Published in final edited form as:

Urology. 2009 September ; 74(3): 660–664. doi:10.1016/j.urology.2008.10.075.

Significant Change in Predicted Risk of Biochemical Recurrence After Radical Prostatectomy More Common in Black Than in White Men

Melissa A. Laudano, Ketan K. Badani, Tara R. McCann, Mark J. Mann, Chad Ritch, Manisha Desai, Mitchell C. Benson, and James M. McKiernan

Department of Urology, Columbia University Medical Center; and Department of Biostatistics, Columbia University Mailman School of Public Health, New York, New York

Abstract

OBJECTIVES—To examine by race how frequently the data after radical prostatectomy translates into a substantial change in prognosis. Many nomograms exist to predict the survival outcomes using the pretreatment clinical parameters and post-treatment pathologic parameters. Race might be an important factor affecting their predictive ability.

METHODS—Kattan nomograms were used to calculate the pretreatment and post-radical prostatectomy 5-year progression-free probability for each patient. The difference between the nomogram scores was used to divide the patients into 3 groups. A decrease in probability of 15 percentage points was classified as a significant increase in the probability of recurrence, an increase of 15 points was classified as a significant decrease in the probability of recurrence, and an absolute change of <15 points was considered no significant change.

RESULTS—The data from 1709 (132 black and 1577 white) men were analyzed. Among the black men, 26.5% had an increase in the probability of recurrence, 57.6% had no change, and 15.9% had a decrease in the probability of recurrence. Among the white men, 13.8% had an increase in the probability of recurrence, 64.5% had no change, and 21.7% had a decrease in the probability of recurrence. Black men were twice as likely to have a significant increase in the probability of recurrence postoperatively compared with white men after adjusting for preoperative prostate-specific antigen level, clinical stage, and biopsy Gleason sum (odds ratio 2.0, 95% confidence interval 1.3–3.1, $P = .002$).

CONCLUSIONS—These data could assist clinicians when counseling black men regarding their treatment options according to their preoperative risk profile.

Prostate cancer (CaP) is the most common solid organ tumor in the United States, with approximately 186 320 new cases expected during 2008.¹ Racial differences in the incidence of CaP have been well described in published studies. Black men are almost 2 times as likely to be diagnosed with CaP compared with white men (255.5/100 000 men vs 161.4/100 000 men, respectively).¹ Additionally, the cancer-related mortality rate for black men vs white men is 62.3 and 25.6 per 100 000, respectively.¹

Although this racial discrepancy in mortality from CaP has been well described, the underlying cause for this difference remains unknown. The present analysis explored a novel issue in the management of CaP in black men. When counseling all patients with CaP, the preferred treatment modality is often chosen according to the available preoperative variables, including prostate-specific antigen (PSA) level, Gleason sum, and clinical stage. Therefore, an accurate preoperative assessment is crucial for appropriate decision making regarding treatment. The postoperative radical prostatectomy (RP) specimen provides the opportunity for definitive data to assess the risk of recurrence, making postoperative outcome models the reference standard for determining the postoperative biochemical disease-free survival (DFS).

The purpose of this study was to describe how frequently the postradical prostatectomy data translates into a substantial change in the prognosis and to determine whether this phenomenon occurs more frequently in black than in white men. The secondary objective was to determine the postoperative parameters that drive the change in risk.

MATERIAL AND METHODS

The institutional review board-approved, Columbia University Comprehensive Urological Oncology database was reviewed; 3663 patients had undergone radical retropubic prostatectomy from 1988 to 2007. From the database, 1709 patients with the self-reported racial designation of black or white who had complete information necessary for the calculation of the 1997 pretreatment and post-RP risk of biochemical failure using the Kattan CaP nomograms were included. Initially, the preoperative and postoperative nomogram scores were compared for the entire cohort. Then, the population was stratified to consider the variations in nomogram scores by race. The necessary parameters for the nomograms included preoperative PSA level, clinical stage, biopsy Gleason sum, pathologic Gleason sum, extraprostatic extension, margin status, and seminal vesical and lymph node involvement.

The predictive nomograms defined by Kattan et al.^{2,3} were used to calculate the pretreatment and post-RP 5-year progression-free probabilities after RP. Progression-free probability was defined in both the nomogram and the present study as biochemical DFS. Patients who were disease free had no evidence of biochemical (detectable PSA level of 0.2 ng/dL) or clinical recurrence. The pretreatment and post-RP DFS probability scores were calculated and compared for each patient. Patients with a decrease in probability of 15 percentage points were classified as having a significant increase in the probability of recurrence, patients with an increase of 15 points were classified as having a significant decrease in the probability of recurrence, and those patients with an absolute change of 15 points were deemed to have no significant change in probability.

Within the black cohort, the percentage of men within each of the 3 possible groups was calculated. The same was done for the white cohort. Additionally, the mean change in probability (postoperative subtracted from preoperative) was calculated for the black and white groups. Thus, a positive value signified an increased probability of recurrence calculated when the postoperative parameters are known. A negative value signified a

decreased risk of recurrence with postoperative information. The odds of having a greater postoperative risk of recurrence than was predicted preoperatively were compared between racial groups using the odds ratio.

Statistical significance was set at $P = .05$ for all analyses. The analyses were performed using Stata SE, version 9.0 (StataCorp LP, College Station, TX).

RESULTS

The study included 1709 patients with a median age of 61.45 years (range 36.50–76.49) and a median follow-up time of 38 months (range 0–195). The mean pretreatment and post-RP progression-free probability was 80.6 (range 2–99) and 83.3 (range 1–99) for all patients. Of the entire cohort, 1093 (64.0%) had no significant change in the nomogram score, 253 (14.8%) had a significant increase in the probability of recurrence, and 363 (21.2%) had a significant decrease in the probability of recurrence. Thirty-seven patients (2.2%) had identical pre-and post-RP nomogram scores. Of the 253 patients with an increased probability of recurrence, 211 (83.4%) had worsened progression-free probability, as represented by a decrease of 20%, 182 (71.9%) had a decrease of 25, and 163 (64.4%) had a decrease of 30. The pretreatment and post-RP patient characteristics are detailed in Table 1.

The cohort was then stratified by race. Of the whole cohort, 132 (7.7%) were black, with a median follow-up of 47 months, and 1577 (92.3%) were white, with a median follow-up of 38 months. A comparison of the preoperative characteristics for the black and white groups was performed (Table 2). Of the black men, 35 (26.5%) had a significant increase in the probability of recurrence by 15% postoperatively. Conversely, 21 black patients (15.9%) had a significant decrease in the probability of recurrence by 15% after RP. Finally, 76 (57.6%) had no significant change in the probability of recurrence from the preoperative to the postoperative prediction (Fig. 1). Of the white patients, 218 (13.8%) had a significant increase in the probability of recurrence by 15% from the preoperative to the postoperative score. Also, 342 white patients (21.7%) had a significant decrease in the probability of recurrence by 15%. Finally, 1017 white men (64.5%) had no significant change (Fig. 1). The distribution of black men with a significant increase, no change, and a significant decrease was significantly different than that for the white men ($P < .001$).

In the black cohort, the mean pretreatment and post-RP progression-free probability was 79.2 (range 15–93) and 73.9 (range 1–99), respectively. In the white patients, the mean pretreatment and post-RP progression-free probability was 80.8 (range 2–99) and 84.1 (range 1–99), respectively. When comparing the mean change in probability, black men had a mean difference of +5.4 (95% confidence interval 1.0–9.8), signifying a significant increase in the probability of recurrence as predicted by the postoperative nomogram. In contrast, white men had a mean difference of –3.3 (95% confidence interval –4.4 to –2.3), signifying a slight improvement in their probability of being disease free (Student's t test; $P < .001$). Additionally, black men were twice as likely to have a significant increase in the probability of recurrence postoperatively compared with white men, even after adjusting for the preoperative PSA level, clinical stage, and biopsy Gleason sum (odds ratio 2.0, 95%

confidence interval 1.3–3.1, $P = .002$). After noting this racial discrepancy, the factors driving the significant increase in the risk of recurrence among black men was explored. The pathologic parameters that significantly contributed to the increase in the probability of recurrence seen more frequently in black men were an increase in the risk of discovering positive lymph nodes and positive surgical margins (Table 3). Differences in biopsy vs pathologic Gleason sum, extraprostatic extension, and seminal vesicle invasion did not significantly contribute to the increase in probability of recurrence seen more commonly among black patients.

COMMENT

Accurate risk predictions both pre- and postoperatively are central to effective patient counseling and optimal management. Underestimating the risk of recurrence in black patients using current preoperative predictive models could lead to suboptimal treatment selection and subsequently contribute to the greater rates of mortality from CaP seen among black men. The present study sought to determine the frequency with which information gained at RP revealed a substantially increased risk of biochemical recurrence in black vs white patients.

In the pretreatment period, the burden of disease can only be determined by the prognostic variables available at the initial assessment such as the PSA level, biopsy Gleason sum, and clinical stage. Typically, the preoperative variables correlate with the postoperative data discovered at RP. A pathologic evaluation of 499 biopsy and associated RP specimens evaluated for concordance at a university medical center revealed that a Gleason sum of <7 predicted for the same Gleason sum 63.9% of the time.⁴ However, that study did not comment on the predictive ability of biopsy in different racial groups. The assessment of disease stage is also subject to change after RP, with the additional knowledge of surgical variables such as extracapsular extension, seminal vesicle involvement, and nodal status.

These preoperative and postoperative variables individually affect DFS and are synthesized in the preoperative and postoperative outcome nomograms developed by Kattan et al.² and others.⁵ The predictive principles of the Kattan nomograms were derived from 983 patients who underwent RP by a single surgeon at a tertiary referral center.² This nomogram was subsequently validated as an outcome model at multiple academic institutions.^{6,7} In an international and multi-institutional study, the predicted outcome and actuarial recurrence differed by $<5\%$ in patients with low- to high-risk CaP. The present study used the Kattan nomograms as outcome models to compare the predicted DFS as determined from the clinical parameters and the predicted DFS as determined from the pathologic parameters. Therefore, a significant decrease from the pre- to postoperative nomogram scores reflected inaccurate preoperative prediction of the postoperative parameters. It did not indicate an inadequacy of the predictive model itself.

The racial disparity seen in the predictive accuracy of the preoperative model can be attributed to differences in the pathologic disease characteristics, which can only be detected after surgical intervention. Sanchez-Ortiz et al.⁸ reviewed the RP specimens from 37 black men with clinical Stage T1c disease and compared them with those from 35 white men

matched for age, clinical stage, PSA level, year of surgery, prostate weight, and prostate biopsy strategy. The black men had a significantly greater pathologic Gleason sum (7 in 76% of black men vs 34% of white men; $P = .01$).⁸ The black patients also had a greater mean tumor volume and had 2.8 times more tumor per 1 ng/mL of serum PSA. That study suggested that some preoperative parameters used to calculate risk, such as PSA level and clinical stage, might not predict for adverse pathologic parameters as accurately in black men.

Similar variations in pathologic outcomes after RP were seen in black men compared with white men in a study performed by Eastham et al.⁹ In that study of 129 consecutive men (56 black men and 73 white men), no statistically significant differences were found by race in patient age, serum PSA level, biopsy Gleason sum, pathologic stage, incidence of lymph node metastases, or incidence of positive surgical margins. However, the pathologic Gleason sum was more heterogeneous in black men than in white men ($P = .02$).⁹ This finding suggests that random prostate biopsies used as a parameter in the preoperative nomogram score might be less accurate at predicting the true pathologic features in black men.

The preoperative nomogram has been called the most widely used disease-specific prediction tool in oncology, which highlights the importance of understanding its limitations.¹⁰ The accurate preoperative prediction of DFS is especially important in patients with low- to moderate-grade disease, because many of these patients might be considered appropriate candidates for nonextirpative management or local ablative therapy, such as radiotherapy or cryotherapy, which do not allow for pathologic confirmation of the disease status.¹¹ With the potential lack of pathologic data to confirm the actual disease status, it is essential to recognize the frequency of a major discrepancy between the preoperative and postoperative risk and how this divergence might vary by race. In the present study, 26.5% of black men had a 15% increase in the predicted risk of biochemical recurrence after analysis of the postoperative parameters. In contrast, an increased risk of recurrence was only seen in 13.8% of white men.

One limitation of the present study was the relatively small number of black patients included in the analysis ($n = 132$). However, black men were 7.7% of the entire cohort, which was reasonable given that the 2000 United States census reported that black men were 12.3% of the general American population. The variation from this nationwide value can be explained by differences in the demographics in the patient population served by our institution. Additionally, additional research is needed to correlate the racial disparities in the accuracy of the preoperative nomograms with the differences in outcomes (biochemical recurrence and death from CaP). The information presented in the present study combined with outcomes data will be pertinent to counseling patients of different races in decision making before therapeutic intervention for localized CaP.

CONCLUSIONS

In the present study, we found that black patients had 2 times the odds of having a significant increase in the risk of recurrence of CaP described only after postoperative data were available compared with white men. The pre-operative parameters significantly

underestimated the probability of recurrence in 13.8% of the white and 26.5% of the black patients. The factors that contributed significantly to the increased risk of recurrence seen in blacks postoperatively were the discovery of positive lymph nodes and positive surgical margins. These data might assist clinicians when counseling black men regarding the treatment options according to their preoperative risk profile.

References

1. Jemal A, Siegel R, Ward E, et al. Cancer statistics, 2008. *CA Cancer J Clin.* 2008; 58:71–96. [PubMed: 18287387]
2. Kattan MW, Eastham JA, Stapleton AM, et al. A preoperative nomogram for disease recurrence following radical prostatectomy for prostate cancer. *J Natl Cancer Inst.* 1998; 90:766–771. [PubMed: 9605647]
3. Kattan MW, Wheeler TM, Scardino PT. Postoperative nomogram for disease recurrence after radical prostatectomy for prostate cancer. *J Clin Oncol.* 1999; 17:1499–1507. [PubMed: 10334537]
4. Steinberg DM, Sauvageot J, Piantadosi S, et al. Correlation of prostate needle biopsy and radical prostatectomy Gleason grade in academic and community settings. *Am J Surg Pathol.* 1997; 21:566–576. [PubMed: 9158682]
5. Partin AW, Mangold LA, Lamm DM, et al. Contemporary update of prostate cancer staging nomograms (Partin Tables) for the new millennium. *Urology.* 2001; 58:843–848. [PubMed: 11744442]
6. Graefen M, Karakiewicz PI, Cagiannos I, et al. International validation of a preoperative nomogram for prostate cancer recurrence after radical prostatectomy. *J Clin Oncol.* 2002; 20:3206–3212. [PubMed: 12149292]
7. Graefen M, Karakiewicz PI, Cagiannos I, et al. A validation of two preoperative nomograms predicting recurrence following radical prostatectomy in a cohort of European men. *Urol Oncol.* 2002; 7:141–146. [PubMed: 12474529]
8. Sanchez-Ortiz RF, Troncoso P, Babaian RJ, et al. African-American men with nonpalpable prostate cancer exhibit greater tumor volume than matched white men. *Cancer.* 2006; 107:75–82. [PubMed: 16736511]
9. Eastham JA, Carver B, Katz J, et al. Clinical stage T1c prostate cancer: pathologic outcomes following radical prostatectomy in black and white men. *Prostate.* 2002; 50:236–240. [PubMed: 11870801]
10. Stephenson AJ, Scardino PT, Eastham JA, et al. Preoperative nomogram predicting the 10-year probability of prostate cancer recurrence after radical prostatectomy. *J Natl Cancer Inst.* 2006; 98:715–717. [PubMed: 16705126]
11. Potters L, Morgenstern C, Calugaru E, et al. 12-Year outcomes following permanent prostate brachytherapy in patients with clinically localized prostate cancer. *J Urol.* 2005; 173:1562–1566. [PubMed: 15821486]

Figure 1. Percentage of patients in each cohort with increase, no change, or decrease in the probability of recurrence found postoperatively.

Table 1

Pretreatment and post-RP patient and prostate cancer characteristics

Characteristic	Entire Cohort (n = 1709)	Change in 5-y Probability of Recurrence		
		Increased (n = 253; 14.8%)	No Change (n = 1093; 64%)	Decreased (n = 363; 21.2%)
Before treatment				
Median age (y)	61.4	62.0	60.9	62.7
Median PSA (ng/mL)	6.0	7.3	5.5	7.9
Biopsy Gleason sum				
6	1039 (60.8)	111 (43.9)	809 (74.0)	119 (32.8)
7	531 (31.1)	83 (32.8)	245 (22.4)	203 (55.9)
8	139 (8.1)	59 (23.3)	39 (3.6)	41 (11.3)
Clinical stage				
T1a	5 (0.3)	0 (0.0)	2 (0.2)	3 (0.8)
T1b	7 (0.4)	1 (0.4)	5 (0.5)	1 (0.3)
T1c	932 (54.5)	142 (56.1)	707 (64.7)	83 (22.9)
T2a	451 (26.3)	57 (22.5)	280 (25.6)	114 (31.4)
T2b	193 (11.3)	31 (12.3)	60 (5.5)	102 (28.1)
T2c *	112 (6.6)	21 (8.3)	37 (3.4)	54 (14.9)
T3a	9 (0.5)	1 (0.4)	2 (0.2)	6 (1.7)
After RP				
Pathologic Gleason sum				
6	691 (40.4)	16 (6.3)	534 (48.9)	141 (38.8)
7 (3 + 4)	824 (48.2)	139 (54.9)	490 (44.8)	115 (53.7)
8	190 (11.1)	97 (38.3)	66 (6.0)	27 (7.4)
EPE				
Negative	822 (48.1)	9 (3.6)	565 (51.7)	248 (68.3)
Invasive	469 (27.4)	32 (12.6)	350 (32.0)	87 (24.0)
Positive	418 (24.5)	212 (83.8)	178 (16.3)	28 (7.7)
Positive margins	394 (23.1)	181 (71.5)	183 (16.7)	30 (8.3)
SVI	113 (6.6)	73 (28.9)	28 (2.6)	12 (3.3)
LNI	17 (0.9)	13 (5.1)	4 (0.4)	0 (0.0)

PSA = prostate-specific antigen; RP = radical prostatectomy; EPE = extraprostatic expansion; SVI = seminal vesicle invasion; LNI = lymph node involvement.

* Four pathologic Gleason sums were unavailable (1 in increased group and 3 in no-change group).

Table 2

Patient demographics by race

Demographic	Black (n = 132; 7.7%)	White (n = 1577; 92.3%)	P Value
Age (y)			< .0010
Median	58.6	61.7	
Range	41.2–75.7	36.5–76.5	
PSA (ng/mL)			.0179
Median	6.7	6.0	
Range	1.6–60.0	0.4–126.0	
Biopsy Gleason sum			.0010
6	61 (46.2)	978 (62.0)	
7	59 (44.7)	472 (29.9)	
8	12 (9.1)	127 (8.1)	
Clinical stage			< .0010
T1a	0	5 (0.3)	
T1b	0	7 (0.4)	
T1c	97 (73.5)	835 (52.9)	
T2a	20 (15.2)	431 (27.3)	
T2b	5 (3.8)	188 (11.9)	
T2c *	8 (6.1)	104 (6.6)	
T3a	2 (1.5)	7 (0.4)	

PSA = prostate-specific antigen.

Data presented as number of patients, with percentages in parentheses, unless otherwise noted.

* Four pathologic Gleason sums were unavailable (1 in increased group and 3 in no-change group).

Table 3

Pathologic parameters by race

Parameter	Black (n = 132)	White (n = 1577)	P Value
Gleason sum difference (pathologic – biopsy)			.624
–3	0	2 (0.1)	
–2	0	22 (1.4)	
–1	10 (7.6)	142 (9.0)	
0	70 (53.0)	880 (55.8)	
+1	42 (31.8)	426 (27.0)	
+2	7 (5.3)	81 (5.1)	
+3 or more	3 (2.3)	20 (1.3)	
EPE	40 (30.3)	378 (24.0)	.104
Positive surgical margin	42 (31.8)	352 (22.3)	.013
SVI	11 (8.3)	102 (6.5)	.407
LNI	5 (3.8)	12 (0.8)	.001

Abbreviations as in Table 1.

Data presented as number of patients, with percentages in parentheses.

Four white patients had unattainable pathologic Gleason sums.