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The impact of socioeconomic factors on prostate cancer outcomes in black patients treated with surgery

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Abstract

Objective—The role of socioeconomic factors in the worse outcome of black men with prostate cancer remains unclear. To determine if socioeconomic factors affect prostate cancer outcomes, we studied a cohort of only black patients to minimize known confounding factors

Methods—Black men treated with radical prostatectomy at New York Veterans Administration Medical Center and Memorial Sloan-Kettering Cancer Center between 1990 and 2005 were studied. A centralized pathology review process determined the Gleason score of all cases. PSA recurrence at both sites was defined as PSA $\geq$ 0.2 with a confirmatory rise. By matching patients' home zip codes to the U.S. Census Bureau database, corresponding socioeconomic data regarding median household income (income) and percentage of population having graduated from high school (education) was obtained. Income, education, clinical and pathological parameters were analyzed for the whole cohort.

Results—430 black patients were studied. They resided in neighborhoods where median household income was $41,498.10 and mean percentage of high school graduates was 73.4%. Eighty-eight (20.9%) patients had PSA recurrence. Median follow-up for survivors was 37 months. Neither income nor education evaluated as continuous or categorical variables were predictors of PSA recurrence. When evaluated as composite categorical variable, the combination of greater income and education did not predict disease free survival.

Conclusions—Data suggest that socioeconomic factors have limited impact on PSA recurrence in black men treated with radical prostatectomy. Thus, biologic factors might play a role in the poor outcomes in this population.

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INTRODUCTION

Several studies have sought to identify differences in outcome between black and white prostate cancer (PCA) patients undergoing radical prostatectomy (RP). These studies have consistently shown that with time, differences in outcome by race, have diminished when adjusted for pathologic features[1–]4. We have recently reported that at our equal-access institution, while disparities in pathologic stage, pretreatment PSA and age at diagnosis between black and white patients have narrowed over time, black patients continue to have significantly worse Gleason scores, suggesting that biological factors might play a role in the poor outcome of PCA in this population5.

Several groups have attempted to determine the impact of socioeconomic factors, such as income, literacy, and access-to-care, on the disparities seen in PCA outcome between black and white patients[6–8]. Data suggested that even when controlling for socioeconomic factors, black race remained an independent predictor of disease recurrence or mortality[6]. Disparities in education and literacy have been found to be predictive of poorer outcome from PCA[9]. While black patients in many studies often have lower income and less education, it remains unclear whether differences in disease presentation and progression are secondary to these socioeconomic factors. Studies addressing the issue of race and PCA compare white and black patients. Our study aims to determine if socioeconomic factors affect PCA outcomes in a cohort of only black patients, thereby minimizing known racial differences in access-to-care, screening participation, and treating physician bias.

We developed a cooperative Translational Research Program of PCA in black men between the New York Veterans Affairs Medical Center (VAMC) and Memorial Sloan-Kettering Cancer Center (MSKCC) in New York. This combined program has allowed us to expand the ethnic and socioeconomic diversity of our patient cohort and build upon our previous studies examining the biologic differences between black and white PCA patients by. In this study, we sought to determine if socioeconomic factors played a role in predicting the disease course of black patients treated with RP.

PATIENTS AND METHODS

We studied 430 black men with PCA who underwent RP (223 VAMC, 207 MSKCC). Institutional Review Board approval was obtained from both institutions. Patients in both cohorts self-identified their race as African-American or black. Patients of African or Afro-Caribbean origin were considered as “black” in this analysis. By matching patients’ home zip codes to the U.S. Census Bureau database, we obtained corresponding socioeconomic data regarding median household income (income) and percentage of high school graduates in the population (education)[10]. Twenty patients were missing zip code address information, preventing estimation of socioeconomic factors. The clinical and pathologic parameters analyzed were patient age, pre-treatment PSA, Gleason score, pathological stage, surgical margin status, recurrence, date of recurrence, and current clinical status, including death and cause of death. The tumors were staged according to the 1997 TNM staging system. The Gleason score of all cases were determined using a centralized pathology review process (VR and PL attending pathologist at MSKCC and VAMC, respectively). Patients were followed with serial post-operative PSA measurements to determine biochemical recurrence. A unified definition of PSA recurrence was used at both institutions: PSA $\geq$ 0.2 ng/dL with a confirmatory rise. The patients who did not achieve PSA nadir <0.1 (n=33) were considered recurrent on the date PSA was $\geq$0.2 ng/dL. Clinical and pathologic variables by socioeconomic strata were compared using Wilcoxon rank sum test for continuous variables and Fisher’s exact test for categorical variables.

In recurrence-free survival analysis, the time to biochemical recurrence is defined as months elapsed between the date of prostatectomy to the date of diagnosis of biochemical recurrence or date of death (if the patient dies prior to biochemical recurrence) or the last follow-up date (for the patient alive without biochemical recurrence at the end of study). Patients of unknown recurrence status (n=9), whose follow-up information were missing (n=3), or whose date of recurrence was not known (n=12) were excluded from the analysis. The effect of the variables of interest on time to biochemical recurrence was examined by treating death as a competing cause of risk. The p-values were obtained using a modified Chi-squared test[11].

In the univariate recurrence-free survival analysis, the following were treated as categorical variables: T stage, Gleason Score (<7, =7, >7), and surgery margin. Age and PSA were treated as continuous variables. Median household income and high school education level in a patient's neighborhood were treated as continuous variable initially. These variables were also divided into quartiles (four groups of approximately equal sample size), and analyses were conducted to estimate the hazard of biochemical recurrence in (i) each of the upper three quartiles with the lowest quartile as the baseline; (ii) the upper 3 quartiles combined versus the lowest quartile; (iii) a composite variable of income and high school level, consisting of three categories, was created: lowest quartiles of both income and high school level, lowest quartile of one of these variables and one of the upper three quartiles of the second variable, and one of the upper three quartiles of both the variables. Patients with missing data for any explanatory variables were eliminated from the corresponding analyses.

RESULTS

The focus of the study was to compare the clinical and pathologic features of patients with PCA stratified by socioeconomic factors. The mean of median household incomes was $41,498.10 (Inter-Quartile range [IQR]: $26,237, $52,445), versus $41,994.00 for the median US household income (Table 1). The mean percentage of high school graduates was 73.4% (IQR: 65.9%, 82.6%) (Table 1). The distribution of socioeconomic factors highlights a broad diversity within this cohort of black patients who received treatment at one of two hospitals in one major city.

To evaluate the parameters clinical and pathologic features, we stratified these parameters by lowest quartile compared to the higher three quartiles of median household income. In Table 2a, the top three income quartiles were grouped as "High Income" and the lowest quartile was termed "Lowest Income." As expected, stratification by median income levels revealed a statistically significant difference in the percentage of high school graduates. Of note, the Lowest Income quartile had more frequent positive surgical margins (Table 2a).

In Table 2b, we further stratified the clinical and pathologic features parameters by the lowest quartile compared to the higher three quartiles of percentage of high school graduates by zip code. We termed these two groups as "Lowest Education" and "High Education," respectively. As expected, difference in income was statistically significant after stratification by education, and again, the Lowest Education quartile had more frequent positive surgical margins (Table 2b).

Of note, the Lowest Income and Lowest Education were comprised of older individuals with higher PSA values at the time of RP, though the latter difference was not statistically significant (Tables 2a and b). Despite these clinical differences at the time of surgery, the distribution of the pathologic stages and Gleason scores remained similar.

Median follow-up for survivors was 37 months. Gleason score, positive surgical margins, and PSA were all statistically significant predictors of recurrence ($p<0.01$). Pathologic stage and

the components of extracapsular extension and seminal vesicle invasion were also significant predictors ($p<0.01$).

Table 3 demonstrates the results of the univariate analysis of the impact of the socioeconomic factors income and education on outcome. The hazard ratios for median household income and percentage high school graduate quartiles were calculated, but none of these quartiles, either independently or in combination, were statistically significant predictors of recurrence (Table 3).

DISCUSSION

In this study, we examined the impact of education and income of black patients treated with radical prostatectomy on PCA outcome. We examined a relatively large cohort of black men with different levels of education and income. Our results have demonstrated the minimal impact of income and/or education on PSA recurrence in this cohort. We hypothesized that if income and/or education are indeed predictors of PCA behavior (either due to PCA baseline characteristics and or suboptimal care), black men of higher socioeconomic class would have better PCA outcome than those with lower socioeconomic class. Taking into consideration that black patients treated at different healthcare systems may present with a spectrum of clinicopathologic features, which may affect outcomes, we selected outcome as the primary endpoint. After controlling for race by studying a large and diverse cohort of black men treated by radical prostatectomy performed at one of two major metropolitan medical centers, our primary finding was that neither income nor education had a statistically significant effect on recurrence-free survival.

We observed significant differences in age at treatment by both income and education. Our data suggest that patients arrive at surgery via a variety of mechanisms. The underlying differences could be that patients of lower socioeconomic class, regardless of access-to-care, are less likely to pursue screening to establish a PCA diagnosis, or once diagnosed, are less likely to pursue surgical treatment. Conversely, patients with higher socioeconomic class pursue screening, diagnosis, and treatment more aggressively. On the other hand, physician biases may result in differences when screening, diagnosing, and treating patients of different education and income levels. Patients who were treated at MSKCC were wealthier (mean of median household incomes $47,650 versus $35,464) and better educated (mean percentage of high school graduates 76.2% versus 70.6%) than those at the VAMC. The VAMC is a comprehensive health system where patients are more likely to be screened, diagnosed and treated under one roof than at MSKCC, a tertiary center specializing in treatment of cancer patients, many of whom enter the center already with an established diagnosis. Patients treated at MSKCC were younger (mean age 56.6 versus 63.6 years) and lower pre-treatment PSA values (mean PSA 13.2 ng/dL versus 8.61 ng/dL). This latter data lends support to different clinical characteristics at the time of surgery based on underlying socioeconomic factors; however, these did not translate into differences in pathologic features or PSA-recurrence outcomes based on socioeconomic factors.

One difference we observed was the presence of positive surgical margin based upon socioeconomic status. While our reported positive margin rate was high, this frequency has been previously reported by several groups[12–14]. The presence of positive of surgical margin depends upon technical aspects of the operation, which may be influenced by the surgical volume of the surgeons performing the operation[15]. Recent data suggest that beyond surgical volume, as surgeons gain experience, their positive surgical margin rates decline[16]. As margin status is very much influenced by the surgical and pathologic techniques, AJCC staging of PCA does not incorporate margin as part of the pathological staging[17].

Besides surgeon volume and experience, it is possible that other factors may have contributed to differences in margin rate. The higher positive surgical margin based upon socioeconomic status could be related to obesity. Obesity is prevalent in the U.S., especially among lower income populations, and while obesity affects the black population, it is a health issue that also crosses racial divisions[18,19]. In a large, diverse cohort, Amling *et al.* observed a higher frequency of positive surgical margins in obese patients and noted that black patients were more often obese[20]. Therefore, since our cohort of only black patients included lower rungs of the socioeconomic ladder, it is possible that more patients were obese and therefore suffered more frequent positive margins. Freedland *et al.* also noted that another source of more frequent positive margins was smaller prostate size, but it is difficult to offer a hypothesis to explain why this would have a greater manifestation and effect on one socioeconomic group over another[21].

The relationship between socioeconomic factors and PCA presentation has been previously studied in patients treated at the VAMC system. Wolf *et al.* reported that in a cohort of newly diagnosed PCA patients, mostly recruited from VAMC centers, that black men had lower literacy than white men [9]. In multivariable analysis, lower literacy was a predictor of PSA>20 ng/mL at presentation, but not black race. The study suggested that education is a more important determinant of high risk disease at presentation than race alone. The discordance of these results with our data may be explained by the fact that patients in the Wolf *et al.* study were identified at the initial diagnosis of PCA. Our study followed PCA patients treated by surgery and evaluated the subsequent PCA outcome. Yanke *et al.* used multivariable analysis to show that after controlling for clinical factors such as PSA, in equal-access-to-care systems, black race alone was a statistically significant predictor of PCA at first biopsy[22]. The results of this study support our hypothesis that even after controlling for cohort populations, there is some basis for the difference in PCA biology between black and white men.

In concordance with our data, Sanchez-Ortiz reported provocative findings from a clinical study of patients exclusively with cT1c PCA[23]. A cohort of black patients who underwent RP was matched to a similar cohort of white patients. The black patients had higher grade tumors, greater tumor volume and greater tumor volume per ng/mL of PSA. These differences were statistically significant, but the differences in stage or the presence of a positive surgical margin were not. Although this is a retrospective study that attempted to control for other factors such as clinically advanced stage and PSA, Sanchez-Ortiz's results suggest that black PCA patients have notable differences in pathologic features that could predispose them to more aggressive disease.

Conclusion

As neither income, education, nor their combinations were significant predictors of PSA-recurrence, socioeconomic factors do not appear to influence outcomes after RP in our study cohort. These data suggest that biologic factors, either genetic or environmental, might play a role in the worse PCA outcomes in black patients.

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Table 1

Clinical and pathologic characteristics of overall cohort of 430 black men treated by radical prostatectomy

Clinical or Pathologic Parameter	Mean (Inter-Quartile range, IQR) or Number (percent)
Percentage High School Graduate	73.4 (65.9, 82.6)
Median Household Incomes	$41,498.10 ($26,237, $52,445.5)
Recurrence	
No	300
Yes	88
Never reach <0.1	33
UNK	9
Age	60.2 (55.3, 66)
Median PSA	7.5 (5.20, 13.00)
Pathologic Stage	
pT2	279
pT3	142
pT4	8
Gleason Grade	
< 7	131
7	248
> 7	47
Margin Status	
Negative	220
Positive	156

Note: Twenty patients were missing zip code address information

Table 2

Clinical and pathologic characteristics of black men treated by radical prostatectomy

Table 2a: Stratified by Income	Lowest Income (Q1) ($14,896 - $26,237) (n = 107)	High Income (Q2–4)($26,237 - $163,046) (n=303)	p-value
Mean % High School Graduate (IQR)	60.0 (55.3, 65.5)	78.1 (71.5, 84.9)	<0.01
Recurrence			
No	65	221	
Yes	34	51	
Never reach <0.1	7	23	
UNK	1	8	
Mean Age (IQR)	62.6 (59, 67)	59.2 (54, 65)	<0.01
Median PSA (IQR)	8.0 (5.0, 14.0)	7.0 (5.3, 12.0)	0.36
Pathologic Stage			
pT2	64	199	0.18
pT3	39	99	
pT4	4	4	
Gleason Grade			
< 7	25	100	0.13
7	71	168	
> 7	11	34	
Margin Status			
Negative	35	174	<0.01
Positive	57	94	

Table 2b: Stratified by Education	Lowest Education (Q1) (44.0 - 65.9%) (n = 114)	High Education (Q2–4) (65.9 - 97.6%) (n = 296)	p-value
Mean of Median Household Incomes(IQR)	$23,665 ($20,839~$26,366)	$48,366 ($37,141~$57,362.5)	<0.01
Recurrence			
No	71	215	
Yes	35	50	
Never reach <0.1	8	22	
UNK	0	9	
Mean Age (IQR)	61.6 (57.3, 66)	59.5 (54~66)	0.02
Median PSA (IQR)	12.1 (5.54, 13.0)	10.4 (5.12, 12.0)	0.11
Pathologic Stage			
pT2	71	192	0.36
pT3	39	99	

Table 2b: Stratified by Education	**Lowest Education (Q1) (44.0 - 65.9%) (n = 114)**	**High Education (Q2–4) (65.9 - 97.6%) (n = 296)**	**p-value**
pT4	4	4	
Gleason Grade			
< 7	31	94	0.61
7	71	168	
> 7	12	33	
Margin Status			
Negative	43	166	<0.01
Positive	57	94	

Table 3

Univariate analysis of socioeconomic factors as predictors of PSA-recurrence

Variable	Hazard ratio (95% CI)	p-value
Median Household Income		
Q1: 14896 ~ 26237	Reference	0.77
Q2: 26237 ~ 38713	0.74 (0.44~1.27)	
Q3: 38713 ~ 52445	0.94 (0.68~1.29)	
Q4: 52445 ~ 163046	0.90 (0.66~1.24)	
Q4: 52445 ~ 163046	0.90 (0.66~1.24)	
Q1: 14896 ~ 26237	Reference	0.48
Q2-4: 26237 ~ 163046	0.86 (0.58~1.28)	
Percentage High School Graduate		
Q1: 44.0 ~ 65.9	Reference	0.66
Q2: 65.9 ~ 72.8	0.70 (0.41~1.20)	
Q3: 72.8 ~ 82.6	0.92 (0.69~1.24)	
Q4: 82.6 ~ 97.6	0.86 (0.64~1.15)	
Q1: 44.0 ~ 65.9	Reference	0.37
Q2-4: 65.9 ~ 97.6	0.82 (0.56~1.21)	
Income & Education		
Q1 education **and** Q1 income	Reference	0.59
Q2-4 education **or** Q2-4 income (not both)	0.78 (0.43~1.41)	
Q2-4 education **and** Q2-income	0.80 (0.57~1.13)	