Ethnic minorities (African American and Hispanic) males prefer prostate cryoablation as aggressive treatment of localized prostate cancer

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KIM FJ, WERAHERA PN, SEHRT DE, GUSTAFSON D, SILVA RD, MOLINA WR. Ethnic minorities (African American and Hispanic) males prefer prostate cryoablation as aggressive treatment of localized prostate cancer. *Can J Urol* 2014;21(3): 7305-7311.

Introduction: *Our safety net hospital offers minimally invasive, traditional open and perineal radical prostatectomies, as well as radiation therapy and medical oncological services when appropriate. Historically, only few African American and Hispanic patients elected surgical procedures due to unknown reasons. Interestingly, after initiation of the prostate cryoablation program (Whole Gland) in 2003 at Denver Health Medical Center (DHMC) we noticed a trend towards cryotherapy in these specific patient populations for the treatment of localized prostate cancer. We analyzed the profile of ethnic minority men evaluated for localized prostate cancer and evaluated the associated factors in the decision making for the treatment of localized prostate cancer.*

Materials and methods: *A retrospective review of 524 patients seen for prostate cancer from January 2003 to January 2012 in our safety net hospital was conducted. The treatment selected by the patient after oncologic consultation was then recorded. The health insurance status, demographic data, and personal statements of reasons for elected procedure were obtained. A multivariate logistic regression for associated factors influencing treatment decisions was then formed. Patients were categorized by using the D'Amico risk stratification criteria.*

Results: *The insurance status revealed that only 1% of African American patients had private health insurance versus 5% Hispanic and 26% of Caucasians. African American men were at higher D'Amico risk with more positive metastasis evaluation yet were less likely to undergo surgery and instead often elected for radiation therapy. Conversely, Hispanic and Caucasian men often elected cryoablation and radical prostatectomy for their treatment. Referrals for surgery were primarily Caucasian males with private health insurance. Most minority patients had indigent health coverage. Statistical analysis further revealed that age, marital status, indigent enrollment, D'Amico risk, and the option of cryoablation may influence patient's selection for surgical management of localized prostate cancer.*

Conclusion: *Many factors influence treatment selection including race, age, marital status, enrollment in an indigent program, and a high D'Amico risk. The less invasive nature of cryoablation appeared to influence patients' opinion regarding surgery for the treatment of localized prostate cancer, especially in African American men.*

Key Words: prostate cancer, minority group, decision making, cryoablation

Introduction

Prostate cancer exhibits the most striking racial disparity, as African American men are at 1.4 times higher risk of being diagnosed, and have a 2-3 times higher risk of dying of prostate cancer compared to Caucasian men.[1] Moreover, African American men have lower odds of undergoing radical prostatectomy compared to Caucasian men.[2] Conversely, they have greater odds of receiving radiation therapy or watchful waiting.[3] According to the Office of Minority Health of the US Department of Health Human Services, new prostate cancer diagnosis in Hispanic males occurs in 116.2 cases out of every 10 men.[4,5] Hispanic American

Accepted for publication April 2014

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men and women generally have lower cancer rates than the non-Hispanic Caucasian population. However, disparities still exist in certain types of cancer and initial diagnosis may have advanced disease and will be not eligible for curative treatment. Therefore, we analyzed the demographic and health insurance profile of men diagnosed with prostate cancer and evaluated the selection factors for the surgical management of localized prostate cancer at our institution because we observed a shift of patients electing cryotherapy, especially African American and Hispanic patients.

Materials and methods

We performed a retrospective chart review of male patients evaluated between January 2003 and January 2012 in a single institution (tertiary hospital). Patients were deemed eligible for the study if they were diagnosed with prostate cancer. The variables included in this study were demographics, insurance status, and tumor registry data. Preoperative data included age, race, marital status, insurance type, residency, census data for Denver, prostate specific antigen (PSA), and Gleason sum (GS). Insurance status was defined as private, Medicare, Medicaid, and Indigent program. Patients eligible for the Indigent program are at or below 25% of the Federal Poverty Level. Residency was considered In- or Out-of-County due to eligibility requirements for the Indigent program. All patients were classified by D'Amico risk stratification. Patients classified as intermediate or high risk underwent evaluation for metastasis according to the American Urological Association (AUA) guidelines. An institutional review board approved the study previous to data collection.

Patients that were consulted for their cancer at our institution were included in a multivariate logistic regression of variables hypothesized to influence the surgical selection of treatment for localized prostate cancer. These factors included age, insurance, marital status, D'Amico risk, and race. Surgical treatment included radical open, perineal and laparoscopic prostatectomy and cryoablation performed by a single surgeon while non-surgical treatment pertained to active surveillance, radiation therapy, and hormonal management. Real-time translation to all non-English patients was offered and provided as our institutional policies mandate.

Statistical analysis was performed in the R Project. Discrete variables were evaluated with a chi-squared test. Data are presented as average ± standard error and frequency (percentage of race) unless otherwise stated. A p value < 0.050 was considered significant.

Results

Retrospective medical chart reviews of 524 men were evaluated between January 2003 until January 2012 due to completeness of medical records and insurance documentation. From the male patients seen, a total of 441 men underwent prostate needle biopsy for elevated PSA and/or abnormal digital rectal exam in our safety net hospital, Table 1. Two hundred and seventy-three patients were diagnosed with prostate cancer and 190 patients were treated for localized prostate cancer by a single surgeon. There were 65 African American, 53 Hispanic, and 72 Caucasian men. Hispanic men were typically older at biopsy ($p = 0.042$) while African American men presented with higher PSA ($p = 0.005$). A total of 83 men with private insurance from out of county were referred to our clinic specifically for surgical management of prostate cancer.

Insurance status

From the total of 441 patients that underwent prostate needle biopsy at our center, 49 (11.2%) patients had major private insurance coverage with the majority of Caucasian men having this coverage. A majority of these private payers were from outside of the county. A majority of the minority patients were considered residents and were largely enrolled in the indigent health care plan.

In evaluating those over the age of 65 and potentially eligible for Medicare, another disparity is seen. Although the majority of coverage is through this entity, over 20% of the Hispanic population and 9% of the African American population was still covered by the Indigent plan ($p = 0.066$). Meanwhile, African American and Hispanic men under 65 heavily relied on the Indigent plan with 70 and 61% enrollment, respectively. Caucasian men under the age of 65, however, had 31% enrollment in private insurance plans.

Oncological profile and outcome

Notably, Hispanic men had a much lower malignancy rate even with similar PSA prior to prostate needle biopsy ($p < 0.001$), Table 1. Additionally, African American men had the highest median PSA and Gleason scores. Caucasian men were primarily diagnosed with Gleason 6 while African American men had more aggressive Gleason 8 and 9 prostate cancers. When stratifying D'Amico classification, Caucasian men had more low risk* cancer ($p = 0.187$) while African American men had significantly more high risk* cancers ($p = 0.035$). Resultantly, African American men had more positive bone scan for metastatic work up ($p < 0.001$). (*D'Amico risk stratification).

TABLE 1. **Demographics and oncologic profile**

	All	African American	Hispanic	Caucasian	p value
Biopsied profile					
N	641	179 (27.9%)	235 (36.7%)	227 (35.4%)	-
Age	63.0 ± 0.4	62.8 ± 0.7	64.4 ± 0.6	61.7 ± 0.6	*0.042
PSA (median)	6.8 (0.2-183.0)	7.6 (0.5-183.0)	6.7 (0.3-103.3)	6.6 (0.2-167.0)	*0.005
Resident	509 (92.1%)	171 (95.9%)	229 (97.5%)	189 (83.3%)	*< 0.001
Insurance					*< 0.001
Private	71 (11.2%)	7 (3.9%)	18 (5.0%)	58 (25.3%)	*< 0.001
Medicare	194 (30.3%)	67 (37.7%)	71 (30.4%)	56 (25%)	0.056
Medicaid	115 (17.8%)	23 (13.1%)	40 (24.8%)	33 (14.5%)	*0.013
Indigent	261 (40.8%)	82 (48.4%)	64 (39.8%)	80 (35.2%)	0.105
Oncologic profile					
Malignant	295 (46%)	94 (52.8%)	96 (40.8%)	105 (46.2%)	< 0.001
Age	63.0 ± 0.4	62.8 ± 0.9	64.4 ± 1.1	61.7 ± 0.8	0.011
PSA (median)	6.8	11.0	9.0	7.6	0.05
Gleason score					
6	50.3%	40.8%	52.8%	57.0%	0.130
7	28.5%	28.2%	26.4%	30.4%	0.881
8	10.8%	19.7%	9.4%	3.8%	*0.007
9	9.4%	11.3%	11.3%	6.3%	0.497
10	0.9%	0.0%	0.0%	2.5%	0.205
Risk category					
Low	39.4%	32.4%	37.7%	46.8%	0.187
Moderate	32.5%	29.6%	34.0%	34.2%	0.807
High	28.1%	38.0%	28.3%	19.0%	*0.035
Positive bone scan	5.9%	9.8%	4.3%	4.5%	0.337

PSA = prostate-specific antigen

Treatment selection of prostate cancer

There was no difference in the selection for curative treatment of localized prostate cancer in population (p = 0.775), Table 2. However, there was a statistical difference between African American and Caucasian men with regards to surgical management (p = 0.041). Other than choosing cryoablation, African American men were more likely to undergo radiation while more Hispanic and Caucasian men underwent prostatectomy.

Out of county referrals

Referrals were common for laparoscopic prostatectomy

TABLE 2. **Selection of treatment for localized prostate cancer**

Treatment	All (n = 295)	African American (n = 94)	Hispanic (n = 96)	Caucasian (n = 105)	p value
Surveillance	35 (11.8%)	12 (12.7%)	7 (7.3%)	16 (15.2%)	0.816
Radiation	32 (10.8%)	18 (19.1%)	6 (6.5%)	8 (7.6%)	0.05
Cryoablation	136 (45%)	45 (53.1%)	43 (44.7%)	48 (45.7%)	0.856
Laparoscopic prostatectomy	92 (28.9%)	19 (20.2%)	40 (41.5%)	33 (31.4%)	0.100
Surgical*	228 (77.2%)	64 (68%)	83 (79%)	81 (77.1%)	0.168

*from 295 patients with prostate cancer 77.2% of men chose a surgical procedure (cryoablation-45% or prostatectomy-28.9%)

and cryoablation of the prostate, Table 3. The laparoscopic prostatectomy referrals were primarily Caucasian men (45: 95.7%) while there were 2 minority men (4.3%). However, cryoablation had more minority patient referrals. Of note: African American men were referred to our institution since we are the safety net hospital for this population. Most of the Hispanic and out-of-county cryoablation patient referrals had private insurance.

Associated factors on surgical treatment selection

Multivariate logistic regression revealed marital status as the only significant factor ($p = 0.036$) which positively influenced the selection of surgical treatment for localized prostate cancer, Table 4. Age and being an African American male all trended to negatively influence the selection of surgery while high risk cancer and offering cryoablation trended towards a positive selection. Further chi-squared testing revealed a significant decrease in the number of prostatectomies once cryoablation was offered. Caucasian and Hispanic men elected significantly less radiotherapy once cryoablation was available in our institution as well ($p < 0.050$). After the introduction of cryoablation, African American men were significantly less likely to undergo prostatectomy and instead elected for more cryoablation ($p = 0.015$).

TABLE 3. **Demographic, residence, insurance data, oncological profile, and disease characteristics of cryoablation by ethnicity**

	African American	Hispanic	Caucasian	p value
N=136	45	43	48	
Age	62.0 ± 7.1	65.8 ± 7.6	62.6 ± 6.5	0.058
Body mass index	25.2 ± 7.9	27.6 ± 8.5	26.6 ± 7.3	0.064
County resident	41 (91%)	33 (76.7%)	23 (47.9%)	< 0.001
Insurance type				
Private	4.8%	11.8%	50.0%	< 0.001
Medicare	31.0%	44.1%	25.0%	
Medicaid	14.3%	14.7%	6%	
Indigent (IP)	51.1%	29.4%	18.7%	< 0.001
Medicare eligibility age (> 65 years old), but elected not to apply for Medicare	4 (9% of 23 IP)	2 (33.3% of 6 IP)		
Oncological profile				
Prostate size	30.5 (23.2-40.8)	32.8 (24.0-43.4)	38.8 (28.1-49.1)	0.053
Prostate length	3.9 (3.3-4.6)	4.1 (3.2-4.7)	4.3 (3.0-4.9)	0.052
Gleason score				
6	42.9%	29.4%	47.4%	0.564
7	42.9%	44.1%	32.9%	
8	11.9%	17.6%	13.2%	
9	2.4%	8.8%	6.6%	
PSA (median)	9.1 (5.5-23.0)	10.4 (6.0-30.2)	7.4 (4.9-12.0)	0.057
D'Amico risk				
Low	31.0%	20.6%	39.5%	0.134
Moderate	38.1%	47.1%	44.7%	
High	31.0%	32.4%	15.8%	
Lymphadenectomy*	64.3%	52.9%	51.3%	0.380

*laparoscopic lymphadenectomy was performed in patients with moderate or high D'Amico risk stratification that agreed to have the procedure done
PSA = prostate-specific antigen
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TABLE 4. **Questionnaire of reason why one treatment was chosen over others**

1) What treatment did you choose to treat your prostate cancer?

a) No treatment but actively follow up the PSA level and have a prostate biopsy once every 6-12 months
b) Remove the prostate with surgery (open or laparoscopically)
c) Freeze the prostate with cryoneedles
d) Radiation of the prostate
e) Hormonal management with injections or remove the testicular tissue

2) State relevant reasons why the procedure was chosen:

a) Degree of invasiveness of procedure
b) Hospitalization time
c) Need for blood transfusion
d) Side effects (unable to control urination, unable to have erections and sexual intercourse) incontinence, and open statement.
e) Open statement:

Treatment	n	Open statement
Surveillance	NA	
Radiation	32 non invasive	2 bad experience with surgery-someone they know
Cryoablation	136 less invasive 88 decreased chance for urinary incontinence issues	Needle surgery, no blood transfusion needed
Laparoscopic	92 less invasive	77 need to remove cause of cancer, 36-their primary doctor recommended to remove it

Discussion

Factors influencing treatment of minority patients with localized prostate cancer remains unclear. Recently, we reported that race interacts with social vulnerability to influence urologist recommendations for radical prostatectomy. Because prostate cancer tends to be more lethal in African Americans, urologists may view such patients as good candidates for radical prostatectomy. However, African American race may amplify perceptions of social vulnerability and heightening urologists' concerns about poor surgical outcomes and follow up.[4] Thus, African Americans historically received prostatectomy less often than Caucasians although they did not receive less curative treatment overall.[6] Our results indicate that the impact of social vulnerability may still exist but is improving. After we instituted a cryoablation program for prostate cancer, we did see an increased number of African American patients that chose prostate cryoablation as curative intent therapy versus other modalities for the treatment of newly diagnosed localized prostate cancer. Often, our African American patients expressed significant concerns towards removal of the prostate, related to possible bleeding, side effects, especially urinary incontinence and surprisingly, violation and spreading of cancer when performing any type of prostatectomy due to "cutting." These concerns were not observed in the other populations. Hispanics have generally elected for aggressive treatment and prostatectomy but now generally select cryoablation after consultation.

Another factor to the vulnerability of these patients is age. Prostate cancer is typically diagnosed in the early 60's but traditional Medicare coverage starts at 65 years old. Approximately 13% of the population between 50 to 65 years old were uninsured in 2007 and this number has been growing.[7] A majority of our population was in this socially vulnerable standing prior to 65, but later many were eligible for Medicare coverage. Thus a paradigm exists as older men are covered but are less likely to select curative treatment while younger men who want to be treated may not be able to because of lack of health coverage. Our data further showed that indigent patients were less likely to select surgical management for their prostate cancer and may be due to the financial burden for surgery. Yet another problem is that many in the Hispanic community will not be eligible for Medicare > 65 years old. Although immigrants after 5 years of continued

residency can purchase Medicare insurance, those in the indigent plan cannot afford this coverage. Thus, many elderly Hispanic men are restricted to where they may seek medical treatment. Whether or not this barrier has resulted in poorer outcomes with prostate cancer remains to be unseen.

Although race, socioeconomic status, and tumor stage are all critical in the determination of the right treatment for the patient, marital status seems to play a critical component as well.[6] In a cohort of 27,920 non-Hispanic Caucasian, African American, and Hispanic men without comorbidities in the 1995–1999 linked to Surveillance, Epidemiology and End Results–Medicare dataset it was shown that marriage was positively associated with curative treatment in general, and with prostatectomy. This study has expanded the influence of marriage to include cryoablation as well. Marriage predicted curative treatment compared with expectant management (adjusted risk ratio [RR] _ 1.28 [1.25-1.30]) and prostatectomy compared with radiotherapy (adjusted RR _ 1.24 [1.20-1.28]). In the study, younger age and higher tumor grade were more robust predictors of curative treatment intent compared with expectant management, prostatectomy, or radiotherapy. Our data further suggests that marital status should not be overlooked.[6]

The primary goal of any prostate cancer surgery is satisfactory oncological outcomes. Retropubic radical prostatectomy is the gold standard in this regard with a biochemical disease free survival at 3 and 5 years of 99% and 98% respectively.[8] The laparoscopic approach has reported a biochemical progression-free survival of 90.5% at 3 years.[9] Robotic assisted laparoscopic prostatectomy (RALP) has reported a 95% PSA progression-free survival with a follow up less than 1 year.[10] Intensity-modulated radiotherapy has an 8 year biochemical relapse between 72%-85% using the ASTRO criteria.[11] Like RALP, cryoablation is an emerging technology in the treatment of prostate cancer. A recent AUA Best Practice Statement describes cryotherapy as a reasonable therapeutic option in both the primary and salvage settings.[12] The 5 year overall biochemical disease free survival of 1198 patients treated with cryoablation has been reported at 77.4%.[13] However, follow up with these patients remain controversial with the definition of biochemical recurrence and biochemical disease free survival. The Cryo On-Line Data Registry (COLD registry) is a multicenter database pooling data from both academic and community centers, and the maturation of this data set will hopefully achieve an evidenced based definition of treatment success and to delineate the role of this therapeutic regimen in patients with localized prostate cancer.

Along with patient and physician preferences for treatment, the cost of surgery should also be strongly considered. A large component of our population is uninsured, making the economics of treatment all the more critical. Radical prostatectomy has been the gold standard not only for oncologic treatment but also for cost analysis. A group evaluating the cost effectiveness of treating prostate cancer noted that radical prostatectomy costs $7300 while radiation modalities such as brachytherapy and intensity modulated radiation therapy costs $19000 and $46900 respectively.[14] Minimally invasive surgeries, on the other hand, have shown to be less expensive than open surgery. Polascik et al reported that the total hospital cost of laparoscopic radical prostatectomy and cryoablation were less than radical prostatectomy with significant difference.[15] However, robotic assisted radical prostatectomy has been shown to be more expensive than open retropubic radical prostatectomy.[15,16] In this study, the authors cited a net loss of $4000 per case with the robotic procedure between charges and the payments received. In our study we have shown that African American men prefer radiation therapy, the most expensive procedure. Compounded with the lack of insurance coverage, radiation therapy places financial strain on the treating institution. Although laparoscopic prostatectomy was not preferred by this demographic, it appears the minimally invasive nature of cryoablation is satisfactory and remains fiscally reasonable. Hispanic men also seem to prefer cryoablation rather than prostatectomy. The change in our patients' preference for surgical treatment after the introduction of cryoablation also seems to suggest that patients desire a less invasive management than prostatectomy. Nonetheless, the application of radical prostatectomy along with the recent addition of cryoablation has allowed our clinic to provide level one care to all, regardless of a patient's ability to pay.

Limitations

Our study has several limitations that deserve to be mentioned. This report is from a single institution, it is a retrospective review with lack of validated questionnaire to understand causes of therapy choice by different ethnic groups and also it reports a small sample of patients. Conversely, this is the best representation of the profile of patients with prostate cancer in our county treated and many by cryoablation of the prostate. Treatment bias is a constant concern when studying surgical options but we tried to minimize it by allowing senior residents present all treatment options prior to attending surgeons with unbiased view.

Regrettably, the mechanisms why minority patients differ electing different treatment modalities for the treatment of localized prostate cancer remain unclear yet very important.

Conclusion

Minority patients that received treatment for localized prostate cancer in our safety net hospital were often enrolled in the state indigent health care program, while Caucasian patients were often referred specifically for laparoscopic prostatectomy and cryoablation from different parts of the country with private insurance. The majority of Caucasian patients were classified as low D'Amico risk versus African American men that were classified intermediate or high risk. Prostate cryoablation seem to be a feasible alternative to different ethnicities that seek aggressive curative intent treatment with minimally invasiveness of the procedure. Although we do not completely understand why patient from different ethnicities may elect and view more favorably cryoablative therapy than other aggressive therapy for prostate cancer, there are still many forces that influence patient's decisions with regards to the treatment of localized prostate cancer. □

References

1. National Cancer Institute. Surveillance, Epidemiology, End Results. Avaiable from URL: http://seer.cancer.gov/statistics/. Accessed February 7th, 2012.
2. Imperato PJ, Nenner RP, Will TO. Radical prostatectomy: lower rates among African-American men. *J Natl Med Assoc* 1996;88(9): 589-594.
3. Moses KA, Paciorek AT, Penson DF et al. Impact of ethnicity on primary treatment choice and mortality in men with prostate cancer: data from CaPSURE. *J Clin Oncol* 2010;28(6):1069-1074.
4. Denberg TD, Kim FJ, Flanigan RC et al. The influence of patient race and social vulnerability on urologist treatment recommendations in localized prostate carcinoma. *Med Care* 2006; 44(12):1137-1141.
5. U.S. Department of Health & Human Services. Cancer and Hispanic Americans. Avaiable from URL: www.minorityhealth.hhs.gov. Accessed July 1st, 2012.
6. Denberg TD, Beaty BL, Kim FJ et al. Marriage and ethnicity predict treatment in localized prostate carcinoma. *Cancer* 2005; 103(9):1819-1825.
7. AARP Public Policy Institute. Health care reform: what's at stake for 50-to 64-year-olds? Avaiable from URL: http://assets.aarp.org/rgcenter/health/i24_hcr.pdf. Accessed July 1st, 2012.
8. Gettman MT, Blute ML. Critical comparison of laparoscopic, robotic, and open radical prostatectomy: techniques, outcomes, and cost. *Curr Urol Rep* 2006;7(3):193-199.
9. Guillonneau B, el-Fettouh H, Baumert H et al. Laparoscopic radical prostatectomy: oncological evaluation after 1,000 cases a Montsouris Institute. *J Urol* 2003;169(4):1261-1266.
10. Patel VR, Tully AS, Holmes R et al. Robotic radical prostatectomy in the community setting--the learning curve and beyond: initial 200 cases. *J Urol* 2005;174(1):269-272.
11. Zelefsky MJ, Chan H, Hunt M et al. Long-term outcome of high dose intensity modulated radiation therapy for patients with clinically localized prostate cancer. *J Urol* 2006;176(4 Pt 1):1415-1419.
12. Babaian RJ, Donnelly B, Bahn D et al. Best practice statement on cryosurgery for the treatment of localized prostate cancer. *J Urol* 2008;180(5):1993-2004.
13. Jones JS, Rewcastle JC, Donnelly BJ et al. Whole gland primary prostate cryoablation: initial results from the cryo on-line data registry. *J Urol* 2008;180(2):554-558.
14. Perlroth DJ, Goldman DP, Garber AM. The potential impact of comparative effectiveness research on U.S. health care expenditures. *Demography* 2010;47 Suppl:S173-S190.
15. Mouraviev V, Nosnik I, Sun L et al. Financial comparative analysis of minimally invasive surgery to open surgery for localized prostate cancer: a single-institution experience. *Urology* 2007;69(2):311-314.
16. Tomaszewski JJ, Matchett JC, Davies BJ et al. Comparative hospital cost-analysis of open and robotic-assisted radical prostatectomy. *Urology* 2012;80(1):126-129.