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Disproportionate Presentation of High Risk Prostate Cancer in a Safety Net Health System

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Purpose: Most prostate cancer research is based on relatively homogenous cohorts of men, often with comparatively high socioeconomic status. We describe prostate cancer characteristics in men treated in a public health system and hypothesize a disproportionate burden of high risk disease in this population.

Materials and Methods: We created a clinical registry from a review of the medical records of 377 men diagnosed with prostate cancer in the San Francisco General Hospital system, which provides care to underserved, uninsured populations. We compared sociodemographic data and cancer characteristics with those in 2 large prostate cancer databases from a community (CaPSURE™) and an academic (University of California-San Francisco tumor registry) setting to assess differences in risk distribution using the D'Amico and Cancer of the Prostate Risk Assessment scoring systems.

Results: Compared to men in CaPSURE or the University of California-San Francisco tumor registry those in the San Francisco General Hospital cohort were nonwhite (76%), insured under Medicaid (31%) or uninsured (8%) and had adverse clinical characteristics, including median prostate specific antigen greater than 10 ng/ml at diagnosis and higher Gleason grade. In addition, the majority of patients (67%) had intermediate or high risk disease based on the D'Amico classification and a higher mean Cancer of the Prostate Risk Assessment score. Using ANOVA for continuous variables and the chi-square test for categorical variables, all comparisons were statistically significant ($p < 0.001$).

Conclusions: Men in the San Francisco General Hospital public health system bear a substantially higher burden of high risk disease that those in an academic or a community setting. Populations such as this would benefit most from targeted efforts for early detection and treatment to decrease prostate cancer morbidity and mortality.

Key Words: prostate, prostatic neoplasms, risk, continental population groups, Medicaid

Abbreviations and Acronyms

CAPRA = Cancer of the Prostate Risk Assessment

IMPACT = Improving Access, Counseling and Treatment for Californians with Prostate Cancer

PSA = prostate specific antigen

SFGH = San Francisco General Hospital

UCSF = University of California-San Francisco

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PROSTATE cancer is the most common noncutaneous cancer diagnosis in men in the United States. In 2009 an estimated 192,280 men were diagnosed with this condition and a large proportion had low risk disease.[1] This stage migration is attributed to widespread PSA screening with improved outcomes and decreasing cancer specific mortality, presumably due to early intervention for disease.[2] However, most of these studies are based on data on patients in academic series, which typically reflect a relatively homogeneous, narrow sociodemographic range.[3]

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Previous studies show that prostate cancer incidence and mortality can vary greatly by race, ethnicity and socioeconomic status.[4,5] Prevailing theories include disparities in health care access, differences in cultural values and physician trust, varying treatment patterns and quality, genetic variation, diet and other environmental factors, and diverse tumor biology.[6–8] Overall prostate cancer risk distribution and outcomes in lower socioeconomic strata remain relatively unknown.

The San Francisco Community Health Network serves all residents of the City and County of San Francisco regardless of insurance status or ability to pay for services. Of the patients served 60% are uninsured or Medicaid recipients and are from various ethnic backgrounds with 75% of the population comprising nonwhite groups, including black, Asian/Pacific Islander and Latino. Most uninsured patients are enrolled in Healthy San Francisco (www.healthysanfrancisco.org), an income based sliding scale program administered by the City and County of San Francisco. Some of these men are also enrolled in IMPACT, which has provided prostate cancer care to uninsured men with an income at or below 200% of the federal poverty level since 2001.[9]

Based on clinical experience and observations in previous studies we hypothesized that men treated in public health systems for prostate cancer comprise a distinct cohort, harbor more aggressive cancer and may not be adequately served by current screening and treatment efforts. Thus, we assessed sociodemographic and clinical characteristics in patients seen in this public health system, and compared them with data from an academic medical center, also in San Francisco, and a national prostate cancer disease registry to determine differences in disease risk and burden.

MATERIALS AND METHODS

SFGH, which is funded and operated by the County of San Francisco Department of Public Health, is designated as a safety net hospital, in that it provides care primarily to low income, uninsured and other vulnerable populations. We reviewed patient data from SFGH pathology logs and the institutional tumor registry to identify all 377 patients diagnosed with prostate cancer between 1998 and 2008. We collected more than 70 data variables, including sociodemographic factors, diagnostic and staging tests, and primary treatments, from electronic and paper medical records.

Comparison groups were 2 large prostate cancer databases, including the CaPSURE registry and the UCSF Helen Diller Family Comprehensive Cancer Center tumor registry. CaPSURE is a longitudinal, observational database of 13,730 men with biopsy proven prostate cancer who have been treated at 31 academic and community based urology practices across the United States since 1995. Additional details on the study population and sociodemographic characteristics were previously reported.[10] The UCSF cohort is derived from an institutional tumor registry of 6,504 patients treated for prostate cancer from 1997 to 2007.

We assessed prostate cancer risk using the D'Amico classification system and the UCSF CAPRA scoring system, which have been used in previous studies to preoperatively predict biochemical recurrence and are well validated.[11,12] The D'Amico system stratifies patients based on clinical stage, PSA and Gleason grade in biopsy specimens. Low risk cases were defined as clinical stage T1 or T2a, PSA 10 ng/ml or less and Gleason score 6. High risk cases were defined as clinical stage T2c-T3a, PSA greater than 20 mg/ml, or Gleason score 8 or greater. Others were classified at intermediate risk.

The CAPRA scoring system, derived from community based data, predicts pathological status, disease recurrence and mortality after prostate cancer treatment. Points are assigned based on patient age, clinical stage, PSA, Gleason grade and percent of cores positive on biopsy.[12] Scores range from 0 to 10 with each 2-point increase approximately doubling the risk of recurrence and progression. A 9-point variation in the CAPRA scoring system can be used if data on the percent of positive biopsy cores are not available, as in the UCSF Cancer Registry. The CAPRA score was imputed in men missing data on exactly 1 contributing variable while those missing more than 1 were excluded from risk analysis. Men with locally advanced (cT3b or cT4) or clinically metastatic disease at presentation cannot be risk stratified with standard instruments, including the D'Amico and the CAPRA systems. They were classified as having advanced disease.

In addition to risk stratification, we compared demographic and clinical features in patients treated at SFGH to those in men in CaPSURE and the UCSF Cancer Registry. These variables include ethnicity, insurance status, primary language, clinical stage, biopsy Gleason score, mean ± SD age at diagnosis and median PSA at diagnosis. Differences in the cohorts were measured using ANOVA for continuous variables and the chi-square test for categorical variables. All analysis was done with Stata®, version 10.1. The study received UCSF and SFGH institutional review board approval.

RESULTS

The table lists patient demographics and clinical characteristics. Mean age in each cohort was similar across the registries, including 64 ± 8.9, 66 ± 8.7 and 63.9 ± 8.8 years in SFGH, CaPSURE and UCSF, respectively. Men in the SFGH cohort were more likely to be nonwhite (76%) and covered by Medicaid (31%) than men in CaPSURE or the UCSF registry. These men also presented with higher clinical stage (greater than cT3aN0M0) (12%), higher median PSA at diagnosis (10.2 ng/ml, range 5.5 to 23.8 vs 6.7, range 4.7 to 11.2 and 6.8, range 4.9 to 10.9, respectively) and higher grade disease on biopsy pathology (Gleason 4 + 3 in 9.6% and 8–10 in 24.4%). All comparisons were statistically significant ($p < 0.001$).

Demographic and clinical characteristics (each p ≤0.01)

	No. SFGH (%)	No. CaPSURE (%)	No. UCSF Registry (%)
Ethnicity:			
Black	122 (33.8)	1,491 (10.9)	483 (7.4)
Asian	83 (23.0)	108 (0.8)	483 (7.4)
White	86 (23.8)	11,747 (85.5)	4,855 (74.7)
Hispanic	66 (18.3)	233 (1.7)	247 (3.8)
Other	4 (1.1)	151 (1.1)	436 (6.7)
Insurance:			
Medicare	185 (51.5)	6,961 (50.7)	1,811 (27.8)
Medicaid	111 (30.9)	0	203 (3.1)
Private	0	5,637 (41.0)	3,777 (58.1)
Sliding scale	29 (8.1)	0	168 (2.6)
Other	34 (9.5)	1,142 (8.3)	544 (8.4)
Clinical stage:			
T1	177 (57.5)	5,953 (46.6)	2,076 (40.5)
T2	120 (39.0)	6,214 (48.6)	2,436 (47.5)
T3	11 (3.6)	359 (2.8)	615 (12.0)
Gleason biopsy:			
2–6	132 (43.6)	8,119 (64.2)	1,947 (53.1)
7 (3 + 4)	68 (22.4)	2,113 (16.7)	791 (21.6)
7 (4 + 3)	29 (9.6)	1,091 (8.6)	271 (7.4)
8–10	74 (24.4)	1,324 (10.5)	659 (18.0)

Prostate cancer risk at presentation was substantially higher in patients diagnosed at SFGH compared with patients diagnosed in the community or academic setting. When classified by the D'Amico system, a higher percent of SFGH patients (67%) had intermediate or high risk disease (p <0.001, fig. 1). Also, mean CAPRA scores were higher in the SFGH population than in CaPSURE or the UCSF registry

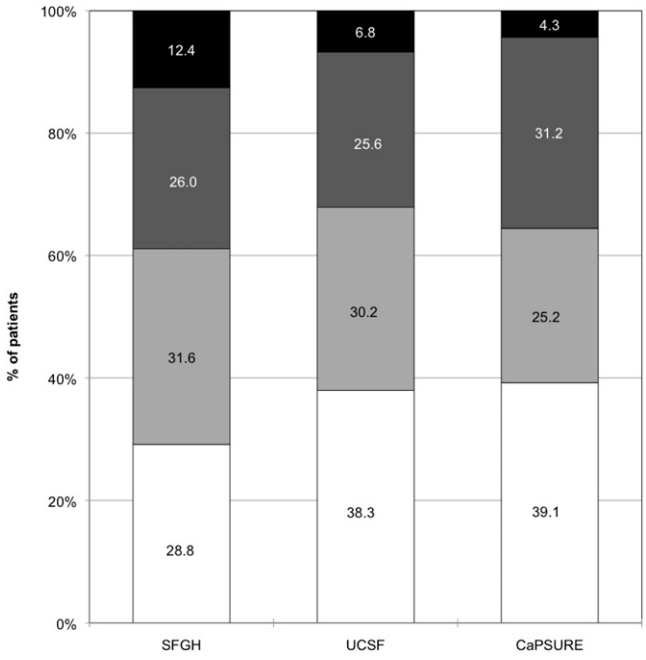

Figure 1. Prostate cancer risk by D'Amico classification. Black bars represent advanced. Dark gray bars represent high. Light gray bars represent intermediate. Open bars represent low.

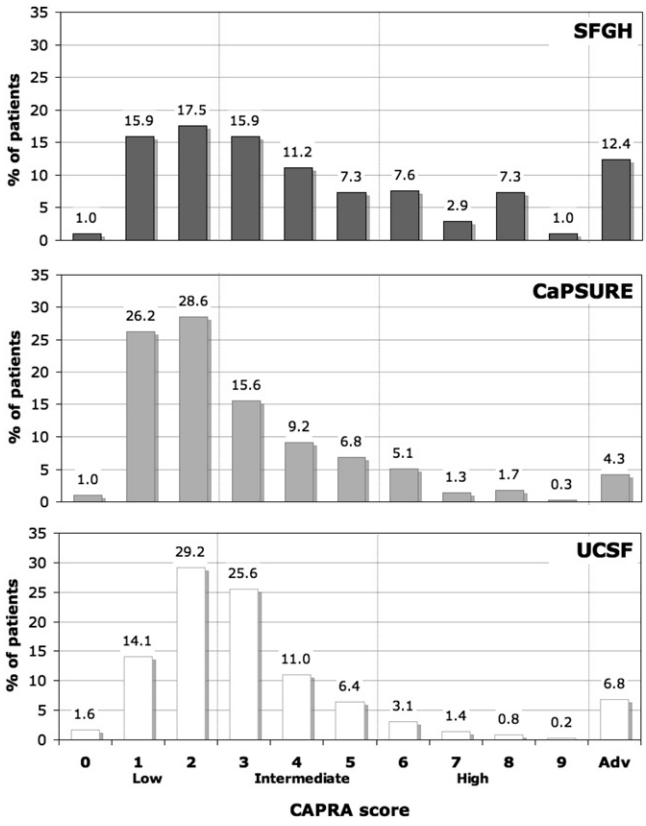

Figure 2. Prostate cancer risk by CAPRA score

(4.05 ± 2.53 vs 3.15 ± 2.10 and 2.74 ± 1.88, respectively, p <0.001, fig. 2). A substantially higher proportion of SFGH patients presented with clinically advanced or metastatic disease compared to those in CaPSURE and the UCSF tumor registry (12.4% vs 4.3% and 6.8%, respectively).

DISCUSSION

During the PSA era in the early 1990s the proportion of men with low risk prostate cancer steadily increased.[3] CaPSURE data showed that 27.5% of men diagnosed with prostate cancer from 1989 to 1992 had low risk characteristics. This proportion increased to 46% in 1999 to 2001 but has remained steady throughout the current decade. Men with low risk disease were more likely to be white and have a higher income and more education, and less likely to be covered by Medicare. Conversely high risk disease in the CaPSURE population decreased from 46% in 1990 to 1994 to 29% in 2000 to 2001, remaining constant since that time.[13]

A recent study using Surveillance, Epidemiology and End Results Program data also showed that a greater percent of men of all races presented with localized disease in 2004 to 2005 than those diagnosed from 1988 to 1989. Although racial disparity

has decreased with time, black men still present with prostate cancer at a younger age and higher stage.[14] Other studies revealed similar trends in the United States and Europe, although most were based on relatively homogenous populations with comparatively high socioeconomic status.[15]

Mokete et al found a lack of stage migration in men from a inner city population in the United Kingdom who underwent PSA screening.[16] From 1994 to 2003 there was no statistically significant difference in the percent of men presenting with localized (38%), locally advanced (37%) or metastatic (25%) disease despite a proportional increase in PSA screening during the 10 years. Based on these observations the stage migration observed in the PSA era may be disproportionately distributed in men in a higher socioeconomic demographic.[5]

A recent study by Miller et al provides additional support for this phenomenon.[17] Trends in prostate cancer characteristics were evaluated in 570 men enrolled in IMPACT with diverse ethnicity and low socioeconomic status. In contrast to their more affluent, insured, educated and white counterparts, low risk disease did not increase with time in these men. Rather, 24% of the men presented with low risk tumor characteristics and this proportion remained stable with time. In about 50% of the men PSA exceeded 10 ng/ml and Gleason score was 7 or greater on biopsy. Approximately 11% of them had clinical stage T2 or greater and 19% had metastatic cancer at diagnosis.

We report similar findings in men in a public health system. Compared to patients in a community and an academic cohort, our patients of lower socioeconomic status presented with higher risk prostate cancer. In approximately half of our patients PSA exceeded 10 ng/ml and Gleason score was 7 or greater on biopsy, in concordance with the population described by Miller et al.[17] Our analysis includes multivariate risk assessment, a longer observation period, and direct comparison to contemporaneous academic and community based registries. Moreover, since it includes Medicare and other low income but insured patients, the SFGH population may be more representative of the breadth of low socioeconomic status than IMPACT, which covers only uninsured men.

There are multiple possible explanations for the disparity in disease presentation among the prostate cancer cohorts analyzed in this study. Studies show that access to quality care and socioeconomic factors that limit access can have a significant role in cancer survival in men of different racial/ethnic backgrounds.[18,19] Potentially the lack of access to early detection programs and cancer screening explains part of the disparity in prostate cancer presentation. However, other investigators reported racial and ethnic disparities that persist after controlling for socioeconomic factors and access to medical care, and found that most cancer in this population is still detected by screening.[20,21] Patients at SFGH were no older on average than those at UCSF and younger than those in CaPSURE, suggesting that delayed diagnosis due to poor access to care does not likely explain a large part of the risk difference.

As yet unknown genetic factors may partially explain the findings. Lichtenstein et al described results from twin studies that heritable factors contribute 42% of prostate cancer risk.[22] Oakley-Girvan et al concluded that after controlling for socioeconomic status and comorbid conditions black and Asian American men were 1.5 times more likely to be diagnosed with advanced prostate cancer.[23] This suggests the potential impact of independent heritable risk factors, although this association remains controversial since other groups noted no influence and specific genetic factors associated with risk remain to be identified across sociodemographic groups.[23,24] We hope in the future to collect tissue specimens from men treated for prostate cancer at SFGH to elucidate further unique biological determinants.

Also, dietary and environmental inputs, and chronic allostatic stress load related to poverty may have a significant role. Potential dietary risk factors include obesity, high consumption of animal fat and intake of toxins such as cadmium.[25] Contemporary studies highlight that comprehensive lifestyle changes targeting these factors may modify the progression of prostate cancer in men with low risk disease, likely via pathways affecting gene expression and oncogene transcription.[26] Klassen et al examined prostate cancer risk in patients based on area resources such as race, income, education, neighborhood and community resources.[27] Those at highest risk for advanced tumor grade were white men with low income and all black men, suggesting the contribution of environment and psychosocial impact.

Chronic allostatic stress or the psychobiological response is defined as the physiological cost of chronic exposure to a repeat stressor such as poverty. It is postulated that frequent activation of the stress response of the body, which is essential to manage acute threats, can with time affect and accelerate various disease states, such as cancer progression.[28] Ellison et al recently proposed a theoretical model linking psychosocial stress to adverse risk factors in black men, potentially due to interaction with immune modulation.[29] In fact, the true explanation for the differences that we observed between the SFGH cohort and the comparison cohorts is almost certainly multifactorial.

Based on our findings, the most significant impact of prostate cancer screening, diagnosis and treatment may be in high risk patients, in particular those of lower socioeconomic status and/or nonwhite race. Recent studies highlight the controversy regarding PSA screening, the risk of over detection and related concerns regarding overtreatment in men with low stage and grade disease.[30] We believe that our findings may help guide future screening policy decisions, such as the allocation of screening efforts specifically to programs serving the communities in which disadvantaged men live and work. Education outreach programs and promoting awareness in other interfaces with the health care systems (primary care, emergency room care and psychiatric care) may be central interventions to help screen and treat these men, in whom under rather than over diagnosis may be a greater problem than in other populations. Such institutions would also provide excellent settings for future research aimed first at identifying risk factors that best explain the higher prevalence of high risk disease in low socioeconomic status settings and then systematically ameliorating these disparities.

Our study has limitations. It is retrospective and nonrandomized in nature and, thus, susceptible to the biases of such studies. The CaPSURE database is driven by urologist based practices and does not include primary care or medical oncology treatments except as reported by the patient or urologist. The UCSF Cancer Registry includes patients from urology practices and medical oncology referrals, which may contribute to a higher proportion of men with more advanced cancer. Also, our findings may not be representative of men of lower socioeconomic status in rural or other geographic regions since our study population included men in San Francisco. We could not account for other confounding variables that may explain the differences observed. Further investigation is needed to elucidate whether the burden of high risk disease results in increased prostate cancer specific mortality and morbidity.

CONCLUSIONS

Men of lower socioeconomic status diagnosed with prostate cancer bear a substantially higher burden of high risk disease compared to men in a community setting and an academic center, and most other previously reported patient cohorts. Multiple theories exist regarding the etiology of this disparity, which is most likely multifactorial. More clinical and research efforts must be directed toward early diagnosis and management of prostate cancer in underserved patient populations.

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