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SOCIODEMOGRAPHIC AND CLINICAL RISK CHARACTERISTICS OF PATIENTS WITH PROSTATE CANCER WITHIN THE VETERANS AFFAIRS HEALTH CARE SYSTEM: DATA FROM CaPSURE

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ABSTRACT

Purpose: Veterans Affairs (VA) health care system investigators perform large clinical trials in prostate cancer treatment but potential differences between VA and other patient cohorts have not been explored systematically.

Materials and Methods: Cancer of the Prostate Strategic Urologic Research Endeavor is an ongoing observational database of men with prostate cancer, comprising 7,202 patients treated at 35 sites across the United States. Three sites that together contribute 241 patients are VA medical centers. Demographic and clinical characteristics were compared between all VA and nonVA patients in the database and a multivariate model was used to explore the interactions between ethnicity and VA status for predicting clinical characteristics.

Results: VA patients were 4 times as likely as nonVA patients to be black. They had lower income, less education and more co-morbidity at presentation (all comparisons $p < 0.0001$). VA patients had higher risk disease. Mean serum prostate specific antigen at diagnosis was 20.1 vs 15.3 ng/ml for nonVA patients ($p = 0.003$). Mean Gleason score was 6.4 for VA patients vs 6.0 for nonVA patients ($p < 0.0001$). Differing ethnic distributions explained the differences in prostate specific antigen between VA and nonVA patients. However, VA status, socioeconomic level and ethnicity independently predicted Gleason score. VA patients were more likely to undergo watchful waiting or primary hormonal therapy and less likely to receive definitive local treatment ($p < 0.0001$).

Conclusions: Significant sociodemographic and clinical differences exist between VA and nonVA patients, which should be borne in mind when extrapolating the results of VA clinical trials to the general population. These observations require validation in larger patient cohorts.

KEY WORDS: prostate, prostatic neoplasms, United States Department of Veterans Affairs, ethnicity

The Veterans Affairs (VA) health care system is the largest integrated health care delivery system in the United States.[1] Its large patient population, standardization of practice patterns and consistency of medical records provide a substrate for large scale clinical trials.[2] From early VA Urology Cooperative Group studies[3] to the ongoing Prostate Cancer Intervention Versus Observation Trial,[4] VA initiatives have had a major role in defining optimal treatment strategies for prostate cancer. However, it is not clear that patients with prostate cancer in the VA system are necessarily representative of the general population or the results of VA studies are fully applicable to patients in other settings. Therefore, we compared sociodemographic and clinical parameters between the VA and nonVA populations of a large national prostate cancer database.

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MATERIALS AND METHODS

Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE) is a longitudinal observational database of men with biopsy proven prostate adenocarcinoma recruited from 35 academic and community based urology practices across the United States. All patients with prostate cancer are recruited consecutively by participating urologists, who report complete clinical data and followup information on diagnostic tests and treatments. Data on patients diagnosed prior to 1995 but still followed by a urologist were initially entered retrospectively. For those diagnosed since 1995, all data entry has been prospective. Informed consent is obtained from each patient. Patients are treated according to the usual practices of their physicians and followed until the time of death or study withdrawal. Data completeness and accuracy are ensured by random sample chart review

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every 6 months. Additional details of the project methodology have been reported previously.[5]

Between June 1995 when the database was opened, and August 2001, 7,379 patients were invited to participate and 7,202 (97.5%) agreed. Demographic and clinical characteristics of all patients in the database were extracted. Patients were stratified into low, intermediate and high risk groups. Those at low risk had serum prostate specific antigen (PSA) 10 ng/ml or less, biopsy Gleason score 6 or less and clinical stage T1 or T2a. Those at intermediate risk had PSA 10.01 to 20 ng/ml, Gleason score 7 or clinical stage T2b. Those at high risk had PSA greater than 20 ng/ml, Gleason score 8 or greater, or clinical stage T3 or T4.[6]

Comparisons between nonVA and VA patients were performed using the chi-square test for categorical variables (ethnicity and treatment type) and the Mantel-Haenszel chi-square test for trend for ordinal and categorized continuous variables (age, education, income, Charlson co-morbidity index,[7] Gleason sum, PSA at diagnosis, clinical T stage and risk). A generalized linear model ANOVA was used to explore the interactions among ethnicity, education, income and VA status for predicting clinical characteristics. All analyses were performed using commercially available software (SAS Institute, Cary, North Carolina).

RESULTS

Three of the 35 sites, accounting for 241 patients (3.3%) in the dataset, are VA medical centers, including 2 on the West Coast and 1 on the East Coast. Of the nonVA patients 53.4% received Medicare with or without supplemental insurance, 33.5% participated in managed care plans, 7.44% had fee for service insurance and 5.6% had other, unknown or no insurance. Table 1 lists the demographic characteristics of nonVA and VA patients. VA patients were 4 times as likely as nonVA patients to be black and they tended to have lower income and less education. Mean age was 67 in each group and there was no significant difference in age distribution.

Table 2 lists the clinical characteristics of the 2 groups. VA patients had more co-morbidity at presentation with a mean Charlson index ± SEM of 3.2 ± 1.1 vs 2.7 ± 1.1 in nonVA patients and were notably more likely to have 4, or 5 or greater co-morbidities. They also had higher risk prostate cancer. Mean serum PSA at diagnosis was 20.1 ± 25.8 ng/ml (median 9.1) vs 15.3 ± 20.6 (median 7.9) in nonVA patients. Mean Gleason score was 6.4 ± 1.6 in VA patients vs 6.0 ± 1.4 in nonVA patients. Differences in clinical T stage distribution were not statistically significant. Figure 1 shows the overall distribution of the 2 groups according to low, intermediate and high risk. On multivariate analysis differences in PSA between VA and nonVA patients were explained at least in part by the different racial distributions between the 2 populations ($p = 0.0006$) and they did not reflect an independent effect of VA status ($p = 0.5$), income ($p = 0.24$) or education ($p = 0.88$). However, Gleason score reflected significant independent variation by ethnicity ($p = 0.0176$), income ($p < 0.0001$) and education ($p < 0.0001$) as well as by VA status ($p = 0.0011$). Patients who had less than a high school education or earned less than $10,000 had a higher mean Gleason score than other patients. Among white and black men VA patients were about twice as likely to have Gleason 8 to 10 disease (21.5% vs 10.5%, $p = 0.0003$) and 27.4% vs 15.9%, $p = 0.014$, respectively).

Figure 2 shows differences in treatment patterns. Overall VA patients were twice as likely as nonVA patients to pursue watchful waiting and they were also more likely to receive primary androgen deprivation therapy. They were less likely to receive any definitive local treatment but the differences among specific local treatment types were not significant.

TABLE 1. *Demographic characteristics of nonVA and VA patients*

	No. NonVA (%)	No. VA (%)	Univariate p Value (chi-square test)
Total pts	6,961	241	
Age:			
Younger than 60	473 (7.2)	23 (10.0)	
60–69	1,145 (17.5)	38 (16.6)	
70–79	2,635 (40.2)	96 (41.9)	0.7423
80 or Greater	2,306 (35.2)	72 (31.4)	
Unknown	402	12	
Ethnicity:			
White	5,986 (86.0)	139 (57.7)	
Black	653 (9.4)	91 (37.8)	
Latino	131 (1.9)	2 (0.8)	<0.0001
Other	191 (2.7)	9 (3.7)	
Unknown	1,614	72	
Education:			
Below high school	389 (7.0)	30 (16.5)	
Some high school	668 (12.0)	41 (22.5)	
High or technical school	1,437 (25.8)	42 (23.1)	
Some college	1,120 (20.1)	40 (22.0)	<0.0001
College graduate	939 (16.9)	16 (8.8)	
Graduate school	1,011 (18.2)	13 (7.1)	
Unknown	1,397	59	
Income:			
Less than $10,000	520 (10.3)	64 (37.4)	
$10,001–30,000	1,588 (31.6)	77 (45.0)	
$30,001–50,000	1,245 (24.8)	18 (10.5)	<0.0001
$50,001–75,000	766 (15.2)	8 (4.7)	
$75,001 or Greater	909 (18.1)	4 (2.3)	
Unknown	1,933	70	

For each category percents and chi-square values were based on nonmissing data within that category.

TABLE 2. *Clinical characteristics of nonVA and VA patients*

	No. NonVA (%)	No. VA (%)	Univariate p Value (chi-square test)
Co-morbidity index:			<0.0001
0	1,944 (36.5)	45 (31.3)	
1	1,410 (26.5)	28 (19.4)	
2	890 (16.7)	25 (17.4)	
3	500 (9.4)	14 (9.7)	
4	315 (5.9)	13 (9.0)	
5 or Greater	264 (5.0)	19 (13.9)	
Unknown	1,638	97	
Gleason sum:			0.0027
2–4	774 (13.1)	27 (14.3)	
5–6	3,254 (54.9)	71 (37.6)	
7	1,239 (20.9)	46 (24.3)	
8–10	658 (11.1)	45 (23.8)	
Unknown	1,036	52	
PSA at diagnosis (ng/ml):			0.0033
Less than 4.0	658 (11.3)	11 (6.4)	
4.0–10.0	2,973 (50.9)	81 (47.4)	
10.01–20	1,194 (20.4)	36 (21.1)	
Greater than 20	1,018 (17.4)	43 (25.1)	
Unknown	1,118	70	
Clinical T stage:			0.6382
T1	1,971 (31.3)	69 (35.8)	
T2	3,825 (60.8)	105 (54.4)	
T3	449 (7.1)	17 (8.8)	
T4	46 (0.7)	2 (1.0)	
Unknown	658	11	

For each category percents and chi-square values were based on nonmissing data within that category.

DISCUSSION

This study is an exploratory analysis of sociodemographic and clinical differences between patients in the VA health care system and those who received health care in other contexts. We found that VA patients with prostate cancer had lower income and education levels, and were more likely to be black and present with multiple co-morbid conditions. VA patients tended to present with higher risk disease than other patients. They presented with higher PSA, which followed racial variations in PSA. They also presented with higher biopsy Gleason scores even after adjustment for eth-

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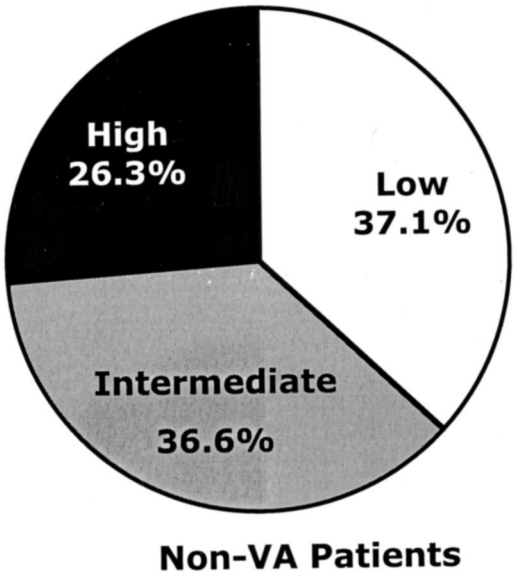

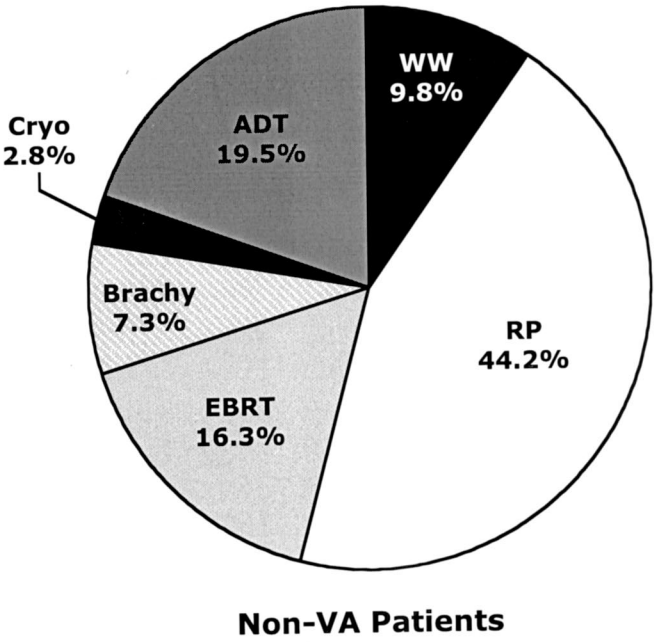

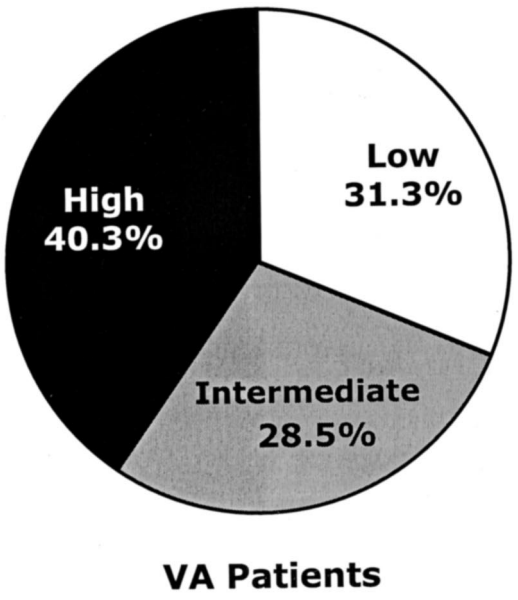

FIG. 1. Clinical risk stratification of nonVA and VA methods. Stratification difference between nonVA and VA patients was statistically significant ($p = 0.0031$).

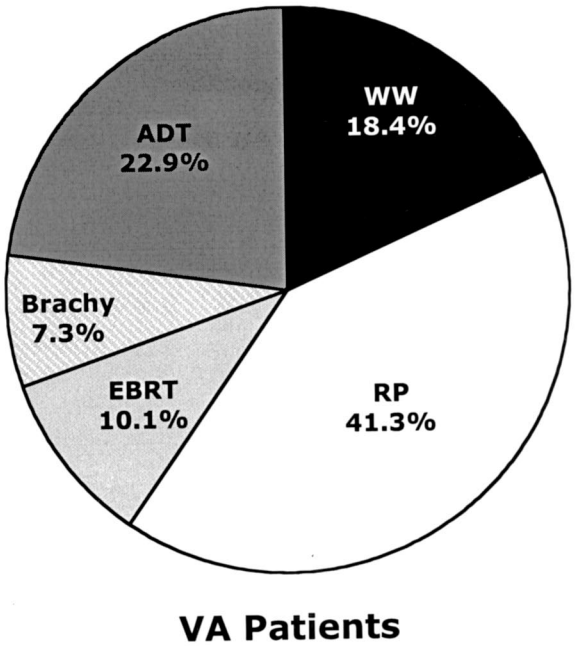

FIG. 2. Primary treatment distributions in VA and nonVA patients. Differences between 2 groups was statistically significant ($p < 0.0001$). *RP*, radical prostatectomy. *EBRT*, external beam radiotherapy. *Brachy*, brachytherapy. *ADT*, androgen deprivation therapy. *WW*, watchful waiting.

nicity and socioeconomic status. In particular, they were more than twice as likely to present with Gleason 8 to 10 disease. On the other hand, they were not less likely to have clinically organ confined disease at presentation based on clinical staging. VA patients were more likely to pursue watchful waiting or primary hormonal therapy and less likely to receive definitive local therapy.

Equal access to the VA system for veterans makes this group of patients an excellent cohort in which to analyze multiple associations between ethnicity and socioeconomic status when determining disease risk. We found that VA status predicted Gleason grade even when adjusted for ethnicity and socioeconomic status. In a study performed in the military health care system Tarman et al found that lower socioeconomic status was related to higher grade independent of patient ethnicity.[8] However, others reported widely divergent results when reviewing the literature on the relationship between socioeconomic status and prostate cancer risk.[9] It should also be emphasized that even within the VA system, in which many but not all barriers to health care access are removed, patients in the lowest strata of education and income still presented with higher grade disease.

Likewise, Stamey et al have previously reported that black men tend to have higher grade prostate cancer than white men.[10] However, like socioeconomic status the relationship

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between ethnicity and prostate cancer risk is complex and remains incompletely defined.[11] Because there is no immediately apparent biological explanation for higher Gleason grade in VA patients, there are likely other features unique to this population that explain the more aggressive disease in these patients. They may include factors that, while important, are uncommonly reported in prostate cancer series, such as body mass index[12] or other dietary parameters, smoking prevalence,[13] other life-style factors and exposure to potential carcinogens during military service.

The different treatment distribution of VA patients compared with nonVA patients may be primarily related to prostate cancer risk differences, but also to educational differences between the cohorts. Kane et al recently examined the impact of patient educational level on treatment received by patients with prostate cancer in CaPSURE and found that educational level was related to treatment selection, particularly for patients older than 75 years.[14] Patients with a higher education level tended to receive definitive local therapy more frequently than those with less education. The VA cohort in CaPSURE is too small to allow detailed subset analysis of treatment patterns between VA and nonVA patients when adequately controlling for clinical and sociodemographic variables. We hope to perform such analysis in the future with larger patient data sets.

The major caveat that must be borne in mind when interpreting these results is that, while CaPSURE represents a mix of locales and practice types, the sites were not chosen at random and, thus, neither the VA nor the nonVA patients can be assumed to represent a statistically valid sample of their respective national populations. For example, white patients are relatively over represented in CaPSURE compared with national census data. Furthermore, only men seen by urologists at the various sites are accessioned to CaPSURE. Thus, patients seen only by medical oncologists or other practitioners would not be included. Because there is no central review of pathological specimens in CaPSURE, subtle differences in Gleason grade may be in part attributable to differing interpretations in various institutions. Finally, socioeconomic data were collected only from patient reported questionnaires and not externally validated. Therefore, if VA patients or any other group was more or less likely to overstate or understate income or education data, our findings with respect to these parameters could be biased.

Despite these cautionary notes, we believe that our data represent one of the best available samplings of patients with prostate cancer across the nation. Validation of these observations must be made in larger VA patient cohorts. We hope to perform further comparisons with data from the newly described Shared Equal Access Regional Cancer Hospital database.[15]

CONCLUSIONS

VA patients in CaPSURE have substantially different sociodemographic characteristics, oncological risk factors and treatment patterns than other patients in the database. Well designed clinical trials can certainly control for such clinical and demographic variables but these potentially significant differences between research and clinical populations should be borne in mind when extrapolating the results of VA clinical trials to patients in general practice. Validation and further exploration of these observations must be made in larger cohorts of VA patients.

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