Factors Associated With Initial Therapy for Clinically Localized Prostate Cancer: Prostate Cancer Outcomes Study

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Background: **Because of the lack of results from randomized clinical trials comparing the efficacy of aggressive therapies with that of more conservative therapies for clinically localized prostate cancer, men and their physicians may select treatments based on other criteria. We examined the association of sociodemographic and clinical characteristics with four management options: radical prostatectomy, radiation therapy, hormonal therapy, and watchful waiting.** ***Methods:*** **We studied 3073 participants of the Prostate Cancer Outcomes Study diagnosed from October 1, 1994, through October 31, 1995, with clinically localized disease (T1 or T2). Participants completed a baseline survey, and diagnostic and treatment information was abstracted from medical records. Multiple logistic regression analysis identified factors associated with initial treatment. All statistical tests were two-sided.** ***Results:*** **Patients with clinically localized disease received the following treatments: radical prostatectomy (47.6%), radiation therapy (23.4%), hormonal therapy (10.5%), or watchful waiting (18.5%). Men aged 75 years or older more often received conservative treatment (i.e., hormonal therapy alone or watchful waiting; 57.9% of men aged 75–79 years and 82.1% of men aged 80 years and older) than aggressive treatment (i.e., radical prostatectomy or radiation therapy) (for all age groups, $P \leq .001$). After adjustment for age, clinical stage, baseline prostate-specific antigen level, and histologic grade, the following factors were associated with conservative treatment: history of a heart attack, being unmarried, geographic region, poor pretreatment bladder control, and impotence. In men younger than 60 years, use of aggressive treatment was similar by race/ethnicity (adjusted percentages = 85.5%, 88.1%, and 85.3% for white, African-American, and Hispanic men, respectively). However, among men 60 years old and older, African-American men underwent aggressive treatment less often than did white men or Hispanic men (adjusted percentages for men aged 60–64 years = 67.1%, 84.7%, and 79.2%, respectively; 65–74 years = 64.8%, 73.4%, and 79.5%, respectively; and 75 years old and older = 25.2%, 45.7%, and 36.6%, respectively).** ***Conclusions:*** **The association of nonclinical factors with treatment suggests that, in the absence of definitive information regarding treatment effectiveness, men diagnosed with prostate cancer should be better informed of the risks and benefits of all treatment options. [J Natl Cancer Inst 2001;93: 1864–71]**

To date, no randomized clinical trials have been completed that definitively establish the efficacy of radical prostatectomy or radiation therapy for the treatment of localized prostate cancer *(1)*. Currently ongoing trials, many years from completion, are testing these aggressive therapies against conservative management consisting of hormonal therapy or observation *(2)*. For older men with early-stage disease, observational studies *(3,4)* have suggested that conservative management is a viable option. For men with low-grade, clinically localized disease and a life expectancy of fewer than 10 years, conservative management has been shown to be an acceptable alternative. Because of

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See "Notes" following "References."

the lack of definitive evidence, no clear consensus exists on the selection of optimal treatment for clinically localized prostate cancer *(5)*. In choosing treatment options, men and their clinicians must also weigh the substantial risk of clinically significant complications of competing therapies *(6–10)*.

Prior research has identified demographic factors associated with treatment of clinically localized prostate cancer, including age at diagnosis, geographic region, comorbidity, and race *(11–15)*. No prior study has comprehensively assessed key clinical factors (such as prostate-specific antigen [PSA], Gleason score, and baseline urinary and sexual functions) and nonclinical factors (such as sociodemographic and economic variables) in a population-based sample. Any of these factors may affect the selection of treatments. To investigate patterns of therapy in a population-based sample of men with prostate cancer, we examined the influence of these factors on patterns of treatment in the four major management options (radical prostatectomy, radiation therapy, hormonal therapy, and watchful waiting) received by men diagnosed with clinically localized prostate cancer.

Materials and Methods

Data

We analyzed data from patients who were participants in the National Cancer Institute (NCI)-sponsored Prostate Cancer Outcomes Study (PCOS). PCOS was initiated in 1994 to describe the diagnosis, the initial therapy and its determinants, the quality of life, and the subsequent treatment for recurrence and/or progression of prostate cancer. Methodologic details of the study have been reported elsewhere *(16)*.

Patients with newly diagnosed prostate cancer were identified within 4 months of initial pathologic diagnosis with systems used by the six participating registries (the states of Connecticut, New Mexico, and Utah and the metropolitan areas of Atlanta, GA, Los Angeles, CA, and Seattle, WA, of the NCI's Surveillance, Epidemiology, and End Results [SEER][1] Program). Men with a first primary prostate cancer diagnosed from October 1, 1994, through October 31, 1995, who were younger than 90 years, were eligible for the study. Men were asked to complete a survey 6 months after their diagnosis of prostate cancer. All men who completed a 6-month questionnaire and those who did not actively refuse to complete the 6-month survey were asked to complete the 12-month survey. Of the 5672 men sampled, 3533 (62%) participated by completing a 6-month survey, a 12-month survey, or both. Participants were similar to nonparticipants with respect to mean age, 67.5 years ± 11.3 years (standard deviation) (range, 39–89 years) and 70.2 years ± 12.2 years (range, 43–89 years), respectively; tumor stage; and grade. Nonparticipants were more often nonwhite and from geographic areas with lower median incomes, although these differences were not large *(16)*. For this analysis, we excluded 47 men with a missing medical records abstract and 413 men diagnosed with clinically advanced disease (T3 and T4), defined as a positive scan, metastatic disease, or disease reported clinically as extending beyond the prostatic capsule, leaving a total sample size of 3073 patients.

Because the primary aims of this study were to investigate quality of life and patterns of therapy in a population-based sample of men with prostate cancer and because we were concerned about patient and physician burden, we believed that it was necessary to survey patients at 6 months rather than to attempt a survey before the initiation of therapy and again at 6 months. The self-administered PCOS patient survey conducted at 6 and 12 months included questions about symptoms; urinary, bowel, and sexual functioning; and comorbidity *(17)*. The 6-month survey also included questions about sociodemographic and economic status; symptoms; and urinary, bowel, and sexual functioning before the diagnosis of prostate cancer. In addition, after written consent was obtained from the patient, medical records were abstracted by trained medical record abstractors in facilities where the patient received treatment (e.g., the physician's offices, radiation facilities, and hospitals) *(17)*. Detailed information on symptoms, clinical stage, Gleason grade *(18)*, PSA values, diagnostic tests, and treatments was recorded.

Initial therapy, abstracted from the medical records, was defined as treatment received in the first 6 months after diagnosis. A hierarchical variable was created to quantify treatment, ranging from the most aggressive therapy to the least aggressive. Men who received a radical prostatectomy were assigned to the prostatectomy category, whether or not they received any other adjuvant therapy, such as radiation therapy or hormonal therapy. Those men who received radiation therapy were categorized as having radiation therapy, whether or not they also received hormonal therapy. Men who were included in the hormone category consisted of those who received only hormonal therapy (medical or surgical), and men who had no reported therapy in the first 6 months after diagnosis were in the watchful-waiting group. Subsequent therapies given 6 months after diagnosis were excluded from the analysis because our goal was to examine factors related to selection of initial therapy.

We created a clinical stage variable that was based on an algorithm using clinical information, diagnostic tests, and biopsy results abstracted from inpatient and outpatient records. A patient assigned to clinical stage T1 had no positive scans, no metastatic disease, no abnormal or suspicious digital rectal examinations, a PSA level of less than 20 ng/mL, and disease reported from clinical examination as confined to the prostate or of unknown extension *(19)*. Patients assigned to T2 had no positive scans and no metastatic disease or disease reported clinically as confined to the prostate or of unknown extension. These patients had one or both of the following test results: unknown, abnormal, suspicious digital rectal examinations, or a PSA level of 20 ng/mL or more. Lymph node status was not considered in assigning clinical stage, because men who undergo surgery would be much more likely to have lymph nodes sampled and their disease upstaged *(20)*.

Comorbid conditions were identified from the patient survey, which queried respondents about the presence of 12 major chronic conditions hypothesized by the PCOS investigators to influence prostate cancer treatment choice and outcomes. A comorbidity score ranging from 0 to 12 was constructed from the responses to these items. If the respondent reported only that a doctor had told him that he had arthritis, diabetes, chronic lung disease, heart failure, hypertension, heart attack, chest pain, gastric ulcers, or depression but had no limitations in daily activities or if the respondent took no prescription medication, then nothing was added to his comorbidity score. For each of these nine conditions, a report of limitation of activity and/or of use of prescription medication added one point to the comorbidity score. Because of the probability that the remaining three conditions (stroke, inflammatory bowel disease, or liver disease) substantially influenced the selection of therapy, one point was added to the comorbidity score, even when no medication or limitation of activity was reported.

Respondents were asked on the 6-month survey about urinary, bowel, and sexual function "just before prostate cancer" was diagnosed and about their function "during the past month." To assess the accuracy of 6-month retrospective recall of urinary, bowel, and sexual function, we conducted a validation study in a convenience sample of 133 men recruited in urologists' offices *(21)*. These patients were asked to complete the PCOS survey first at diagnosis and before treatment of prostate cancer and then again 6 months later. There was high overall agreement between prediagnostic sexual, bowel, and bladder function. However, men participating in the validation were younger, had higher educational levels and higher incomes, and were more likely to have a radical prostatectomy. These characteristics may limit the generalizability of the validation study.

Statistical Analysis

In bivariate analysis, we examined the association between the four major treatment types and the following clinical information: stage, PSA level at diagnosis, Gleason score, results of digital rectal examination, urinary symptoms, urinary infection, weight loss or anorexia, fatigue, bone pain, other symptoms, and comorbidity score. We also investigated the association between treatment and the sociodemographic variables of age at diagnosis, race/ethnicity, marital status, number of individuals living in the home, educational level, income, insurance coverage, and geographic location. In addition, we explored the relationship among urinary, bowel, and bladder functions before therapy; the patient–physician discussion of therapy options; and the therapy selected.

Descriptive analyses were conducted by use of SAS (SAS Institute, Inc., Cary, NC), and multiple logistic regression models were performed by use of the Survey Data Analysis statistical computer package (Research Triangle Institute, Research Triangle Park, NC) to compute the appropriate variances on the basis of the PCOS survey design. The Horvitz–Thompson weight, which, in this case, was calculated as the inverse of the sampling proportion for each PCOS sampling stratum (defined by age, race,

and/or study area), was used to obtain estimates. The data presented in the tables, graphs, and the multiple logistic regressions are weighted to reflect all of the eligible prostate cancer patients in the PCOS study areas. The outcome variables were bivariate, aggressive versus conservative management, in the logistic regression models and were radiation therapy versus radical prostatectomy in the second model. We determined *a priori* that the independent variables entered in the logistic models would be those statistically significantly associated with initial therapy in the bivariate analyses, by use of statistical significance level of .05. We examined statistical interactions of age and race, age and comorbidity, and race and several comorbid conditions in our multivariate models. Only the interaction of age and race was statistically significantly associated with aggressive versus conservative therapy.

Results of the logistic regression models are shown as adjusted percentages of patients receiving the treatment of interest, according to each of the independent variables. The logistic regression models were used to generate these estimates of the probability for each individual (or predicted values from the models) receiving the treatments, according to each independent variable. The percentages in each group were then directly standardized to the distribution of the covariates among the weighted sample used in each model *(22)*. The odds ratio for the statistical interaction term was calculated by combining the interaction between age and race with the main effects for age and race. All statistical tests were two-sided.

RESULTS

For patients with clinically localized disease, radical prostatectomy was the most frequently selected therapy overall (47.6%), followed by radiation therapy (23.4%), watchful waiting (18.5%), and hormonal therapy (10.5%). Clinical factors were associated with treatments used for men diagnosed with clinically localized prostate cancer in bivariate analyses (Table 1). We found a statistically significant ($P \leqslant .001$) difference in treatment selection between men with clinical stage T1 and T2 disease. For clinical stage T1 disease, 52.4% underwent a radical prostatectomy and, for stage T2, only 45.7% underwent this surgery. Hormonal therapy alone was received more frequently by patients at stage T2 than at stage T1 (12.7% versus 5.2%). More than one half of the men with PSA levels of less than 10 ng/mL received a radical prostatectomy compared with 20.6% of the men with PSA levels of more than 50 ng/mL. The proportion of men receiving radical prostatectomy decreased to less than 50% when the Gleason score was 7 or higher or was unknown. In general, the presence of pretreatment disease symptoms and more comorbidity were related to increasingly less aggressive treatments.

Table 1. Distribution of tumor characteristics and symptoms at diagnosis by initial therapy*

	Unweighted No.	Weighted % for each therapy				
		Radical prostatectomy	Radiation therapy	Hormonal therapy	WW	*P*
Clinical stage						
T1	857	52.4	23.8	5.2	18.7	⩽.001
T2	2216	45.7	23.2	12.7	18.4	
PSA, ng/mL at diagnosis						
0–4	323	50.6	18.4	6.9	24.1	⩽.001
>4–10	1508	53.8	24.4	5.7	16.1	
>10–20	621	44.9	28.1	9.6	17.4	
>20–50	293	33.4	26.4	22.6	17.5	
>50	122	20.6	14.5	48.9	16.0	
Unknown	206	39.6	9.9	17.0	33.5	
Gleason score						
2–4	443	50.1	21.6	5.8	22.5	⩽.001
5	549	52.4	25.9	5.7	15.9	
6	809	52.5	21.7	9.3	16.4	
7	605	43.7	28.8	14.3	13.2	
8–10	234	37.2	27.8	26.1	9.0	
Unknown	433	40.6	15.1	9.8	34.5	
Digital rectal examination						
Negative	1056	49.5	22.9	6.8	20.7	⩽.001
Positive	1601	47.5	23.8	12.2	16.5	
Unknown	416	42.6	23.1	13.8	20.5	
Urinary symptoms						
Yes	1673	43.3	25.7	11.2	19.8	⩽.001
No/unknown	1400	52.7	20.6	9.8	16.9	
Urinary infection						
Yes	323	50.9	16.6	11.2	21.4	.088
No/unknown	2750	47.2	24.1	10.5	18.2	
Weight loss–anorexia						
Yes	31	18.6	11.7	26.5	43.2	⩽.001
No/unknown	3042	47.8	23.5	10.4	18.2	
Fatigue						
Yes	41	16.0	47.3	16.1	20.6	⩽.001
No/unknown	3032	48.0	23.1	10.5	18.4	
Bone pain						
Yes	26	26.1	16.4	28.1	29.4	.005
No/unknown	3047	47.8	23.5	10.4	18.4	
Other symptoms						
Yes	290	46.4	21.3	10.5	21.9	.499
No/unknown	2783	47.7	23.7	10.6	18.0	
Comorbidity score						
0	2132	52.7	22.0	9.2	16.2	⩽.001
1	595	40.7	23.7	12.0	23.6	
2	179	32.5	30.3	15.2	22.0	
⩾3	167	23.5	33.0	17.6	26.0	

*Two-sided χ^2 tests were used to compare the distribution of treatments across levels of the variable. WW = watchful waiting; PSA = prostate-specific antigen.

Table 2 shows the distribution of selected sociodemographic and economic characteristics among the four initial treatments. Patient age at diagnosis was an important determinant of therapy, with 79.3% of the men younger than 60 years at diagnosis having a radical prostatectomy, but the proportion of men receiving hormonal therapy or watchful waiting increased substantially with age for men 75 years old and older, with 57.9% of the men aged 75–79 years and 82.1% of the men aged 80 years old and older receiving hormonal therapy or watchful waiting. Men 75 years old and older were also more likely to receive conservative therapy than either radical prostatectomy or radiation therapy. In addition, race/ethnicity, marital status, number living in the home, educational level, income, insurance coverage, and geographic region also were related to treatments received. Hispanic men received radical prostatectomy more often than non-Hispanic whites or African-Americans ($P \leqslant .001$), and radical prostatectomy was received less fre-

Table 2. Distribution of sociodemographic and economic characteristics by initial therapy*

Characteristic	Unweighted No.	Weighted† % for each therapy: Radical prostatectomy	Radiation therapy	Hormonal therapy	WW	*P*
Age at diagnosis, y						
<60	720	79.3	10.8	2.8	7.0	⩽.001
60–64	532	69.6	14.8	3.8	11.9	
65–69	684	56.0	23.6	7.9	12.5	
70–74	612	29.5	38.4	10.5	21.6	
75–79	349	10.4	31.6	23.3	34.6	
⩾80	176	4.3	13.6	35.5	46.6	
Race/ethnicity						
NH white	2120	46.5	25.3	9.8	18.4	⩽.001
NH African-American	520	48.5	18.6	13.6	19.3	
Hispanic	433	54.5	15.6	12.0	17.9	
Marital status						
Married	2435	49.7	23.9	9.3	17.2	⩽.001
Not married/unknown	638	39.7	21.5	15.4	23.4	
No. in home						
Alone	476	36.1	26.0	14.0	23.9	⩽.001
1 other	1834	47.6	24.1	10.0	18.3	
⩾2 others	700	57.1	19.5	10.0	13.4	
Unknown	63	38.6	22.1	8.2	31.2	
Educational level						
⩽8th grade	298	39.6	19.7	18.5	22.2	⩽.001
Some high school	359	38.7	24.7	18.2	18.4	
High school graduate	623	51.0	23.8	7.2	18.0	
Some college	728	48.6	22.7	10.0	18.7	
College graduate	444	44.9	26.7	9.7	18.7	
Advance/graduate school	572	54.3	22.0	7.8	15.8	
Unknown	49	43.6	23.7	2.6	30.0	
Income						
<$20 000	730	38.9	21.6	14.1	25.5	⩽.001
$20 000–50 000	1185	47.1	25.8	10.2	16.9	
⩾$50 000	822	59.4	21.3	6.0	13.3	
Unknown	336	37.9	23.7	15.8	22.6	
Insurance						
Private	2521	48.6	23.6	10.2	17.5	⩽.001
Public	269	36.8	24.5	13.5	25.1	
Unknown	283	48.8	19.9	11.0	20.3	
Registry						
Connecticut	587	40.5	33.1	8.0	18.4	⩽.001
New Mexico	304	41.6	18.3	10.0	30.1	
Seattle (WA)	360	42.8	25.4	11.5	20.3	
Utah	542	53.0	21.2	7.9	17.9	
Atlanta (GA)	327	55.6	28.0	9.0	7.4	
Los Angeles (CA)	953	49.3	18.0	13.3	19.4	

*Two-sided χ^2 test was used to compare the distribution of treatments across levels of the variable. WW = watchful waiting; NH = non-Hispanic.

†Weighted to reflect all eligible prostate cancer patients in the study area.

quently by patients with lower educational levels and incomes.

Poorer pretreatment urinary, bowel, and sexual functions were associated with less aggressive treatments (Table 3). Patients who received radical prostatectomy reported less baseline incontinence or impotence than did patients who received other therapies. Men who reported being sexually impotent before treatment were also less often treated with surgery compared with potent men. In men who were younger than age 70 years at diagnosis, 71.0% without impotence received a radical prostatectomy compared with 53.3% who reported being impotent. This observation also was true for men 70 years old and older.

As might be expected, the therapy selected was related to the type of therapy discussed with the physician. Those patients not discussing aggressive therapy were less likely to receive it. In the younger age group, 58.6% of those receiving watchful waiting had a discussion about aggressive and conservative therapies, and in the older age groups, 54.8% discussed both aggressive and conservative therapies.

Table 4 shows the adjusted percentage distributions for the variables that were statistically significantly associated with treatments in multiple logistic regression models. First, among all of the patients with clinically localized prostate cancer, conservative therapy was associated with unmarried status, geographic location, a high PSA level, history of heart attack, baseline impotence or poor bladder control, and no reported discussion of an aggressive therapy option (Table 4). A difference in the effect of age by race/ethnicity group was observed. Similar proportions of white, African-American, and Hispanic men younger than 60 years of age received aggressive therapy (adjusted percentages = 85.5%, 88.1%, and 85.3%, respectively). However, there was a decrease in the proportion of African-American men 60 years old and older who received aggressive therapy (adjusted percentages for men aged 60–64 years = 67.1%, 65–74 years = 64.8%, and ⩾75 years = 25.2%) relative to white men (adjusted percentages for men aged 60–64 years = 84.7%, 65–74 years = 73.4%, and ⩾75 years = 45.7%), but no difference between white and Hispanic men (adjusted percentages for men aged 60–64 years = 79.2%, 65–74 years = 79.5%, and ⩾75 years = 36.6%) was observed.

Among only those men receiving aggressive therapies, we next examined factors associated with the use of radical prostatectomy versus radiation therapy (Table 4). After adjustment for clinically significant characteristics, such as PSA level and comorbidity, age was positively associated with radiation therapy. In the youngest age group, men younger than 60 years, 13.9% (adjusted percentages) received radiation therapy, whereas 70.5% (adjusted percentages) of men 75 years old and older received radiation therapy. Regional differences also emerged, with men living in Atlanta (36.4% = adjusted percentage) or Connecticut (43.4% = adjusted percentage) being more likely to receive radiation therapy than men residing in the other four areas. Non-Hispanic white and African-American men were equally likely (33.8% = adjusted percentage) and Hispanic men were less likely (25.8% = adjusted percentage) to receive radiation therapy after adjustment for other clinical and nonclinical factors.

DISCUSSION

The choice of initial treatment for clinically localized prostate cancer is difficult for both the physician and patient,

Table 3. Distribution of function and treatment discussed by age and initial therapy*

	Unweighted No.	Weighted† % for each therapy: Radical prostatectomy	Radiation therapy	Hormonal therapy	WW	*P*
Age <70 y						
Urinary control before cancer						
Total control	1431	71.5	14.5	4.2	9.8	⩽.001
Some incontinence	285	46.9	31.3	8.4	13.4	
>3 bowel movements/day before cancer						
Rarely/never	1306	68.8	16.2	4.9	10.1	.003
Some days/every day	418	61.4	20.9	5.7	12.0	
Erection sufficient for intercourse before cancer						
Yes	1388	71.0	15.2	4.2	9.6	⩽.001
No	322	53.3	24.3	8.8	13.6	
Discussed treatment options						
C and A‡	998	68.0	16.2	3.6	12.2	
A only	679	69.1	19.5	6.3	5.1	⩽.001
Not discussed A/unknown	259	58.4	13.8	7.8	20.0	
Age ⩾70 y						
Urinary control before cancer						
Total control	719	22.8	33.1	17.2	26.9	⩽.001
Some incontinence	317	11.3	32.3	21.7	34.7	
>3 bowel movements/day before cancer						
Rarely/never	826	20.3	29.7	19.6	30.4	⩽.001
Some days/every day	216	15.5	45.0	13.2	26.3	
Erection sufficient for intercourse before cancer						
Yes	521	24.7	33.6	13.4	28.3	⩽.001
No	508	15.0	31.9	23.7	29.4	
Discussed treatment options						
C & A‡	569	18.8	37.4	12.6	31.2	⩽.001
A only	332	28.4	39.1	21.5	11.0	
Not discussed A/unknown	236	9.7	10.8	28.8	50.7	

*Two-sided χ^2 test was used to compare the distribution of treatments across levels of the variable. WW = watchful waiting.

†Weighted to reflect all eligible prostate cancer patients in the study area.

‡Discussed both conservative (C) and aggressive (A) therapies.

given the scientific uncertainties about the relative efficacy of each therapeutic strategy. We found substantial variations in the treatments used across regions and in population subgroups. Although such variations do not necessarily indicate poor or inappropriate treatments, they raise important questions. Do all men with clinically localized prostate cancer have access to all treatment options? Are they informed of the potential risks and benefits? Are clinicians providing information about all options to their patients?

We found that treatment patterns were related partly to prognostic factors, such as the baseline PSA value and Gleason score (Table 1), known determinants of outcome *(23,24).* When the PSA level was more than 50 ng/mL, men were more likely to be treated conservatively. The distribution of therapy by PSA level suggests that some older patients who have aggressive forms of cancer and are poor surgical candidates receive hormonal therapy rather than radiotherapy. Higher PSA levels may also raise concerns about clinically inapparent spread of the disease, which is treated with hormonal therapy to delay possible metastatic progression.

We observed that 10.5% of the men with clinically localized prostate cancer received hormonal therapy only. The reason for hormonal therapy at this time is unclear, given the lack of definitive evidence that hormonal therapy is effective against early-stage prostate cancer. Perhaps hormonal therapy is given because some patients with favorable prognostic factors prefer to do something other than watching and waiting. For other patients at higher risk of progression, as reflected by a high level of PSA or a high Gleason score, the goal of hormonal therapy may be to delay progression to metastatic prostate cancer. Some of these patients, especially older men and those with other comorbidities, may be poor surgical candidates and may wish to avoid the potential complications associated with radiation therapy. This observation is supported by the finding that men with a history of heart attack were more likely to be treated conservatively, 36.6% (adjusted percentage) of men with a history of heart attack versus 28.3% (adjusted percentage) of men without such a history.

We observed that age at diagnosis was inversely associated with the proportion of men receiving aggressive treatment, consistent with results in previous studies *(11,13).* Age is generally considered to be a key prognostic factor in treatment decision making, perhaps as important as PSA level and Gleason score. Given the long natural history of localized prostate cancer, the majority of older men with prostate cancer will die of other causes *(4,25).* Furthermore, because radical prostatectomy and radiation therapy have potential serious long-term complications *(9,10, 26),* the tendency for older men to be treated more conservatively may be reasonable and appropriate.

Unmarried men in the current study were more often treated conservatively than married men, even after adjustment for age and other factors, 33.1% versus 27.9%. Other studies have reported similar findings. Married patients with lung cancer more often were treated surgically *(27),* and married women with breast cancer more often had definitive therapy *(28).* Unmarried men have poor survival from a variety of diseases and may have other physical and psychologic health issues that prohibit aggressive treatment or may lack emotional support and encouragement to select aggressive therapy for their cancer *(29).*

The geographic variation in therapies that we found suggests a lack of consensus among physicians, particularly in the absence of evidence on the relative outcomes of competing therapies *(30,31).* We observed statistically significant ($P \leqslant .001$) regional variations in treatments, with a range of 18.8%–37.4% of the patients receiving conservative treatment across the six regions studied. Such variations across geographic regions have

Table 4. Adjusted percentage (Adj. %) distributions for patients with clinically localized prostate cancer to receive therapy

	Conservative* therapy among all patients		Radiation† therapy among patients receiving aggressive therapy	
	Adj. %	OR (95% CI)‡	Adj. %	OR (95% CI)‡
Age at diagnosis, y				
<60			13.9	1.0 (referent)
60–64			18.4	1.4 (1.0 to 2.1)
65–74			41.1	5.1 (3.7 to 7.0)
⩾75			70.5	19.6 (11.9 to 32.4)
Race§				
NH white			33.8	1.0 (referent)
NH Afrian-American			33.8	1.0 (0.7 to 1.4)
Hispanic			25.8	0.6 (0.4 to 0.9)
Marital status				
Married	27.9	1.0 (referent)		
Not married/unknown	33.1	1.4 (1.1 to 1.8)		
Registry				
Los Angeles (CA)	32.3	1.0 (referent)	28.7	1.0 (referent)
Atlanta (GA)	18.8	0.4 (0.2 to 0.6)	36.4	1.6 (1.0 to 2.5)
Utah	26.5	0.7 (0.5 to 0.9)	24.8	0.8 (0.5 to 1.1)
Seattle (WA)	27.1	0.7 (0.5 to 1.0)	29.8	1.1 (0.7 to 1.6)
New Mexico	37.4	1.4 (0.9 to 2.0)	32.5	1.3 (0.8 to 2.1)
Connecticut	27.3	0.7 (0.5 to 1.0)	43.4	2.3 (1.6 to 3.2)
Comorbidity score				
0			30.8	1.0 (referent)
1			34.5	1.1 (0.8 to 1.5)
2			42.5	1.6 (1.0 to 2.7)
⩾3			48.8	2.6 (1.5 to 4.6)
Heart attack				
No	28.3	1.0 (referent)		
Yes	36.6	1.7 (1.2 to 2.5)		
Weight loss and/or fatigue				
No/unknown			32.7	1.0 (referent)
Yes			53.6	3.1 (1.5 to 6.6)
Impotence before diagnosis				
No	28.5	1.0 (referent)	29.8	1.0 (referent)
Yes	32.6	1.3 (1.0 to 1.7)	36.5	1.5 (1.1 to 2.0)
Unknown	23.0	0.7 (0.3 to 1.7)	45.0	2.4 (1.1 to 5.2)
Bladder control				
Total	29.4	1.0 (referent)	31.0	1.0 (referent)
Other	36.3	1.6 (1.2 to 2.0)	47.8	2.5 (1.8 to 3.4)
Unknown	17.7	0.4 (0.1 to 1.2)	23.5	0.7 (0.3 to 1.4)
PSA at diagnosis, ng/mL				
0–4	26.3	1.0 (referent)	27.6	1.0 (referent)
>4–10	24.7	0.7 (0.5 to 1.0)	33.2	1.4 (0.9 to 2.2)
>10–20	34.1	0.6 (0.4 to 0.9)	34.3	1.5 (0.9 to 2.4)
>20–50	53.2	1.1 (0.7 to 1.8)	41.8	2.3 (1.3 to 3.9)
>50	37.8	3.3 (1.7 to 6.4)	32.6	1.4 (0.5 to 3.8)
Unknown	32.0	1.4 (0.8 to 2.3)	21.5	0.7 (0.3 to 1.4)
Discussed treatment options				
C and A	27.5	1.0 (referent)		
A only	18.7	0.5 (0.4 to 0.7)		
A not discussed/unknown	63.3	7.4 (4.8 to 11.6)		
Interaction of age, y, and race/ethnicity				
<60, white	14.5	1.0 (referent)		
<60, African-American	11.9	0.8 (0.4 to 1.5)		
<60, Hispanic	14.7	1.0 (0.5 to 2.1)		
60–64, white	15.4	1.1 (0.6 to 1.8)		
60–64, African-American	32.9	3.6 (2.0 to 6.6)		
60–64, Hispanic	20.8	1.7 (0.9 to 3.2)		
65–74, white	26.6	2.5 (1.7 to 3.7)		
65–74, African-American	35.2	4.1 (2.6 to 6.6)		
65–74, Hispanic	20.5	1.7 (1.0 to 2.8)		
⩾75, white	54.3	10.5 (6.9 to 15.9)		
⩾75, African-American	74.8	29.8 (13.2 to 67.5)		
⩾75, Hispanic	63.4	16.3 (7.3 to 36.4)		

*C = conservative (homonal therapy and watchful waiting).

†A = aggressive (radical prostatectomy and radiation therapy).

‡OR = odds ratio; CI = confidence interval.

§NH = non-Hispanic; PSA = prostate-specific antigen.

been noted previously *(11,13,32)*. Urban–rural differences in treatments of other cancers have also been observed, possibly associated with distance to treatment facilities *(27,28)*. However, the urban–rural disparity was not apparent in our data. Little difference in treatment practices was observed in Los Angeles and New Mexico, and men in Utah received aggressive therapy more frequently than men in Los Angeles.

As the comorbidity score increased in this study, men were statistically significantly more likely to receive radiation therapy rather than radical prostatectomy, even after adjustment for other variables (Table 4), confirming previous results *(12,33)*. Men with clinically significant medical conditions are not candidates for radical prostatectomy, which carries nontrivial risks of acute complications *(34)*.

To our knowledge, this is the first study of prostate cancer treatment patterns to include measurements of prediagnostic disease-related urinary, bowel, and sexual functions. A new finding is that pretreatment impotence and poor bladder control emerged as statistically significant independent determinants of the treatment received (Table 4). We found that such men were more likely to receive conservative therapy, even after adjustment for other variables, including age and comorbidity. Perhaps, men and their clinicians may avoid aggressive therapies that may exacerbate an existing problem to minimize further losses in function, or perhaps these problems exist more often in men with other diminished functions that we did not measure.

After adjustment for clinical factors, the use of conservative treatment did not appear to be associated with income, educational level, or insurance coverage. In our study, among men 60 years old and older, African-American men were more likely to be treated conservatively than white men, consistent with previous reports *(11–13,35)*. Although previous studies have found a difference in aggressive versus conservative therapy, Demark-Wahnefried et al. *(15)* reported that, stage for stage, African-American (n = 117) and white (n = 114) men participating in their study received comparable treatment. However, their study population was younger (average age, 64.7 years), and men older than 74 years were excluded. Indeed, we found no difference in the treatment, conservative or aggressive, given to African-American and white men younger than 60 years. When comparisons were made within the group receiving aggressive therapy, although there were differences by age, the selection of radiation therapy or radical prostatectomy was not different for African-American (33.8% = adjusted percentage) and white (33.8% = adjusted percentage) men. However, when aggressive and conservative therapies were compared, it was unclear why older African-American men in our study received less aggressive therapy than white men. Demark-Wahnefried et al. *(15)* also queried men about which treatment options were discussed. They observed that white men were somewhat more likely to discuss each of the listed treatment options with their physicians. Our data are not strictly comparable. After adjustment for a number of clinical and socioeconomic variables, including educational level and income, our data suggest that African-American men were more likely to have discussed both aggressive and conservative treatments but that white men were more likely to have discussed only aggressive therapies (data not shown). Possible reasons for the differences in the treatment patterns include variables that we did not measure, such as patient preferences, poorer access to physician specialists, bias in referral patterns, or physician recommendations for treatment, or some other variable, such as attitudes toward the medical system.

Most previous studies of treatment for prostate cancer *(11,13,35)* have been hospital based or lacked information on multiple patient clinical and health factors that may affect the selection of treatments. This study includes extensive information collected from hospital charts, physician records, and patients. However, certain limitations remain.

Although the current study provides detailed information on the therapy given, functional status, and coexisting illnesses, we do not have information about the process of decision making in the selection of therapy. We do have information regarding the types of therapies discussed, which suggests that a discussion that includes only the aggressive therapy option strongly influences treatment choice toward more aggressive therapy. However, it remains difficult to clearly delineate the extent to which the decision for specific treatments is influenced by the physician's recommendation and by patient preferences that are, in turn, based on a complex set of expectations, desire for specific outcomes, and fear of particular complications. Because men completed the surveys 6 months after diagnosis, our study has the potential for recall bias; thus, future surveys may wish to track the discussion and decision-making process more closely in time to the discussion. Clearly, the primary goal for most patients remains cure. Research into the complex dynamics of decision making about treatment of prostate cancer requires better understanding of the patients' perception of the trade-offs between quantity and quality of life. This information will be critical in guiding future research into the underlying patient, provider, and health system factors that may influence patterns of care.

In summary, we found that, in addition to prognostic factors (such as age and PSA value), baseline disease-related function (such as impotence and bladder control), nonclinical variables, and marital status are important determinants of treatment of clinically localized prostate cancer. These results showing the variation in treatment by geographic region and other nonclinical factors underscore the lack of consensus for care of this disease, probably attributable to the lack of definitive evidence of the efficacy of one approach versus another. Until such evidence can be obtained, we urge that men diagnosed with prostate cancer be informed of the potential risks and the potential benefits of all four main treatment options so that they might make an informed decision.

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NOTES

Editor's note: SEER is a set of geographically defined, population-based, central cancer registries in the United States, operated by local nonprofit organizations under contract to the National Cancer Institute (NCI). Registry data are submitted electronically without personal identifiers to the NCI on a biannual basis, and the NCI makes the data available to the public for scientific research.

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