

*Null Results in Brief*Plasma Leptin Is Not Associated with Prostate Cancer Risk¹

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Introduction

Leptin, the adipocyte-produced hormone, has been shown to induce angiogenesis and proliferation in several tissues, and leptin receptors have been demonstrated in the prostate (1, 2). Circulating levels of leptin are strongly related to the amount of adipose tissue and androgenicity (1, 3). We hypothesized that leptin may provide a link between a Western lifestyle often resulting in excess weight, and prostate cancer. In a previous prospective study in The Northern Sweden Health and Disease Cohort, we found a significantly increased risk of prostate cancer up to a relative risk of 2.4 for intermediately elevated levels of plasma leptin (2). The aim of the present study was to investigate the consistency of our previous finding in a different study population while taking putative hormonal confounders into consideration.

Materials and Methods

In a longitudinal study, we used prediagnostic serum samples from 200 cases of prostate cancer and 397 controls in the Janus Project in Norway, for which the procedure for recruitment and blood collection have been described in detail previously (4). Cases, diagnosed at the earliest 3 months after blood collection, were identified through linkage with the Cancer Registry. Two controls were randomly selected from sets matched to the index case on age (± 1 year) and date (± 6 months) at blood sampling and on county. The study was approved by the Research Ethics Committee of Umeå University Hospital.

Leptin was determined with a double antibody radioimmunoassay (Linco Res., St. Louis, MO). Intra-batch coefficients of variation were between 3–5%, and interassay coefficient of variation was 6–12%. Testosterone and estradiol were quantitated by a time-resolved fluoroimmunoassay (DELFLIA; Wallac, Turku, Finland). SHBG³ was quantitated by fluoroimmunoas-

say (AutoDELFLIA; Wallac, Turku, Finland). Samples of matched subjects were analyzed in the same batch, without knowledge of the case-control status.

The relation between the hormones was evaluated by the Pearson correlation analysis. Conditional logistic regression analysis was used to estimate the odds ratios and 95% CIs. Calculations were made with the software SPSS (Chicago, IL). With 200 cases and 400 controls, there is 0.80 power (at a significance level of 0.05) to detect a mean difference in exposure corresponding to an expected odds ratio of disease of 1.84 between the top and bottom quartiles (assuming normal exposure distributions, rare disease, and a loglinear relationship of exposure to disease risk).

Results

The mean age of the subjects at blood collection was 49 years (SD, 7.3), and the mean time between blood collection and diagnosis was 17 years (SD, 5.5). There were weak but significant correlations between leptin and testosterone ($r = -0.11$; $P = 0.007$), and SHBG ($r = -0.09$; $P = 0.02$) but not to estradiol ($r = -0.05$; $P = 0.2$). No significant association between plasma leptin levels and prostate cancer risk was found, either in the whole study group or in strata of age or follow-up time (Table 1). Adjustments for testosterone, estradiol, and SHBG, separately or combined, did not affect the odds ratio estimates.

Discussion

Prostate cancer risk was slightly increased for younger men with the highest levels of leptin and for men with the longest follow-up time. However, at variance with our earlier finding (2), but in accordance with a recent case-control study (5), we found no support for the hypothesis that elevated levels of

Table 1 Odds ratios with (95% CI) of prostate cancer by quartiles of serum leptin

	Odds ratios (95% CI) Quartiles			
	1	2	3	4
Leptin unadjusted	1.00 (ref)	1.0 (0.6–1.6)	0.7 (0.4–1.1)	0.9 (0.6–1.6)
Leptin adjusted ^a	1.00 (ref)	1.0 (0.6–1.7)	0.7 (0.4–1.1)	0.9 (0.6–1.6)
Leptin				
Age < median ^b	1.00 (ref)	1.4 (0.7–2.6)	0.8 (0.4–1.7)	1.4 (0.7–2.7)
Age \geq median	1.00 (ref)	0.7 (0.3–1.4)	0.5 (0.2–1.1)	0.7 (0.3–1.3)
F-U < median ^c	1.00 (ref)	0.7 (0.3–1.5)	0.8 (0.4–1.5)	0.7 (0.4–1.4)
F-U \geq median	1.00	1.4 (0.7–2.6)	0.5 (0.2–1.1)	1.2 (0.6–2.4)

^a Adjusted for serum levels of testosterone, estradiol, and SHBG.

^b Subgroup analysis in two groups according to age. The cut-point was the median age at the time of blood collection (49 years).

^c Subgroup analysis in two groups according to follow-up (F-U) time (time between blood collection and diagnosis for the cases). The cut-point was the median follow-up time (17 years).

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³ The abbreviations used are: SHBG, sex hormone-binding globulin; CI, confidence interval.

circulating leptin are associated with overall increased risk of prostate cancer.

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