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Original article

African American men with low-grade prostate cancer have increased disease recurrence after prostatectomy compared with Caucasian men

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Abstract

Purpose: To explore whether disparities in outcomes exist between African American (AA) and Caucasian (CS) men with low-grade prostate cancer and similar cancer of the prostate risk assessment—postsurgery (CAPRA-S) features following prostatectomy (RP).

Methods: The overall cohort consisted of 1,265 men (234 AA and 1,031 CS) who met the National comprehensive cancer network criteria for low- to intermediate-risk prostate cancer and underwent RP between 1990 and 2012. We first evaluated whether clinical factors were associated with adverse pathologic outcomes and freedom from biochemical failure (FFbF) using the entire cohort. Next, we studied a subset of 705 men (112 AA and 593 CS) who had pathologic Gleason score ≤ 6 (low-grade disease). Using this cohort, we determined whether race affected FFbF in men with RP-proven low-grade disease and similar CAPRA-S scores.

Results: With a median follow-up time of 27 months, the overall 7-year FFbF rate was 86% vs. 79% in CS and AA men, respectively ($P = 0.035$). There was no significant difference in one or more adverse pathologic features between CS vs. AA men (27% vs. 31%; $P = 0.35$) or CAPRA-S score ($P = 0.28$). In the subset analysis of patients with low-grade disease, AA race was associated with worse FFbF outcomes ($P = 0.002$). Furthermore, AA race was a significant predictor of FFbF in men with low-grade disease (hazard ratio = 2.01, 95% CI: 1.08–3.72; $P = 0.029$).

Conclusions: AA race is a predictor of worse FFbF outcomes in men with low-grade disease after RP. These results suggest that a subset of AA men with low-grade disease may benefit from more aggressive treatment.

Keywords: African American race; Disparities; Biochemical failure; Adverse pathologic features

1. Introduction

Men of African descent are known to experience greater incidence of and mortality due to prostate cancer (PCa) than men of other races [1]. African American (AA) men have been shown to experience PCa at an earlier age than Caucasian (CS) men. Furthermore, AA men often present with higher grade and stage of disease at the time of diagnosis [2]. This observation has been partly attributed to socioeconomic factors and inadequate access to health care [3]. However, there is recent evidence suggesting that differences in genetic susceptibility play a major role in this disparity [4,5].

Owing to the relatively indolent nature of most PCas diagnosed in the United States, the decision-making process for determining whether to pursue active surveillance (AS) or alternative management options is complicated by the balance between the life expectancy, comorbidities, clinical

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benefits and side effects of treatment [6]. The ability to predict clinical outcomes is critical in recommending appropriate treatment options for patients with PCa. Current National Comprehensive Cancer Network (NCCN) guidelines recommend AS as the preferred option for very low-risk PCa in men, defined as prostate-specific antigen (PSA) <10 ng/ml, clinical stage $\leq$T1c, Gleason score (GS) ≤ 6, positive cores ≤ 2, and cancer involvement of $\leq 50\%$ per core. The goal of these recommendations is to prevent overtreatment of indolent cancers while identifying patients who develop disease progression and offering treatment with curative intent. However, most predictive tools currently used to risk stratify patients with PCa for treatment recommendations have not been developed or validated in AA men [7]. Furthermore, randomized clinical trials reporting on low-risk PCa treatment outcomes have been unable to effectively address whether interventions depend on race because of the inadequate numbers of AA participants [8].

Whether AA race acts as a prognostic factor for freedom from biochemical failure (FFbF) in patients with pathologic GS $\leq$ 6 disease (referred to here as low-grade disease) and minimal adverse pathologic features after prostatectomy (RP) is poorly understood. The goal of this study is to determine whether disparities in adverse pathologic features and FFbF outcomes exist among an identical cohort of AA and CS men using a prospective cohort of patients with PCa treated with RP.

2. Patients and methods

2.1. Patient selection

The present study is a retrospective analysis of a prospective cohort of 2,012 men (298 AA, 1,673 CS, and 41 other race) with PCa treated with RP at the University of Pennsylvania Health System (UPHS; Philadelphia, PA) recruited to the Study of Clinical Outcomes, Risk and Ethnicity between 1990 and 2012 [9]. Patients without adequate preclinical data including initial PSA or biopsy GS at diagnosis were excluded from the analysis ($n = 457$). Patients of non-CS and non-AA ethnicity were excluded ($n = 41$). Patients with the following criteria were excluded from the study ($n = 249$): tumors $>$T3 category, GS between 7 (4 + 3) and 10, PSA level $\geq$20 ng/ml, or regional lymph node metastasis on imaging or following bilateral pelvic lymph node dissection. We selected the remaining 1,265 patients for this study, which comprised the overall cohort who met the following NCCN criteria for low- to intermediate-risk PCa: biopsy GS $\leq$ 7 (3 + 4), T-stage $\leq$T2c, PSA $\leq$ 20 ng/ml, and undergoing a RP [10]. Of the 1,265 patients, a subset of 705 men (112 AA and 593 CS) with pathologic GS $\leq$ 6 (low-grade disease determined post-RP) was further analyzed in this study. We selected low- to intermediate-risk patients in the overall cohort to include patients with biopsy GS 7 (3 + 4) who were downgraded to pathologic GS 6 (3 + 3) following RP.

2.2. Preoperative staging

The patients were evaluated at the time of diagnosis by a thorough history and physical examination (including digital rectal examination) followed by routine laboratory studies, including serum PSA levels and GS determined by needle biopsy, and were reviewed at the UPHS. All the patients were staged according to the 1992 American Joint Committee on Cancer staging system [11].

2.3. Treatment

Surgical treatment consisted of a radical retropubic RP or robotic-assisted radical RP and bilateral pelvic lymph node sampling. All pathology slides were prepared as per standard institutional protocol. The RP specimen was initially coated with india ink and fixed in formalin. The whole gland was step-sectioned at 3-mm intervals and the resulting sections were fixed into tissue cassettes. Tissue sections were embedded in paraffin blocks, from which sections were prepared and stained with hematoxylin and eosin for routine histologic analysis by a dedicated genitourinary pathologist. Adverse pathologic features consisting of extraprostatic extension (EPE), seminal vesicle invasion (SVI), and surgical margin status (SM) were noted and recorded. At the discretion of the treating physician, patients with adverse pathologic features including EPE, SVI, or positive surgical margins were treated with adjuvant radiation therapy (RT) or androgen deprivation therapy (ADT) or a combination of both. ADT consisted of a gonadotropin-releasing hormone agonist (leuprolide acetate or goserelin acetate) with or without an antiandrogen (e.g., flutamide and bicalutamide).

2.4. Follow-up and treatment end points

Patient information at each follow-up visit including digital rectal examination and serial PSA values were noted and recorded. PSA failure was defined as a single PSA $\geq$ 0.2 ng/ml along with documentation of failure by a physician or when 2 consecutive PSA values of 0.2 ng/ml were obtained after an undetectable value. Start of the prospective follow-up (i.e., time zero) was defined at the date of surgery for all patients. If PSA was never undetectable postoperatively, then PSA failure was assigned at time zero. Patients with no follow-up PSA measurements ($n =$ 190, 14.5%) were included for the evaluation of differences in preoperative and pathologic characteristics but not for the analysis on FFbF outcomes.