Predicting Prostate Biopsy Results

The Importance of PSA, Age, and Race

M. Natalie Grunkemeier, MD, and Robin T. Vollmer, MD

Key Words: Prostate cancer; Prostate-specific antigen; Age; Race; Probability

Abstract

We studied whether age and race have a significant role in predicting the results of prostate biopsy after consideration of prostate-specific antigen (PSA) alone. We evaluated the results of 884 prostate biopsies performed on 695 men, including 188 black men. We used logistic regression analysis to evaluate relationships between presence of cancer in the biopsy specimen and the key predictor variables of PSA, age, and black race. We also evaluated the importance of a Bayes-derived positive predictive value (PPV), which used age- and race-specific values of specificity and sensitivity of PSA and age- and race-specific Surveillance, Epidemiology, and End Results incidences of prostate cancer. In univariate analysis, the Bayes PPV was associated significantly with presence of cancer ($\chi^2 = 216; P \sim .000$); however, serum PSA provided more information ($\chi^2 = 248; P \sim .000$). With serum PSA in the logistic model, the Bayes PPV provided no further information ($P > .08$), and as additional variables, neither age nor black race contributed further information ($P > .1$). Serum PSA provides the most predictive information about the results of biopsy of the prostate, probably because it naturally correlates with age and race. Decisions about whether to biopsy should rest on values of serum PSA and need not consider age and race.

During the past decade, many authors have reported that the sensitivity and specificity of serum prostate-specific antigen (PSA) for the presence of prostate cancer was age- and race-specific. As a result, lower thresholds in PSA have been recommended for evaluating men who are younger or black. Although the best test of whether thresholds in PSA should be tailored to age and race would involve trials that randomly assign men to different thresholds and then examine the outcomes, another way to examine the issue is to see whether the prevalence of tumor in biopsy specimens depends critically on age or race. We present an analysis of biopsy results from more than 600 men, including 188 black men, who underwent biopsies of their prostates, and we report how the results of their biopsies related to PSA, age, and race.

Materials and Methods

Patients

The patients comprised 695 American veterans who underwent biopsies of their prostate at the Veterans Administration Medical Center, Durham, NC, during the time from January 1992 to December 1995. A total of 884 biopsy specimens were obtained; 740 were from needle biopsies and 144 from transurethral biopsies. For needle biopsies, the number of core biopsy specimens ranged from 1 to 10 (median, 6; mean, 5.6). In addition, if any of the men had follow-up biopsies, their results were included. We obtained age data at the time of biopsy, race if it was reported, the value of serum PSA, and the outcome of the biopsy, ie, whether positive or negative for the presence of prostate cancer. Because the
results of digital rectal examination were not recorded consistently in the medical records, we did not obtain this information. If either age or value of serum PSA were missing, the case was deleted from the study.

Bayes Rule for Positive Predictive Value

For each study patient and each biopsy episode we estimated the positive predictive value (PPV) of prostate cancer according to the following formula:

\[
PPV = \frac{1}{1 + \frac{FP \times (1 - P(Ca))}{Sensitivity \times P(Ca)}}
\]

Here FP represents the false-positive probability of PSA, and it was made to be age- and race-specific by using the methods previously reported. P(Ca) represents an age- and race-specific incidence of prostate cancer as reported by the National Cancer Institute–sponsored Surveillance, Epidemiology, and End Results from its Web site (http://cancerseer.cancer.gov/) devcan2001 program. Sensitivity of PSA also was adjusted to be age- and race-specific using methods previously reported.

Statistical Methods

The outcome for this study was the presence of tumor in a set of biopsy specimens of the prostate all performed on 1 occasion, and we used logistic regression to relate the presence of tumor to PSA, to the age- and race-adjusted PPV, and to age and race as raw explanatory variables. All reported P values are for 2-sided tests.

Results

Altogether, there were 884 biopsy occasions for 695 men, which included 188 black men. Table II gives the results of the logistic regression analysis. We found that the type of biopsy, ie, needle vs transurethral specimen, was related significantly to the presence of a positive biopsy result (P = .001), so that all subsequent analyses controlled for this variable. Although the Bayes PPV was related significantly to presence of tumor in the biopsy (\(\chi^2 = 216; P \sim .000\)), PPV provided less information than did PSA, which also was related significantly to a positive biopsy result (\(\chi^2 = 248; P \sim .000\)). With PSA in the model, the Bayes PPV provided no additional information (P > .8). By contrast, with PPV forced into the model, PSA provided significant information (P < 2 \times 10^{-9}). As separate variables, neither age nor race provided further significant information (P > 0.1), and the number of core biopsy specimens also was not related significantly to a positive biopsy result (P > .1). Thus, among these variables and after controlling for the type of specimen, serum PSA was of greatest importance.

![Figure 1](https://academic.oup.com/ajcp/article-abstract/126/1/110/1759989/plot-of-the-probability-of-obtaining-a-positive-needle-biopsy-of-the-prostate-for-carcinoma-vs-prostate-specific-antigen-psa-level. The smooth line comes from a logistic regression model, which used serum PSA as the only explanatory variable and which obtained a nearly perfect fit of our data.)

Table II

<table>
<thead>
<tr>
<th>Variable</th>
<th>Coefficient*</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSA</td>
<td>0.087</td>
<td>~.000</td>
</tr>
<tr>
<td>PPV</td>
<td>—</td>
<td>&gt;.08</td>
</tr>
<tr>
<td>Age</td>
<td>—</td>
<td>&gt;.8</td>
</tr>
<tr>
<td>Black race</td>
<td>—</td>
<td>&gt;.1</td>
</tr>
<tr>
<td>No. of cores</td>
<td>—</td>
<td>&gt;.1</td>
</tr>
</tbody>
</table>

PPV, positive predictive value; PSA, prostate-specific antigen.
* The coefficient is given only if the variable was related significantly to a positive biopsy result, and all analyses controlled for the effect of specimen type, ie, needle biopsy vs transurethral biopsy.

Discussion

Although several have suggested that there be race- and age-specific thresholds in PSA for further evaluation of the prostate for cancer, our results suggest that once PSA has been considered, neither race nor age provides further information.
about the likelihood of finding tumor in a routine set of biopsy specimens of the prostate. The reason that neither race nor age provides more diagnostic information is most likely because of the way in which serum PSA depends on both race and age. PSA is higher in black men, and PSA continuously rises with age. Thus, as a serum marker, PSA naturally incorporates information about race, age, and the presence of tumor.

Yet, it has become clear that PSA is not a perfect predictor for the presence of tumor, much less a perfect predictor of clinically significant tumor. Many men with tumor have normal levels of PSA, and many men without detectable tumor have elevated levels of PSA. For men whose elevated levels of PSA lead to a positive biopsy, it is unclear who requires treatment. Even so, it is clear that once the tumor is detected, PSA provides further important staging and prognostic information.

Although our results do not favor making PSA-based algorithms for biopsy of the prostate race- or age-specific, it still is possible that race and age may have important roles in the way PSA is used for further decisions about treatment and prognosis. Thus, we favor continuing study of the roles that race and age may have in the way PSA is used for treatment decisions, once the diagnosis of cancer has been made.

From Laboratory Medicine, Veterans Administration and Duke University Medical Centers, Durham, NC.

Address reprint requests to Dr Vollmer: Laboratory Medicine 113, VA Medical Center, 508 Fulton St, Durham, NC 27705.

References

17. Fowler JE, Bigler SA, Farabaugh PB. Prospective study of cancer detection in black and white men with normal digital rectal examination but prostate specific antigen equal or greater than 4.0 ng/mL. Cancer. 2002;94:1661-1667.