	*7 (1.56%)*	
Family History of Renal or Bladder Cancer[c]			0.0541			0.6672
Yes	6 (3.75%)	4 (1.26%)		5 (2.40%)	9 (2.01%)	
No	131 (81.88%)	288 (90.57%)		177 (85.10%)	406 (90.63%)	
Missing	*23 (14.38%)*	*26 (8.18%)*		*26 (12.50%)*	*33 (7.37%)*	
Smoking (Pack Years)			0.1274			<.0001
0	59 (36.88%)	130 (40.88%)		38 (18.27%)	187 (41.74%)	
>0-30	10 (6.25%)	32 (10.06%)		12 (5.77%)	26 (5.80%)	
>31-45	12 (7.50%)	10 (3.14%)		11 (5.29%)	12 (2.68%)	
>46-64	7 (4.38%)	16 (5.03%)		15 (7.21%)	20 (4.46%)	
>65	72 (45.00%)	129 (40.57%)		130 (62.50%)	203 (45.31%)	
Missing	*0 (0%)*	*1 (0.31%)*		*2 (0.96%)*	*0 (0.00%)*	
Alcohol Consumption (average drinks/week)	3.48 (3.22)	3.21 (3.28)	0.3627	4.43 (4.07)	3.39 (3.64)	0.0021
Missing	*30 (18.75%)*	*57 (17.92%)*		*40 (19.23%)*	*76 (16.96%)*	

Epidemiological Variable	Renal Cancer Study Population			Bladder Cancer Study Population		
	Cases (N = 160)[a]	Controls (N = 318)[a]	p-value[b]	Cases (N = 208)[a]	Controls (N = 448)[a]	p-value[b]
Lifetime Recreational Inactivity			0.0198			0.016
Active	71 (44.38%)	177 (55.66%)		78 (37.50%)	213 (47.54%)	
Inactive	89 (55.63%)	141 (44.34%)		130 (62.50%)	235 (52.46%)	

[a] Numbers may not sum to total due to missing data

[b] P-values represent t-test for continuous variables; Chi-square for categorical variables

[c] Family history was defined as first-degree history of renal or bladder cancer, respectively.

Table 2

Odds Ratios and 95% Confidence Intervals Representing the Associations of Lifetime Recreational Physical Inactivity with Renal and Bladder Cancer Risk

Tumor Site	Physical (In)activity Status	Multivariable-Adjusted Models[b]		
		Cases (N[a])	Controls (N[a])	OR (95% CI)
Renal Cancer (n=160 cases; 318 controls)	Active	50	140	1.00
	Inactive	68	102	1.77 (1.10, 2.85)
Bladder Cancer (n=208 cases; 448 controls)	Active	53	176	1.00
	Inactive	**104**	**173**	**1.73 (1.13, 2.63)**

[a]Numbers do not sum to total due to missing data.

[b]Multivariable models were adjusted for age (continuous), BMI (continuous), first-degree family history of renal or bladder cancer (yes/no), smoking pack-years (0, <30, 31-45, 46-64,>65), alcohol consumption (average drinks per week), and sex (male/female).

Table 3

Sex- and Obesity-Stratified Odds Ratios and 95% Confidence Intervals Representing the Associations of Lifetime Recreational Physical Inactivity with Renal and Bladder Cancer Risk.

Sub group	Tumor Site	Physical (In)activity Status	Multivariable-Adjusted Model[b,c]		
			Cases (N[a])	Controls (N[a])	OR (95% CI)
Males	***Renal***	Active	28	50	1.00
		Inactive	42	47	1.32 (0.67, 2.60)
	Bladder	Active	38	80	1.00
		Inactive	80	89	1.62 (0.96, 2.72)
Females	***Renal***	Active	22	90	1.00
		Inactive	26	55	2.18 (1.08, 4.40)
	Bladder	Active	15	96	1.00
		Inactive	24	84	2.03 (0.94, 4.39)
Non-obese (BMI<30)	***Renal***	Active	53	152	1.00
		Inactive	68	113	1.75 (1.03-2.98)
	Bladder	Active	63	181	1.00
		Inactive	103	182	1.70 (1.08-2.69)
Obese (BMI≥30)	***Renal***	Active	18	24	1.00
		Inactive	20	23	1.33 (0.42-4.14)
	Bladder	Active	14	31	1.00
		Inactive	**27**	**47**	**1.34 (0.40-4.44)**

[a] Numbers do not sum to total due to missing data.

[b] Sex-stratified multivariable models were adjusted for age (continuous), BMI (continuous), first-degree family history of renal or bladder cancer (yes/no), smoking pack-years (0, <30, 31-45, 46-64,>65), alcohol consumption (average drinks per week).

[c] Obesity-stratified multivariable models were adjusted for age (continuous), first-degree family history of renal or bladder cancer (yes/no), smoking pack-years (0, <30, 31-45, 46-64,>65), alcohol consumption (average drinks per week),and sex (male/female).