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PRINCIPAL INVESTIGATOR: Katrine L. Wallace, M.A.

CONTRACTING ORGANIZATION: University of Illinois  
Chicago, IL 60612-7205

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**INTRODUCTION:**

Prostate cancer has a huge and growing burden of disease, yet its natural history has not been fully elucidated. Several studies have shown a positive association between IGF-1 and prostate cancer, suggesting that perhaps increased levels of this hormone could be considered a risk factor for the disease. The ProCEED study was undertaken to examine whether levels of serum IGF-1 were higher in prostate cancer patients vs patients without prostate cancer.

Prostate cancer cases and non-cancer controls were recruited in a Veteran's Administration general urology clinic setting. Clinical / sociodemographic data and blood draws for ascertainment of laboratory assays were collected during the study visit and by reviewing medical records. Only African-American and Caucasian men over the age of 50 who lived in the state of Illinois were included in the study. Patients were classified as prostate cancer cases if they had recent biopsy-proven adenocarcinoma. Controls were required to have a negative digital rectal exam at the study visit, no history of BPH or prostate cancer, and two normal PSA values (one within one year of study entry). Univariate group means were compared using t-tests or Cochran Mantel-Haenszel tests as appropriate. Multivariable analysis was performed using logistic regression methods, with prostate cancer status as the dependent variable.

## **BODY:**

The final year of the grant was dedicated to statistical data analysis and final report preparation.

## PUBLICATIONS:

- One manuscript was submitted under this grant:

“Racial trends in prostate cancer incidence rates for Illinois and the United States; 1986-2000” Journal of Registry Management, 2006 • Volume 33 • Number 4. 85

- Two additional manuscripts are currently being prepared.

## FUNDING:

- Two additional small grants were secured under this grant, both in 2006:

Paul D. Doolen Graduate Scholarship for the Study of Aging

Midwest Roybal Center for Health Promotion and Behavior Change

## RESEARCH ACTIVITIES AND STATEMENT OF WORK:

Below is the approved statement of work with final updates:

### Task 1. Identification/recruitment subjects – Ongoing until month 30

100% complete - As of the end of the reporting period there were 84 evaluable subjects (59 cases and 25 controls).

### Task 2. Subject Recruitment and Data Collection, Months 2-29

*When patients come in for a 60-minute study visit, the following tasks will take place:*

- i. Informed consent*
- ii. Demographic interview*
- iii. Waist/hip circumference and Height/weight measurement*
- iv. Blood sample*
- v. 24-hour dietary recall*
- vi. Work and social history questionnaire*
- vii. IPAQ exercise questionnaire*
- viii. Block Brief food frequency questionnaire*
- ix. Patient incentive given*

100% complete - Subject recruitment and data collection was completed in 2009 for this study

### Task 3. Determination of serum levels of IGF-1, IGFBP-3, PSA and testosterone, Months 2-29 (for collections and storage), Months 29-31 (for assays and data entry)

100% complete - Laboratory processing was completed in 2010 for this study

Task 4. Statistical Analyses, Months 30-36

100% complete – final results are included in this report

**KEY RESEARCH ACCOMPLISHMENTS OVER THE COURSE OF THE GRANT:**

- Manuscript published: "Racial trends in prostate cancer incidence rates for Illinois and the United States; 1986-2000"  
Journal of Registry Management, 2006 • Volume 33 • Number 4. 85
- Additional funding secured - Paul D. Doolen Graduate Scholarship for the Study of Aging
- Additional funding secured - Midwest Roybal Center for Health Promotion and Behavior Change
- pending two additional manuscripts - currently being prepared

## REPORTABLE OUTCOMES:

A total of 84 subjects were enrolled in the study: 59 prostate cancer cases and 25 controls. Table 1 displays baseline characteristics of the study population. The cases were significantly older than controls (70.6 vs 63.2 years old,  $p=0.0020$ ). Racial makeup was proportional between groups, with mostly African-Americans in both groups (83% cases were African-American vs 84% of controls). Body mass index and waist circumference were comparable between groups. Significantly more cases than controls reported that they were “not working” at the time of the study (84.8% vs 62.5%  $p=0.0053$ ). Controls were more likely to smoke than cases, and cases were significantly more likely to currently drink alcohol at the time of the study visit than controls (64.4% vs 8.3%,  $p<0.0001$ ). Cases were less likely to have graduated from high school than controls (37.3% cases with less than a high school education vs 13.0% of controls,  $p=0.0232$ ). Cases were more likely to have a family history of cancer (overall) and prostate cancer, but these differences between groups were not statistically significant. Cases were more likely than controls to have the following co-morbidities: overactive bladder disorder, erectile dysfunction, degenerative joint disease, and polyps (any location) (all  $p<0.05$ ).

Prostate cases enrolled in the ProCEED study had been seen in the JBVMAC General Urology clinic for the following treatments: hormone therapy (37%), watchful waiting (27%), radical prostatectomy (37%), radiation (22%), brachytherapy (2%). Patients often receive more than one of the aforementioned treatments so the totals are greater than 100%. The total Gleason scores for the prostate cancer cases were distributed as follows: 5 (1.7%), 6 (42.4%), 7 (37.3%), 8 (8.5%), 9 (10.2%).

Table 2 shows that the laboratory data for plasma IGF-1, IGFBP-3 and the IGF-1/IGFBP-3 molar ratio were not statistically significant between groups. Mean free testosterone and mean free PSA were statistically significant between groups, but this is likely due to the prostate cancer disease status.

Table 3 displays the multivariable analysis for the association of prostate cancer and IGF-1. After controlling for covariates that were significant in the univariate analyses (age, current alcohol use, work status, education, free testosterone, free PSA, overactive bladder status, erectile dysfunction status, family prostate cancer history) there was a null association between IGF-1 and prostate cancer status in this predominantly African-American veteran population (OR 1.047, C.I. 1.006-1.089).

**TABLE 1. PATIENT SOCIODEMOGRAPHIC CHARACTERISTICS BY PROSTATE CANCER STATUS**

Variable	CASES (n=59)	CONTROLS (n=25)	p-value
AGE (mean, sd)	70.6 (14.4)	63.2 (6.5)	<b>0.0020*</b>
RACE (n, %)			0.9155**
African-American	49 (83.1)	4 (16.0)	
White	10 (16.9)	21 (84.0)	
BMI (mean, sd)	30.9 (7.7)	29.8 (6.1)	0.2422*
WAIST CIRCUMFERENCE (mean, sd)	109.3 (10.8)	107.3 (11.0)	0.5316*
WORK STATUS			<b>0.0053**</b>
Not working	50 (84.8)	15 (62.5)	
Part time	6 (10.2)	2 (8.3)	
Full time	3 (5.1)	7 (29.2)	
SMOKING STATUS			0.2081**
Smokes currently	17 (28.8)	9 (37.5)	
Never smoked	9 (15.3)	6 (25.0)	
Used to smoke / Quit	33 (55.9)	9 (37.5)	
ALCOHOL STATUS			<b>&lt;0.0001**</b>
Drinks alcohol currently	38 (64.4)	2 (8.3)	
Never drank alcohol	3 (5.1)	10 (41.7)	
Used to drink alcohol / quit	18 (30.5)	12 (50.0)	
EDUCATION LEVEL			<b>0.0232**</b>
Did not graduate HS	22 (37.3)	3 (13.0)	
High school graduate	15 (25.4)	6 (26.1)	
Any college	22 (37.3)	14 (60.9)	
FAMILY HX OF CANCER	31 (52.5)	7 (29.2)	0.0541
FAMILY HX OF PROSTATE CANCER	15 (25.4)	2 (8.3)	0.0821

\*Paired t-test

\*\*CMH = Cochran Mantel-Haenzel test

**Table 2– LABORATORY DATA\***

Variable	CASES (n=59)	CONTROLS (n=25)	paired t-test p-value
IGF-1 (mean, sd)	153.2 (50.7)	166.4 (48.3)	0.2793
IGFBP-3 (mean, sd)	2.9 (0.9)	3.0 (0.7)	0.7450
IGF-1 / IGFBP-3 RATIO (mean, sd)	54.6 (16.9)	56.9 (14.7)	0.5638
FREE TESTOSTERONE (mean, sd)	35.5 (48.3)	52.8 (24.6)	<b>0.0001</b>
FREE PSA (mean, sd)	1.12 (1.86)	0.5 (1.15)	<b>0.0319</b>

\*the N varied for the laboratory testing: IGF-1 test had 58 cases / 24 controls, IGFBP-3 had 59 cases / 25 controls, Free testosterone had 57 cases/ 24 controls, and Free PSA had 33 cases / 24 controls

Table 3 – LOGISTIC REGRESSION OF IGF-1 AND PROSTATE CANCER STATUS

Variable	Point Estimate	p-value	OR (C.I.) for the association of IGF-1 and Prostate Cancer status
IGF-1	0.0459	0.0233	1.047(1.006-1.089)
AGE	-0.0783	0.2187	
ALCOHOL USE	0.9057	0.4727	
WORK STATUS	-0.6217	0.0525	
EDUCATION	-0.7325	0.3649	
FREE TESTOSTERONE	-0.00120	0.9257	
FREE PSA	0.1948	0.5279	
OVERACTIVE BLADDER	-12.7042	0.9641	
ERECTILE DYSFUNCTION	1.5194	0.2367	
FAMILY CANCER HISTORY	-0.3049	0.8390	
FAMILY PROSTATE CANCER HISTORY	-2.6936	0.3516	

## **CONCLUSIONS:**

This study found a null association between IGF-1 and prostate cancer in an older African-American population, after controlling for important covariates.

The current study has a number of limitations that should be mentioned. Participants were enrolled at one Veteran's Administration hospital in a major urban area, and were predominantly low-income and African-American. Thus, the generalizability of our findings to men with prostate cancer seen in non-VA or in other urology settings may be limited. The sociodemographic homogeneity of participants also may limit the generalizability of our findings to the prostate cancer population at large. Additionally, the number of controls enrolled was less than planned due to the difficulty of finding appropriate subjects meeting the criteria. This made it difficult to perform stratified analyses of the IGF-1 levels. As with any case-control study, the subjects' ability to recall information from past behavior, exposures and experiences may be limited, and can affect the quality of the data.