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The Changing Face of Low-risk Prostate Cancer: Trends in Clinical Presentation and Primary Management

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Abstract

Purpose—Early intervention for prostate cancer is associated with excellent long-term survival, but many affected men, especially those with low-risk disease characteristics, might not suffer adverse impact to quantity or quality of life were treatment deferred. We sought to characterize temporal trends in clinical presentation and primary disease management among patients with low-risk prostate cancer.

Methods—Data were abstracted from CaPSURE, a disease registry of 8685 men with various stages of prostate cancer. 2078 men were included who were diagnosed between 1989 and 2001 and had a serum prostate specific antigen (PSA) ≤ 10 ng/ml, Gleason sum ≤ 6, and clinical T-stage ≤ 2a. Trends in risk distribution, tumor characteristics, and primary treatment were evaluated.

Results—The proportion of patients with low-risk tumor characteristics rose from 29.8% in 1989–1992 to 45.3% in 1999–2001 (p<.0001). There have been sharp increases in the use of brachytherapy and androgen deprivation monotherapy, from 3.1 and 3.1%, to 12.0 and 21.7%, respectively. Utilization rates for prostatectomy, external-beam EBRT, and observation have fallen accordingly, from 63.8, 16.1, and 13.8% to 51.6, 6.8, and 7.9% (p<.0001 for all except prostatectomy, p=.0019). Age and socioeconomic status were significantly associated with treatment selection, but overall the treatment trends were echoed on subgroup analysis of patients 75 years old or greater.

Conclusions—Low-risk features characterize a growing proportion of prostate cancer patients, and there have been significant shifts in the management of low-risk disease. Over-treatment may be a growing problem, especially among older patients.

Introduction

With an estimated incidence in 2003 of 220,900, prostate cancer is the most common malignancy in the United States.[1] The rising prevalence of prostate specific antigen (PSA)-based screening for this tumor has facilitated great strides in its early diagnosis and treatment. However, the natural history of cases diagnosed early, by PSA screening or otherwise, may be prolonged; as a result, only 25 to 33% of men diagnosed with prostate cancer actually die of the disease.[2,3] Recent reports have drawn attention to this problem of

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overdiagnosis, arguing that a significant fraction of tumors detected by screening might not have adversely affect patients' lifespan or quality of life if they were to remain undetected.[4]

While local therapy yields excellent long-term survival rates among patients with clinically localized disease,[5–7] and has been recently been shown to reduce prostate cancer metastases and cause-specific mortality,[8] all available active treatments exert a significant impact on patient health-related quality of life (HRQOL).[9] In an effort to avoid such treatment-related morbidity, several recent studies have highlighted the feasibility of active surveillance as a viable initial treatment alternative in carefully selected patients with low-risk disease characteristics.[10,11] More than ever, therefore, it is crucial that prostate cancer treatment decisions be informed by estimates of the likelihood of future disease progression, morbidity, and mortality.

A number of instruments have been developed in the past decade to predict prostate tumors' clinical behavior; the best validated of these are based on the serum PSA at diagnosis, the Gleason score of the diagnostic biopsy, and the clinical T stage. There appears to exist good consensus especially on those clinical characteristics defining low-risk cancers: serum PSA at diagnosis ≤ 10 ng/ml, diagnostic biopsy Gleason score less than 7 with no pattern 4 or 5 disease, and clinical stage T1 or T2a.[12,13]

Patients with low-risk tumors enjoy the greatest likelihood of prolonged disease-free survival following definitive local treatment; however, they are also the most likely to remain free of progression on active surveillance protocols. To our knowledge, however, contemporary practice patterns in terms of treatments for these patients, have not been well described at the national level. Therefore, we identified a cohort of patients with low-risk tumors from a large, community-based database of men with prostate cancer, and analyzed temporal trends in their presentation and management.

Methods

Description of the disease registry

CaPSURE™ (Cancer of the Prostate Strategic Urologic Research Endeavor) is a longitudinal, observational database of men with biopsy-proven prostate adenocarcinoma, recruited from over 30 academic- and community-based urology practices across the United States. All newly-diagnosed prostate cancer patients are recruited consecutively by participating urologists, who report complete clinical data and follow-up information on diagnostic tests and treatments. Informed consent is obtained from each patient under local institutional review board supervision. Patients are treated according to their physicians' usual practices, and are followed until time of death or withdrawal from the study. Completeness and accuracy of the data are assured by periodic random sample chart review.[14,15]

Study population

Between June 1, 1995, when the database was opened, and July 31, 2002, 8685 patients agreed to participate in the CaPSURE project, representing roughly 90–95% of those invited at each practice site. 7636 were diagnosed between 1989 and 2001; of these, 1820 were excluded because they had unknown PSA at diagnosis, diagnostic biopsy Gleason score, and/or clinical T stage, and 251 because they had an unknown primary treatment. Finally, we excluded 222 patients who received cryotherapy as primary therapy. Overall, these accounted for only 2% of patients since 1996, 68% of these were treated at a single practice site in the early 1990s in the context of a clinical trial.

Analysis: predictors of low-risk stratification

Among the 5343 patients who met the inclusion parameters, we identified low-risk patients according to the PSA, Gleason score, and clinical stage criteria noted above.[12] Sociodemographic variables were compared between low-risk patients and those in higher risk strata, using the χ^2 test for categorical variables and the Mantel-Haenszel χ^2 test for ordinal and categorized continuous variables. Predictors of diagnosis of tumors with low-risk features were identified by building these sociodemographic variables into a logistic regression model, also controlling for year of diagnosis. For these variables, odds ratios (OR) with 95% confidence intervals (CI) were calculated for the likelihood of low-risk classification for patients at each level of each variable.

Analysis: temporal trends in risk factors at diagnosis and primary treatment selection

Temporal trend data were analyzed by year of diagnosis, grouped as follows: 1989–1992, 1993–1995, 1996–1998, and 1999–2001. First, the overall percentage of men in each time period with low-risk disease features were examined, followed by an analysis of time trends within each of the risk factors (PSA, Gleason score, and T stage) among low-risk patients. We next analyzed changes over time in the distribution of low-risk patients among the various primary treatment alternatives: radical prostatectomy (RP), external-beam radiotherapy (EBRT), interstitial radiotherapy (brachytherapy), primary androgen deprivation therapy (PADT), and watchful waiting (WW). We also examined the proportion of patients receiving definitive local treatment (RP, EBRT, or brachytherapy) who first received neoadjuvant androgen deprivation therapy (NADT). We performed a subgroup analysis of patients 75 years of age or older. 75 represents the 90th percentile for age in our dataset, and has been used as a threshold for previous studies of prostate cancer treatment patterns among older patients.[16,17] The significance of each of these time trends was assessed via the Mantel-Haenszel χ^2 test for trend. Finally, we assessed the association of sociodemographic variables with treatment selection, using the χ^2 or Mantel-Haenszel χ^2 test, as appropriate. All statistical tests were conducted at the two-sided p=.05 level of significance. As this was an exploratory analysis of several temporal trends in disease management, we did not specifically control for multiple comparisons.

Results

1990 of 5343 men in the analysis (37.2%) met the criteria for low-risk disease, 29.8% of those diagnosed in 1989–1992, 32.6% in 1993–1995, 32.7% in 1996–1998, and 45.3% in 1999–2001 (p<.0001 for trend).

Table 1 compares the sociodemographic characteristics of low-risk and non-low-risk patients in the dataset. Compared to those in higher risk strata, low-risk patients are significantly younger, and have higher incomes and more education. They are less likely to be covered by Medicare, more likely to be Caucasian, and slightly more likely to be seen in a community setting. In multivariable analysis, year of diagnosis, age, ethnicity, and geographic region were significant predictors of low-risk diagnosis. Patients diagnosed in all time periods after 1989–1992 are more likely to be diagnosed with low-risk tumors than those in 1989–1992. The likelihood of a low-risk diagnosis decreases steadily with advancing age, and is less likely among African-Americans than among Caucasians. Patients in the South are also more likely than those in the West to be diagnosed at low-risk. The time trend toward increasing low-risk diagnoses in the more recent years of the analysis was seen in all ethnic groups and geographic regions studied,

Figure 1 illustrates the shifts over time in the clinical characteristics of low-risk tumors. In terms of clinical stage (panel A), screen-detected T1c cancers now represent nearly two-

thirds of incident low-risk cases, whereas unilaterally palpable T2a tumors have fallen from nearly three-quarters to 36% of cases. T1a and T1b tumors, diagnosed incidentally on pathological analysis of resected benign prostatic hypertrophy tissue, have fallen to a total of only 2% of tumors. Panel B demonstrates a shift toward higher Gleason scores within the low-risk group; the proportion of low-risk tumors graded 5–6 has risen from 59.5 to 96.1% over the study period. As shown in panel C, the proportion of low-risk tumors associated with a serum PSA <4 ng/ml has fallen from 25.5 to 17.2%. Although this is a statistically significant trend over the entire study period, there has been little change in the PSA distribution since 1993.

The distribution of primary treatment modality selected by patients with low-risk tumors is presented in Figure 2. The most striking trends are the four- and seven-fold increases in the use of PADT and brachytherapy, from 3.1 and 3.1%, respectively, in 1989–1992 to 12.0 and 21.7% in 1999–2001. EBRT and observation utilization have each fallen by roughly half, from 16.1 to 6.8% and from 13.8 to 7.9%, respectively. These trends are all statistically significant ($p<.0001$ for each). The use of RP has also fallen, from 63.8 to 51.6% ($p=.0019$), but this trend has been less pronounced, and rates have been relatively stable since 1993. Use of NADT in conjunction with local treatment increased steadily, with 3.9, 6.5, 8.8, and 10.7% of treated low-risk patients in each year group, respectively, receiving neoadjuvant therapy ($p=.0001$ for trend). Across the time periods, 4.1% of RP patients, 26.3% of brachytherapy patients, and 25.1% of EBRT patients received NADT. Overall, 18.1% of the low-risk patient in our analysis received primary or neoadjuvant androgen ablation.

We analyzed sociodemographic factors associated with differing treatment patterns among low-risk patients (Table 2). Among patients younger than 60 years, the vast majority (86.3%) received RP; with advancing age, the proportion dropped precipitously, with only 18.5% of those 70–79, and no patients 80 or older undergoing RP. EBRT use, including both EBRT and brachytherapy, increased with age up to the 70–79 group, among whom a total of 39.4% received EBRT. Compared to RP, however, the associations between other local treatments and age are less pronounced. PADT and observation use both increased sharply with advancing age, accounting for 36.4 and 38.6% of patients over 80, respectively.

Although African-American patients were notably less likely than other patients to receive brachytherapy, ethnicity was not significantly associated with treatment selection. Socioeconomic status, by contrast, as reflected by income and education, was strongly associated with treatment. Patients with annual incomes over $50,000 were nearly twice as likely as those earning less than $10,000 to undergo RP; those with higher education were also more likely than those with less education to receive surgery. Likelihoods of receiving brachytherapy or PADT were both inversely associated with income. Low-risk patients with high incomes were also less likely to pursue observation; there was no clear association with income and EBRT use. Similar trends, though less consistent, are also evident with respect to education.

Insurance type also was associated with treatment selection, with fee-for-service patients most likely, and uninsured patients least likely, to receive RP. VA patients were most likely to opt for WW or brachytherapy. Medicare patients were the most evenly distributed among the various alternatives, whereas patients participating in managed care plans appeared intermediate to fee-for-service and Medicare patients. Patients in the East and Midwest are more likely than those in the West and South to receive surgery and less likely to receive PADT or pursue observation. There were no significant associations with practice type.

Finally, we performed a subgroup analysis of treatment patterns for the 250 patients in the database ≥ 75 years old. The proportion of patients in this group varied only slightly among

time periods in the study, from a low of 11.3% in 1993–1995 to 13.4% in 1989–1992, with no significant trend over time (p=.94). Patients in this age group were found to be less likely to undergo RP (3.6%, vs. 59.9% for patients <75), and are more likely to receive EBRT (15.6% vs 8.7%), brachytherapy (18.0 vs 12.0%), or PADT (26.0 vs 7.3%), or to pursue observation (35.2 vs 8.8%). The trends over time in this group, however, largely parallel those of the overall dataset, as presented in Figure 3. Use of brachytherapy has increased roughly five-fold (p<.0001), and use of PADT has more than doubled (p=.058), whereas that of EBRT has fallen by three-quarters (p=.004). Observation in this group has fallen from a peak of 51.7% of patients in 1993–1995 to 24.4% in the most contemporary group (p=.0037). NADT use among patients ≥ 75 years old increased steadily from 3.2% in 1989–1992 to 19.3% in 1999–2001 (p=.0020).

Discussion

Nearly 29,000 men are expected to die of the prostate cancer in 2003, more than those felled by any other neoplasm except lung cancer,[1] and evidence increasingly suggests that early treatment can decrease cancer-specific mortality. A recent trial randomizing patients with clinically-detected prostate tumors to RP or WW found that RP yielded a 6.6% reduction in disease-specific mortality; a comparable reduction in overall survival was not statistically significant, although the study was underpowered with respect to this secondary outcome.[8] Non-randomized cohort trials of RP, EBRT, and brachytherapy have consistently demonstrated excellent long-term disease-free survival rates for low-risk patients.[5–7]

Although these studies have offered evidence of the success of local therapy in select groups of patients, other recent papers in both the urologic and general medical literature have paid increasing attention to the question of overdiagnosis in prostate cancer. There exists general agreement that some proportion of patients diagnosed with prostate cancer would not suffer significant adverse impact to the length or quality of their lives were the cancer never detected. Estimates of the overdiagnosis rate vary dramatically depending on such factors as the definition of overdiagnosis used, variation in rates and patterns of cancer screening, the average lead time between screening and clinical presentation, and secular trends in cancer incidence.[4,18,19], Perhaps the best estimate to date was recently reported by Etzioni et al, who calculated overdiagnosis rates of 15% among white men and 37% among black men.[4]

However, what should be considered in these discussions is that overdiagnosis is a problem primarily to the extent that it leads to the over-*treatment* of patients with tumors unlikely to reduce their life expectancy or quality of life. A major challenge in prostate cancer research, therefore, remains distinguishing those at mortal risk from a curable cancer from those harboring more indolent tumors. While biomedical research continues to advance toward the goal of better tissue-, serum-, and urine-based prognostic markers, algorithms based on the clinical variables measured in standard practice have steadily progressed in sophistication and currently are the primary means of risk stratification.

Compared with higher risk groups, there exists relatively good agreement among various classification schemes regarding the definition of low-risk patients. Using the D'Amico classification we have employed in this study, a low-risk patient should expect 5-year disease-free survival rates after surgery better than 85%.[13] Likewise, under the Kattan nomogram,[20] these patients would have 5-year recurrence-free survival rates of 81–96%. Within the low-risk group, stage T1c carries a better prognosis than does T2a disease; likewise, lower PSA and Gleason score within the low-risk ranges predict better long-term recurrence free survival.[13,20]

A previous study from CaPSURE demonstrated that the proportion of patients diagnosed with low-risk disease has risen dramatically in the PSA era.[21] In the present analysis, we found that even within this group, both stage and PSA at diagnosis have fallen significantly. While Gleason scores have risen, this has been shown to be at least in part an artifact of changes over time in pathologists' grading methods.[22] The sharp fall in T1a and T1b tumors, from over 10% to 2% of low-risk cases, is of tangential interest: this trend is likely attributable to a combination of the high prevalence of PSA screening among benign prostatic hypertrophy patients[23] and to the contemporary decline in surgical management of this condition, thus reducing the incidence of prostate cancers incidentally identified in transurethral resection prostate specimens.

The American Urological Association's clinical practice guidelines for prostate cancer suggest that localized prostate cancer should be managed with one of three local treatment options—RP, EBRT, or brachytherapy—or with observation.[24] Although the guidelines were published in 1995, these remain the modalities whose use is best supported by the medical literature. While they have been and remain the strategies most commonly employed for the management of low-risk disease, we have identified dramatic shifts over time in the proportional frequency with which they are employed. Utilizations rates for RP, EBRT, and observation have all fallen significantly, with the greatest absolute drop (12.2%) in RP use, and large proportional declines in EBRT (57.7%) and observation (42.8%) use. There have been concomitant sevenfold and four-fold increases in the rates of brachytherapy and PADT use.

In our analysis, 18.1% of the low-risk patients overall received androgen ablation, either as monotherapy or as neoadjuvant therapy prior to definitive local treatment. In the AUA practice guidelines,[24] PADT is considered to be an experimental approach in the setting of localized disease. Indeed, eight years after the guidelines' publication, while androgen deprivation remains the mainstay of therapy for recurrent and metastatic prostate cancer, few studies have formally evaluated its use as monotherapy for localized disease. Three extant analyses reported favorable rates of PSA control, but all were non-randomized cohort studies of selected patients medically unfit for or otherwise averse to standard local treatment.[25–27] To date no trials have compared PADT to observation or to local treatment strategies in terms of oncologic or quality of life outcomes.

A large study has found significant benefit for immediate versus deferred treatment of locally advanced or metastatic prostate cancer.[28] Good evidence moreover supports the use of NADT in association with EBRT in high risk disease,[29,30] and investigators have recently reported favorable experience using NADT with RP for locally advanced disease.[31] Other recent studies in patients with more favorable risk factors, in contrast, have demonstrated that NADT prior to RP does not improve outcomes.[32,33] The benefit for NADT prior to EBRT, likewise, appears to be restricted to patients with higher risk tumors. In the case of brachytherapy, NADT is used to shrink large prostate glands prior to implantation. This approach does result in effective cytoreduction, but does not change clinical outcomes.[34] Moreover, NADT increases treatment costs,[35] and in association with any primary local treatment exerts an additive impact on HRQOL.[9] A recent critical review of the appropriate role for hormonal therapy in prostate cancer found no indication for its use in low-risk, localized disease.[36] Plausible reasons for the increased use of PADT and NADT in low-risk prostate cancer include physician financial incentives, specific patient requests for this form of treatment, and a decrease in patients' and/or physicians' psychological willingness to manage any form of cancer conservatively. The true explanation is most likely multifactorial, but is not answerable with the data collected in CaPSURE. Population-based data from the Prostate Cancer Outcomes Study indicated that among prostate cancer patients in all risk groups diagnosed between 1994 and 1995, 8.4% of men ≥ 75 elected RP, 25.6%

opted for EBRT, 27.4% chose PADT, and 38.6% pursued WW.[16] A recently published Markov model decision analysis found no benefit in terms of either life expectancy or quality-adjusted life expectancy gains for aggressive therapy (RP or EBRT vs WW) among patients ≥ 75 with Gleason scores up to 7, although those with Gleason score 8–10 tumors experienced a clear benefit with either RP or EBRT.[17] Patients in our dataset 75 and older remain unlikely to undergo RP; brachytherapy and PADT now account for 61% of their primary treatment selections, and are less clearly associated with age than is RP.

Overall, 39.4% of these older patients received either PADT or NADT, 49.6% of those diagnosed between 1999 and 2001—more than in the overall cohort. Even in the absence of androgen deprivation, elderly men face a higher risk of anemia[37] and osteoporotic fractures[38] than younger men. Testosterone suppression, which in older men can be prolonged even after the discontinuation of therapy,[39] can exacerbate these problems. Although there is evidence that many older men with higher-risk tumors may in fact be *under*-treated,[40] patients in this age group are also those for whom competing causes of mortality are most relevant—cause-specific mortality is inversely proportional to age[17,41,42]—and for whom overdiagnosis and over-treatment of *low*-risk prostate cancer are of greatest concern. Pursuit of WW among this group, however, has fallen by half in the PSA era, with fewer than one-quarter of low-risk patients over 75 electing initial observation.

We found no significant associations between ethnicity and treatment patterns; however, patients of higher socioeconomic status and those with fee-for-service insurance were significantly more likely to undergo surgery, while those with lower income and education levels and no insurance were more likely to receive PADT. These associations, along with the geographic regional variation we observed, raise the concern that non-clinical factors may be influencing treatment selection.

CaPSURE tracks utilization patterns in actual community practice, free of the constraints typically imposed by clinical trial protocols. Moreover, all data since 1995 have been collected prospectively, irrespective of any specific research objectives. The practice sites in the database project have not been chosen at random, and therefore cannot be assumed to represent a statistically valid sample of the United States patient population. Nevertheless, they do represent a broad range of geographic locales, and a mix of academic and community practices.

We elected to exclude patients treated primarily with cryotherapy. These constitute a small fraction (<2%) of the contemporary low-risk patients in CaPSURE. A recent poll by the American Urological Association found likewise that between 1997 and 2001 the percentage of American urologists offering cryotherapy remained constant at 2% (during the same period, by comparison, the percentage of urologists offering brachytherapy increased from 16 to 51%).[43] Moreover, over two-thirds of the CaPSURE cryotherapy patients were treated at a single practice site. We therefore felt that including cryotherapy in this study would increase the complexity of the analysis unnecessarily without contributing significantly to our understanding of national treatment trends.

CaPSURE data are submitted only by patients and urologists; therefore any treatments by other practitioners which are not reported by patients either to their urologists or in their questionnaires may be missed. Quality assurance mechanisms, including chart review of all hospital admissions, help to minimize this problem. An enrollment bias may persist which could artificially lower the proportion of observation patients: patients who are diagnosed with prostate cancer but who elect not to undergo treatment may simply follow their PSA with their primary care provider, or not at all. If diagnosed by a CaPSURE urologist and enrolled in the database, however, patients should have completed at least one treatment

questionnaire, even if they were not followed in more extended follow-up. Despite these caveats, we believe our data provide the best available description of national practice patterns.

As a result of patient education and screening protocols, low-risk features characterize a growing proportion of newly-diagnosed prostate cancers, and are increasingly likely to be associated with clinical stage T1c, Gleason score 5–6, and serum PSA 4–10 ng/ml. A growing number of patients with low-risk features are choosing brachytherapy, PADT, and NADT, and fewer than previously are receiving RP or EBRT or pursuing observation. Age and socioeconomic status are associated with treatment selection; we also found significant geographic variability. These data highlight the concern that a significant and growing number of low-risk prostate cancer patients are being possibly over-treated. We hope that future clinical trials and updated practice guidelines will clarify optimal, evidence-based treatment for these low-risk patients.

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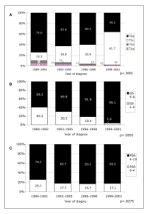

Figure 1.

Time trends in clinical characteristics among low-risk patients

For each time period, percentages of tumors in each clinical T stage (panel A), Gleason score (panel B), and PSA range (panel C) are presented.

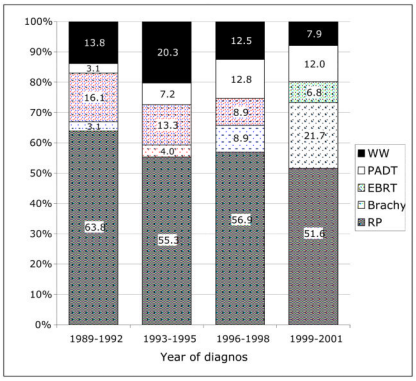

Figure 2.

Treatment trends among low-risk prostate cancer patients

Trends for each primary treatment alternative are significant at the p<.0001 level, with the exception of RP, which is significant with p=.0019.

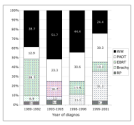

Figure 3.
Treatment trends among low-risk prostate cancer patients 75 years of age or older
p-values for significant trends are as follows: EBRT p=.0005, brachy p<.0001, PADT p=.0492, WW p=.0048. The trend for RP is not significant, p=.96.

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Table 1

Sociodemographic characteristics of low-risk patients

		Low-risk No. (%)	Non-Low-risk No. (%)	P (univariate)	OR (95% CI) (multivariate)
Total		**1990**	**3353**		
Year of diagnosis	1989–1992	224 (11.3)	527 (15.7)		Ref (p<.0001)
	1993–1995	503 (25.3)	1040 (31.0)		1.28 (1.02–1.61)
	1996–1998	304 (15.3)	626 (18.7)		1.31 (1.02–1.69)
	1999–2001	959 (48.2)	1160 (34.6)	p<.0001	2.17 (1.73–2.72)
Age at diagnosis	Younger than 60	503 (25.3)	556 (16.6)		4.68 (3.10–7.07)
	60–69	887 (44.6)	1284 (38.3)		3.99 (2.73–5.81)
	70–79	556 (27.9)	1257 (37.5)		2.48 (1.70–3.60)
	80 or greater	44 (2.2)	256 (7.6)	p<.0001	Ref (p<.0001)
Ethnicity	Caucasian	1777 (89.3)	2838 (84.6)		Ref (p=.0012)
	African-American	152 (7.6)	392 (11.7)		0.66 (0.50–0.86)
	Latino	35 (1.8)	58 (1.7)		0.81 (0.48–1.36)
	Other	26 (1.3)	65 (1.9)	p<.0001	0.61 (0.33–1.13)
Income	Less than $10,000	150 (7.5)	328 (9.8)		Ref (p=.0209)
	$10,001–30,000	421 (21.2)	821 (24.5)		1.07 (0.84–1.36)
	$30,001–50,000	369 (18.5)	595 (17.7)		1.12 (0.86–1.46)
	$50,001–75,000	271 (13.6)	327 (9.8)		1.33 (0.99–1.77)
	$75,001 or more	313 (15.7)	379 (11.3)	p<.0001	1.29 (0.96–1.74)
	Unknown/missing	*466 (23.4)*	*903 (26.9)*		
Education	Below high school	102 (5.1)	244 (7.3)		NS (p=.3422)
	Some high school	165 (8.3)	380 (11.3)		
	High school graduate	435 (21.9)	728 (21.7)		
	Some college	341 (17.1)	484 (14.4)		
	College graduate	298 (15.0)	426 (12.7)		
	Graduate school	307 (15.4)	471 (14.0)	p<.0001	

		Low-risk No. (%)	Non-Low-risk No. (%)	P (univariate)	OR (95% CI) (multivariate)
Total		**1990**	**3353**		
	Unknown/missing	*342 (17.2)*	*620 (18.5)*		
Insurance type	FFS	198 (9.9)	250 (7.5)		NS (p=.0908)
	HMO/PPO	783 (39.3)	968 (28.9)		
	Medicare	906 (45.5)	1885 (56.2)		
	None	14 (0.7)	66 (2.0)		
	Other/Unknown	33 (1.7)	73 (2.2)		
	VA	56 (2.8)	111 (3.3)	p<.0001	
Geographic region	West	301 (15.1)	545 (16.3)		Ref (p=.0445)
	East	830 (41.7)	1475 (44.0)		1.03 (0.83–1.29)
	Midwest	406 (20.4)	593 (17.7)		1.19 (0.93–1.53)
	South	453 (22.8)	740 (22.1)	p=.052	1.32 (1.03–1.68)
Site type	Community	1815 (91.2)	2980 (88.9)		Ref (p=.0085)
	Academic	175 (8.8)	373 (11.1)	p=.007	0.71 (0.55–0.92)

For each variable, numbers and percentages of patients in each group are presented. Univariate p-values are calculated from the χ^2 or Mantel-Haenszel χ^2 test, as appropriate. Multivariate odds ratios (OR) with 95% confidence intervals (CI) are calculated via logistic regression. Ref = reference level.

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Table 2

Sociodemographic factors associated with treatment patterns among low-risk patients

Variable		Percent of patients receiving each treatment					p
		RP	Brachy	EBRT	PADT	WW	
Age at diagnosis	Younger than 60	86.3	5.4	2.2	3.4	2.8	
	60–69	62.2	13.9	7.4	7.3	9.1	
	70–79	18.5	19.4	20.0	17.8	24.3	
	80 or greater	0.0	9.1	15.9	36.4	38.6	p<.0001
Ethnicity	Caucasian	54.8	13.6	9.8	9.2	12.6	
	African-American	54.6	5.9	11.8	16.5	11.2	
	Latino	54.3	17.1	5.7	11.4	11.4	
	Other	50.0	19.2	3.9	15.4	11.5	p=.107
Income	Less than $10,000	38.7	19.3	8.7	19.3	14.0	
	$10,001–30,000	42.3	18.5	11.9	11.6	15.7	
	$30,001–50,000	51.8	14.9	10.6	9.2	13.6	
	$50,001–75,000	72.7	7.8	5.5	6.6	7.4	
	$75,001 or more	72.8	6.7	9.0	3.8	7.7	p<.0001
Education	Below high school	38.2	17.7	15.7	14.7	13.7	
	Some high school	41.8	13.9	9.7	17.0	17.6	
	High school or tech	54.0	13.1	9.2	9.9	13.8	
	Some college	57.5	15.0	8.2	7.9	11.4	
	College graduate	67.8	8.4	9.4	5.4	9.1	
	Graduate school	61.2	12.4	10.1	6.8	9.5	p<.0001
Insurance type	FFS	79.3	5.6	4.6	5.1	5.6	
	HMO/PPO	67.9	12.5	5.5	7.2	6.9	
	Medicare	38.7	15.3	14.7	13.6	17.7	
	None	28.6	0.0	28.6	14.3	28.6	
	Other/Unknown	66.7	9.1	15.2	6.1	3.0	
	VA	41.1	19.6	1.8	7.1	30.4	p<.0001
Geographic region	West	48.2	10.3	8.3	10.6	22.6	p<.0001

Variable		Percent of patients receiving each treatment					p
		RP	Brachy	EBRT	PADT	WW	
	East	59.0	8.8	13.4	7.0	11.8	
	Midwest	57.4	19.0	6.2	9.6	7.9	
	South	48.8	17.9	7.5	15.0	10.8	
Site type	Community	54.7	13.6	9.7	10.0	12.1	
	Academic	55.4	9.1	10.9	9.1	15.4	p=.391

For each variable, the percent of patients receiving each primary treatment at the various levels of the variables are presented. p values are calculated from the χ^2 or Mantel-Haenszel χ^2 test, as appropriate.