Prediagnostic C-Peptide and Risk of Prostate Cancer
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Introduction

Components of metabolic syndrome, including elevated serum insulin and C-peptide levels, seem to affect risk of developing prostate cancer, but inconsistently. Recently, an inverse association was reported in a prospective U.S. study (1), whereas a prospective Norwegian study reported the opposite result that metabolic syndrome predicted prostate cancer (2). We therefore wanted to examine the question, and we investigated the association of prediagnostic C-peptide and risk of developing prostate cancer in a U.S. and Canadian cohort, which was multiethnic and would allow us to explore possible effects of ethnicity on the findings.

Materials and Methods

In 1990 to 1992, we collected blood samples from 760 men who had served as controls in three study centers [San Francisco (United States), Hawaii (United States), and Vancouver (Canada)] of a multiethnic case-control study of prostate cancer (3). We followed these men for prostate cancer occurrence from study enrollment until 2003. Prostate cancer occurred 1 or more years after blood draw in 58 of the men with enough sera for analysis. Men known to be alive and free of prostate cancer at the time the case was diagnosed were matched to each case on age, ethnicity (Black, White, Chinese, and Japanese), and area of residence in a ratio of about four controls for each case. One case was excluded due to an extremely high C-peptide value, leaving 57 cases and 243 controls. Outcome ascertainment was conducted by linkage to state and provincial cancer registries and vital statistics data in California (United States), Hawaii (United States), and British Columbia (Canada).

For each subject, a single 1.0-mL vial of serum was removed from storage in California or Hawaii, packed in dry ice, and shipped to the laboratory of one of us (M.D.P.) at the Lady Davis Institute for Medical Research (Montreal, Quebec, Canada). Laboratory staff used ELISA (Diagnostic Systems Laboratories, Inc.) to analyze samples and were blinded to subject ethnicity, study center, and disease status.

We used SPSS version 11 statistical software (4) for logistic regression analysis, adjusting for age at blood draw. C-peptide values were log transformed to approximate a normal distribution. The study had 80% power to detect a relative risk of 2.88 or greater for the highest versus the lowest tertile, with an \(\alpha = 0.05\), two sided. Tests for interactions were done for age, weight, height, body mass index, waist circumference, study center, ethnicity, and levels of testosterone, free testosterone, percentage free testosterone, and sex hormone–binding globulin.

Results

Prediagnostic levels of C-peptide were similar in cases (mean, 2.22 ng/mL; SD, 1.69) and controls (mean, 2.12 ng/mL; SD, 1.42), although levels did vary by ethnic group, with the highest levels (mean, 2.79 ng/mL; SD, 2.12) in White cases (Table 1). In univariate and age-adjusted analyses, for both continuous and categorical variables, C-peptide was not associated with risk of developing prostate cancer in any ethnic group or in the whole group combined. C-peptide was more strongly negatively correlated with androgens (testosterone and dihydrotestosterone) and sex hormone–binding globulin in cases than in controls (data not shown), although tests for interaction were not statistically significant, and adjustment for these and other variables (e.g., time since last meal, body mass index, waist circumference, caloric intake, and dietary vitamin D intake) did not alter results.

Discussion

We saw no association between C-peptide and risk of prostate cancer. This result supports neither the inverse association reported by Tande et al. (1) nor the positive
C-peptide levels (nanogram per milliliter) by race and disease status, with odds ratios and 95% confidence intervals

<table>
<thead>
<tr>
<th>Race</th>
<th>Cases n</th>
<th>Mean (SD)</th>
<th>Controls n</th>
<th>Mean (SD)</th>
<th>P&gt;0.05</th>
<th>OR (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>All groups</td>
<td>57</td>
<td>2.22 (1.69)</td>
<td>243</td>
<td>2.12 (1.42)</td>
<td>0.18</td>
<td>1.12 (0.59-2.29)</td>
</tr>
<tr>
<td>Black</td>
<td>13</td>
<td>1.67 (0.87)</td>
<td>58</td>
<td>2.03 (1.48)</td>
<td>0.41</td>
<td>0.80 (0.16-3.87)</td>
</tr>
<tr>
<td>White</td>
<td>19</td>
<td>2.79 (2.12)</td>
<td>78</td>
<td>2.38 (1.42)</td>
<td>0.32</td>
<td>1.15 (0.34-3.90)</td>
</tr>
<tr>
<td>Chinese</td>
<td>9</td>
<td>2.50 (2.25)</td>
<td>42</td>
<td>2.42 (1.85)</td>
<td>0.91</td>
<td>1.04 (0.19-5.60)</td>
</tr>
<tr>
<td>Japanese</td>
<td>16</td>
<td>1.83 (1.07)</td>
<td>63</td>
<td>1.66 (0.80)</td>
<td>0.47</td>
<td>1.82 (0.47-7.12)</td>
</tr>
<tr>
<td>Asian†</td>
<td></td>
<td></td>
<td>All groups</td>
<td>57</td>
<td>2.22 (1.69)</td>
<td>243</td>
</tr>
</tbody>
</table>

*Highest tertile compared with lowest (reference) tertile, age adjusted.
†Chinese and Japanese groups combined.

NOTE: Excludes all those diagnosed in the 1st year after enrollment. Abbreviations: OR, odds ratio; 95% CI, 95% confidence interval.

References