Increased Low Density Lipoprotein and Increased Likelihood of Positive Prostate Biopsy in Black Americans

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Purpose: Differences in prostate cancer incidence, grade and stage at diagnosis, and survival in black vs nonblack men are well documented. Recent studies indicate that lipids may have a role in oncogenesis, including that of prostate cancer. We investigated the relationship between circulating lipids in black and nonblack patients, and newly diagnosed prostate cancer.

Materials and Methods: The study population included consecutive patients who underwent prostate biopsy for increased prostate specific antigen and/or abnormal digital rectal examination at Atlanta Veterans Affairs Medical Center. Age, race, prostate specific antigen, prostate volume, body mass index, family history, high and low density lipoprotein, triglyceride and cholesterol lowering medications were included in data analysis.

Results: A total of 1,775 men with complete information were included in data analysis. A total of 521 black and 451 white men had positive biopsies. Using 100 mg/dl or less as the referent the adjusted OR reflecting the association of low density lipoprotein and prostate cancer diagnosis in black men was 1.49 (95% CI 1.04–2.13, p = 0.031), 1.51 (95% CI 0.96–2.39, p = 0.076) and 3.24 (95% CI 1.59–6.92, p = 0.002) for low density lipoprotein greater than 100 to 130, greater than 130 to 160 and greater than 160 mg/dl, respectively. Corresponding results in nonblack men showed no significant association.

Conclusions: Increased serum low density lipoprotein is associated with an increased likelihood of prostate cancer diagnosis in black men but not in nonblack men. This association is strongest in the highest low density lipoprotein risk category. The reasons for the racial differences are unknown but may include genetic, dietary or other environmental factors.

Key Words: prostate; prostatic neoplasms; African Americans; cholesterol, LDL; risk

Abbreviations and Acronyms

AA = African American
AR = androgen receptor
BMI = body mass index
CaP = prostate cancer
DRE = digital rectal examination
HDL = high density lipoprotein
hMG Co-A = 3-hydroxy-3-methylglutaryl-coenzyme A
LDL = low density lipoprotein
Lp(a) = lipoprotein a
PIN = prostatic intraepithelial neoplasia
PSA = prostate specific antigen
TG = triglyceride
VA = Veterans Affairs

Submitted for publication March 16, 2009.

Study received approval from the Atlanta VA Medical Center research and development committee, and Emory University institutional review board.

* Financial interest and/or other relationship with American Urological Association.

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PROSTATE cancer mortality has decreased steadily since 1994, coinciding with widespread PSA screening. However, CaP remains the most common solid tumor in men and the second leading cause of cancer death in the United States.[1] Because of variation in the CaP incidence worldwide, there is great interest in the role of dietary components and their relationship to prostate carcinogenesis.

Dietary supplements have been a focus of attention based on observations that vitamin E or selenium may prevent CaP.[2,3] However, data from prospective clinical trials show that neither decreases the overall

0022-5347/09/1825-2219/0
THE JOURNAL OF UROLOGY®

Vol. 182, 2219-2225, November 2009
Printed in U.S.A.
DOI:10.1016/j.juro.2009.07.039

risk.[4] Other supplements that have shown promise, such as lycopene and soy, may have protective effects or slow CaP progression.[5] However, larger, well designed trials of these supplements are lacking.

The higher incidence of CaP in Western countries, particularly in AA men, has led many researchers to investigate the role of fat intake and body mass in prostate carcinogenesis. Multiple studies show that immigrant populations in the United States have a higher CaP incidence than native counterparts with implications that diet may have a significant role.[6,7] Recent studies also show that higher BMI is associated with an increased risk of CaP diagnosis and higher grade disease, suggesting that metabolic factors in overweight and obese men may have a significant role.[8,9]

An area of recent interest is the potential role of cholesterol in carcinogenesis and tumor progression. Initial studies of statin drugs showed a decreased incidence of some cancers, including CaP.[10–12] Investigators subsequently postulated that this is due to a decrease in the downstream targets of hMG Co-A reductase metabolism.[13] Statin drugs have been shown to increase HDL and decrease LDL but to our knowledge it is not determined which lipid profile components may or may not confer a risk of CaP. Thus, we analyzed our prostate biopsy database to determine whether measured lipid profile components are associated with CaP diagnosis at biopsy.

MATERIALS AND METHODS

Data Collection

We evaluated data on 2,073 consecutive patients who underwent ultrasound guided prostate biopsy at Atlanta VA Medical Center between January 2000 and June 2007. The study was approved by the Atlanta VA Medical Center research and development committee, and the Emory University institutional review board. Clinical records were reviewed and patient interviews were done at biopsy and entered in a comprehensive database. Indications for biopsy were increased serum PSA and/or abnormal DRE. Biopsies showing only PIN, high grade PIN or atypical small acinar proliferation were excluded from analysis. In patients who underwent more than 1 biopsy only the first biopsy was considered in analysis. Information on fasting lipid profiles was obtained in each patient from VA medical records. All VA patients are screened for dyslipidemia during the annual history and physical examination. The test is done more frequently when indicated clinically. In those with more than 1 lipid profile test the one closest to the biopsy date was used.

Patients were categorized into 4 groups by LDL using American Heart Association cutoffs for cardiovascular risk, including 100, 130 and 160 mg/dl, respectively. LDL was calculated using the Friedewald equation, (LDL = total cholesterol – HDL – TG/5). NonHDL was calculated by subtracting HDL from total cholesterol.

Additional information considered in analysis was age biopsy, total serum PSA, prostate volume, BMI, DRE findings, CaP family history and whether patients were on lipid lowering medication. Race was determined by self-identification and/or military records.

Statistical Analysis

Descriptive frequency analysis was done to examine the distribution of demographic, clinical and pathological characteristics in patients with and without CaP evidence on the biopsy result. These descriptive analyses were done using the t test for continuous variables and the chi-square or Fisher exact test for categorical variables.

The association between positive biopsy and serum LDL was examined by calculating crude and adjusted ORs, and the corresponding 95% CI using logistic regression models. The initial model contained LDL as the main exposure variable plus all potential, a priori selected confounders as well as interaction terms between LDL and all other covariates. We arrived at our final model using the hierarchical backward selection method, which eliminated nonsignificant interaction terms 1 at a time in order of decreasing p values.[14] Only significant interaction terms and all potential confounding variables selected based on a priori criteria were retained in the final model. All regression models were tested for colinearity using condition indexes and variance decomposition proportions. The final model was tested for goodness of fit using the Hosmer-Lemeshow test. All tests were 2-tailed with $p < 0.05$ considered significant. Test of trend was done using LDL as a continuous variable in the model. All statistical analysis was done with SAS®, version 9.1.

RESULTS

Of 2,073 men enrolled in the study 1,775 had complete data available for the multivariate logistic model, including 972 (46.9%) with CaP confirmed on pathological evaluation. Of the men 1,101 (53.1%) had negative biopsy. Table 1 lists study population descriptive characteristics. Patient age was 40 to 89 years (mean 64, median 63). Measured PSA varied widely from 0.1 to 5,000 ng/ml but 90% of patients had PSA less than 16 ng/ml.

As expected, age, high PSA and abnormal DRE were associated with increasing odds of CaP (table 2). The adjusted OR for age greater than 65 years, PSA 4 to 10 ng/dl and PSA greater than 10 ng/dl was 1.55, 7.37 and 22.24, respectively ($p < 0.001$). Normal DRE and large prostate volume were associated with lower odds of positive biopsy. The odds of positive biopsy in those with normal DRE were about half the odds in those with abnormal DRE (OR 0.58, $p < 0.001$). Similarly compared with men with a prostate volume of 30 cm^3 or less the adjusted OR in