A Population-Based Study of Men With Low-Volume Low-Risk Prostate Cancer: Does African-American Race Predict for More Aggressive Disease?

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Abstract

We used the Surveillance, Epidemiology, and End Results database to identify 1794 men with low-risk low-volume prostate cancer who underwent surgery. We compared the pathologic findings according to race and found no significant differences in pathologic stage or grade between African-American and Caucasian men. These data support the continued use of active surveillance in the African-American population.

Background: Because of recent reports that suggested more pathologically aggressive disease in African-American (AA) men, we sought to compare pathologic features between AA and Caucasian-American men with low-risk, low-volume prostate cancer. **Materials and Methods:** We analyzed the Surveillance, Epidemiology, and End Results database for pathologic differences based on race. Data on all men who were diagnosed between 2010 and 2011 with prostate cancer, T1cN0M0, Gleason score of 6 (3+3), prostate-specific antigen < 10 ng/mL, via a 12-core biopsy and had ≤ 2 positive samples, and underwent radical prostatectomy were abstracted. Univariate and multivariate logistic regression were performed to detect predictors for adverse pathology, which was primarily defined as pT2 and Gleason $\geq 4+3$, or pT3a and Gleason 3+3 with positive margins, pT3a and Gleason $\geq 3+4$, or pT3b-pT4 with any Gleason score. **Results:** There were 1794 men who met the target study criteria. AA men were a median of 3 years younger ($P < .001$), and were more likely to have 2 positive cores ($P = .02$). However, there were no statistically significant differences between Caucasian and AA men regarding pathologic Gleason score ($P = .99$), pathologic extent of disease ($P = .34$), margins ($P = .43$), Cancer of the Prostate Risk Assessment score ($P = .56$), or adverse features ($P = .45$). On multivariate analysis, there were no differences between AA and Caucasian men with regard to adverse pathologic features (odds ratio, 1.43; 95% confidence interval, 0.87-1.24; $P = .16$). **Conclusion:** In the absence of definitive data to support a more aggressive natural history of very low risk prostate cancer in AA men, these data support continued use of active surveillance in this population.

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Introduction

Multiple recent studies have suggested that active surveillance is a viable alternative to active treatments for very low-risk prostate cancer.[1] This has led to its adoption as part of the management algorithm in the United States by the National Cancer Care Network (NCCN),[2] and in Europe by the European Association of Urology.[3] However, the applicability of these guidelines to African-American (AA) men is less clear. Men with AA race have been reported to have increased incidence and mortality from prostate cancer compared with Caucasian (CA) men.[4] In fact, several recent studies that compared outcomes have confirmed that AA men appear to do worse than their CA counterparts.[5-7]

Further adding to the concern are several recent studies, specifically pertaining to active surveillance, reporting that AA men

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are at greater risk for more aggressive pathologic features, clinical progression during surveillance, and/or biochemical recurrence.[8-10] This has led to some concern regarding the applicability of the current active surveillance guidelines to the AA population. The available studies to date have been single-institution and are limited by relatively low patient numbers. The largest such study was by Sundi et al, who reported on 1801 men treated since 1992.[8] However, in their subset of patients reflecting modern practice with $\geq$ 10 biopsy samples there were far fewer patients (223 CA, 101 AA, 35 other).

In the current study we sought to use the Surveillance, Epidemiology, and End Results (SEER) database to identify patients with clinically very low-risk prostate cancer and analyze whether race plays a role with regard to pathologic upstaging to more aggressive disease or Gleason score upgrading to higher-risk disease.

Materials and Methods

Surveillance, Epidemiology, and End Results is a National Cancer Institute program that collects and reports on the incidence and survival from regional cancer registries across the United States, representing approximately 26% of the United States population. Demographic, clinical, and pathologic parameters, and survival outcomes are all abstracted, deidentified, and made accessible to the public.

Since 2006, SEER has collected the primary and secondary Gleason score, and the serum prostate-specific antigen (PSA) at diagnosis. The coding of the Gleason score was designed to be based on the largest sample. Therefore, patients who underwent surgery had their pathologic Gleason scores reported from the surgical specimen, whereas those who did not undergo surgery had their biopsy scores reported. Starting in 2010, SEER started separately collecting the biopsy and pathologic Gleason scores. Furthermore, starting in 2010, SEER started identifying how many cores were used in the prostate biopsy and how many of these cores were positive. Therefore, in this study we were able to select patients with very low-risk prostate cancer, who closely mimic the optimal candidates for active surveillance according to the NCCN.[2] These patients were diagnosed with T1cNx-0Mx-0 adenocarcinoma of the prostate and underwent radical prostatectomy as their definitive treatment. They had to be diagnosed via $\geq$ 12 core biopsy and the prostate cancer was limited to $\leq$ 2 positive cores. The biopsy Gleason score of all patients was 6 (3+3) and their presenting PSA was $<$ 10 ng/mL. The NCCN guidelines do also recommend a PSA density $<$ 0.15 ng/mL/g and $\leq$ 50% cancer in any positive core. However, these 2 parameters are not available in the SEER database.

There were 8444 men who underwent a radical prostatectomy for T1cN0M0 low-risk prostate cancer, with a Gleason score of 6 and a PSA $<$ 10 ng/mL from 2010 to 2011. After excluding patients who did not have complete pathologic data regarding their T-stage or pathologic Gleason score, there were 8401 patients remaining. Of the remaining patients, 4910 (58.4%) men had codes that identified the number of biopsy cores sampled, and of these, 3734 men had $\geq$ 12 biopsy samples. A total of 3541 of these men had codes that identified the number of cores positive and of these 1794 had $\leq$ 2 positive biopsy cores, thus comprising our targeted study cohort.

The demographic information abstracted included race (CA or AA), age, SEER registry, and year of diagnosis. The additional clinical and pathologic information abstracted included the pathologic T-stage, margin status, and pathologic lymph node status.

We used χ^2 or Mann–Whitney test where appropriate to compare patient characteristics, pathologic upstaging, pathologic stage, and pathologic margin status according to race. We also analyzed adverse pathology as one metric, defined previously as pT2 and Gleason $\geq$ 4+3, or pT3a and Gleason 3+3 with positive margins, or pT3a and Gleason $\geq$ 3+4, or pT3b-pT4 with any Gleason score.[8] In addition, we calculated the Cancer of the Prostate Risk Assessment score (CAPRA-S) for each patient.[11] In this calculation, a PSA $>$ 6 ng/mL was assigned 1 point, positive surgical margins was assigned 2 points, seminal vesicle invasion was assigned 2 points, extracapsular extension was assigned 1 point, and Gleason score was assigned 1 point for Gleason 3+4, 2 points for Gleason 4+3, and 3 points for Gleason 8 to 10. Univariate and multivariate logistic regression analyses were performed to detect predictors for adverse pathology. Variables used included race, PSA, biopsy Gleason score, age, and percentage of positive cores. Because so many patients were excluded based on not having the codes for the total number of biopsy cores sampled or positive, we also repeated all analyses including the entire cohort of 8401 patients. Statistical significance was defined as $P < .05$. All analyses were performed using SPSS version 21.0 (IBM Inc, Armonk, NY).

Results

There were a total of 8401 men with low-risk prostate cancer and 1794 patients who met the selection criteria including data regarding prostate biopsy cores, of whom 1565 (87.2%) were CA and 229 (12.8%) were AA (Table 1). The median age of all patients was 59 years (interquartile range, 54-64 years) and the median PSA was 5 ng/mL (interquartile range, 4.1-6.3). The median age of AA men was 3 years younger than CA men ($P < .001$) and AA men were more likely to have 2 positive biopsy samples than CA men ($P = .02$). However, there were no statistically significant differences between CA and AA men with regard to the pathologic Gleason score ($P = .99$), pathologic extent of disease ($P = .34$), margins ($P = .43$), CAPRA-S score ($P = .56$), or adverse features ($P = .45$). There were noted to be significant differences in distribution of AA and CA men based on the location of each SEER registry ($P < .001$), with 4 registries including 0 AA men who met the selection criteria.

On univariate and multivariate logistic regression, only increasing PSA and increasing age were significant predictors for adverse pathology (Table 2). AA race was not predictive for adverse pathologic features on univariate (odds ratio [OR], 1.19; 95% confidence interval [CI], 0.75-1.88; $P = .45$) or multivariate analysis (OR, 1.43; 95% CI, 0.87-2.33; $P = .16$). The percentage of positive cores was also not predictive for adverse pathology in univariate or multivariate analysis (OR, 1.19; 95% CI, 0.86-1.66; $P = .29$). The logistic regression was also run using the percentage of positive cores as a continuous variable and it remained nonsignificant. None of the SEER registry locations were found to be significant predictors for adverse pathologic features.

Because of the high number of patients initially excluded because of missing codes regarding the number of biopsy cores or the number of positive biopsy cores, we performed an additional