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Research Article

Hypertension in adolescence is not an independent risk factor for renal cancer: A cohort study of 918,965 males

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Abstract

Background: Hypertension has been repeatedly linked to renal cell cancer, independent of overweight and anti-hypertensive drug use, but its role remains unclear, especially within the growing group of relatively young-middle aged renal cancer patients. In order to delineate the role of hypertension in early onset renal cancer, we examined the association of blood pressure measured at age 17 with the incidence of renal cancer.

Methods: Sociodemographic and medical data of 918,965 adolescent males examined for fitness for military service from 1967 to 2005 were linked to the National Cancer Registry in this nationwide population-based cohort study (12,910,585 person years) to obtain cancer incidence. A single measurement of blood pressure at age 17 was stratified as optimal ($<$120/80), normal ($\geq$120/80 $<$ 130/85), high normal ($\geq$130/85 $<$ 140/90), or high ($\geq$140/90). We used Cox proportional hazards modeling to estimate the hazard ratio of the blood pressure categories for renal cancer, adjusted for year of birth, body mass index, origin of parents, and height. We also assessed the role of a clinical diagnosis of persistent hypertension (n = 4223, based on multiple measurements).

Results: Of those who had their blood pressure recorded, 90 examinees developed renal cancer. In a multivariable model, the higher categories of blood pressure were associated with a decreased risk of renal cancer (hazard ratio, 0.32; 95% confidence interval, 0.12-0.84; $P = .021$ for blood pressure $\geq$140/90 vs $<$ 120/80). Furthermore, there was no evidence of increased risk for those with an established diagnosis of hypertension (hazard ratio, 1.28; 95% confidence interval, 0.17-9.50; $P = .81$).

Conclusions: It is unlikely that hypertension in adolescents carries an increased risk for renal cancer. J Am Soc Hypertens 2013;7(4):283–288.

Keywords: Hypertension; adolescence; renal cancer; white coat hypertension; obesity.

Introduction

A history of hypertension has been associated with an increased risk of renal cell cancer (RCC). Elevated blood pressure (BP) in adulthood, regardless of accompanying obesity or anti-hypertensive drug use, showed a dose-response relationship with incidence of RCC in a few case-control and cohort studies.[1–3] The association was evident mainly for stage II hypertension (BP $>$160/100) or medically treated hypertension.[4] However, an association between hypertension originating in adolescence and RCC remains to be demonstrated.

In order to further examine the role of adolescent hypertension, we linked both measured BP values and a clinical diagnosis of hypertension as determined at age 17 in over 900,000 Israeli males, with the Israel National Cancer

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Registry database to obtain the incidence of RCC in early to mid-adulthood. We previously reported that ethnic origin, year of birth, and body mass index (BMI) at age 17 are related to future incidence of RCC. Height showed borderline significance.[5] Consequently, we further analyzed BP as a predictor of RCC adjusted for year of birth, ethnic origin, height, and BMI.

Methods

Study Population

Israeli adolescents are called to recruitment centers, predominantly at age 17, for an obligatory medical board examination to assess their suitability for military service. We restricted the analysis to Jewish males aged 16 to 19 years who were examined from 1967 to 2005; 84% were aged 17 years at examination. We excluded males with any cancer diagnosis before the date of their medical examination. We also excluded those who had no documented BP measurement at age 17 years. The cohort comprised 918,965 adolescent males followed by data linkage for 12,910,585 person years to obtain cancer incidence. The appearance of a first malignancy of any sort during the follow-up excluded further follow-up. Females were not studied because their data were available to us only from 1989 onwards.

Sociodemographic Variables

Baseline adolescent data included year of birth, country of birth, country of origin (father's place of birth or grandfather's place of birth if the father was Israeli-born, grouped as Europe [including countries of emigration from Europe], Asia, Africa, and Israel), socioeconomic status of the city/town/village/settlement (on a 1 [lowest] to 10 [highest] scale as defined by the Central Bureau of Statistics, and grouped as 1–4, 5–7, and 8–10), school type (religious/secular), and years of education.

Anthropometrics

Height and weight, as well as other health data, were measured and recorded during the medical examination. BMI, calculated as weight in kilograms divided by height in meters squared, was grouped in 2.5 kg/m^2 increments (BMI $<$22.5, 22.5–25, 25–27.5, $>$27.5 kg/m^2). Height was categorized into quintiles.

Blood Pressure Recording

Each examinee had a single seated measurement of BP taken at the recruitment center by medical personnel using a standard mercury sphygmomanometer. Measures were available for 918,965 adolescents. BP was analyzed according to adult categories of optimal ($<$120/80), normal ($\geq$120/80 $<$ 130/85), high normal ($\geq$130/85 $<$ 140/90), and high ($\geq$140/90). Being aware of the limitations of a single BP measurement, we also used the military induction health examination computerized database to retrieve the information regarding individuals who received a clinical diagnosis of hypertension at age 17 years, according to accepted criteria (multiple BP measurements above goal).

Ascertainment of Renal Cancer Incidence

We linked the cohort to the Israel National Cancer Registry by way of the personal identification number given to all Israeli citizens at birth or immigration. This population-based registry has been in operation since 1960, and meets internationally accepted requirements for the coding system (ICDO-Version 3) and completeness of data. Reporting is mandatory since 1982, and was excellent before this date; coverage exceeds 93% for solid tumors.[6] We included all malignant tumors of the renal parenchyma, of which the vast majority are ''hypernephroma'' and ''clear cell adenocarcinoma.'' We also included a few cases of kidney cancer that had ''uncertain'' histological classification or ''NOS–not otherwise specified.'' We excluded nephroblastoma (Wilm's tumor), liposarcoma, or transitional cancer of the renal pelvis.

Statistical Analysis

Baseline characteristics are presented in Table 1 for the four BP categories as arithmetic means ($\pm$SD) or as percentages. Cox proportional hazard models were used to estimate the hazard ratios (HR) and 95% confidence interval (CI) for developing RCC, initially with an unadjusted model and subsequently incorporating variables found to be predictors of RCC in a previous analysis.[5] First we introduced year of birth to control for a cohort effect. Then height (in quintiles) and BMI according to 2.5 kg/m^2 increments (as described above) were added to the model, and ethnic origin was included in the final model. Trend tests were undertaken with the BP categories coded as an ordinal variable (Table 2). Log minus log plots for each variable were inspected to verify the assumption of proportionality of the hazards, which was confirmed for all variables studied. Similar models were constructed to assess the risk for those with an established diagnosis of hypertension. IBM SPSS Statistics for Windows, version 19.0 (IBM Corporation, Armonk, NY) software was used for statistical analyses.

Ethics

The Israel Defense Forces Medical Corps Institutional Review Board approved the study. After data linkage at the INCR, personal identifiers were permanently deleted from the computer file so that all analyses were undertaken on anonymous records.