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<thead>
<tr>
<th>a. REPORT</th>
<th>b. ABSTRACT</th>
<th>c. THIS PAGE</th>
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# Table of Contents

Introduction ........................................................................................................4

Body ..................................................................................................................5

Key Research Accomplishments .................................................................7

Reportable Outcomes .....................................................................................8

Conclusions ......................................................................................................12
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:


• 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:


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

*Paired t-test  
**CMH = Cochran Mantel-Haenzel test
### Table 2– LABORATORY DATA*

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

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