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PATTERNS OF TREATMENT OF PATIENTS WITH PROSTATE CANCER INITIALLY MANAGED WITH SURVEILLANCE: RESULTS FROM THE CaPSURE DATABASE

THERESA M. KOPPIE, GARY D. GROSSFELD, DAVID MILLER,* JENNY YU,† DAVID STIER,* JEANETTE M. BROERING, DEBORAH LUBECK,* JAMES M. HENNING, SCOTT C. FLANDERS* AND PETER R. CARROLL‡

From the Department of Urology, Center for Urologic Outcomes, University of California-San Francisco, University of California-San Francisco-Mt. Zion Cancer Center and Lewin TAG, San Francisco, California, and TAP Holdings, Deerfield, Illinois

ABSTRACT

Purpose: We determined the demographic and clinical profile of men who elect surveillance as the initial management of prostate cancer as well as the incidence and predictors of secondary treatment of these patients.

Materials and Methods: The Cancer of the Prostate Strategic Urological Research Endeavor (CaPSURE) is a national disease registry of patients with various stages and treatments of prostate cancer. Using this database of 4,458 men we identified 329 (8.2%) who elected surveillance as the initial management of prostate cancer. Patients choosing watchful waiting were compared to other CaPSURE participants using the chi-square test. The likelihood of treatment initiation in the watchful waiting group was calculated using the Kaplan-Meier method. After adjusting for patient age, race, prostate specific antigen (PSA) at diagnosis, clinical T stage and total Gleason score the Cox proportional hazards regression model was used to determine significant predictors of treatment initiation.

Results: Compared with others in the database, patients on watchful waiting were more likely to be 75 years old or older (51% versus 16%, $p < 0.001$), white (93% versus 85%, $p < 0.001$), and have lower serum PSA ($p < 0.001$), organ confined disease (97% versus 88%, $p < 0.001$) and a total Gleason score of 7 or less (97% versus 88%, $p < 0.001$). In the watchful waiting group there was a 52% likelihood of treatment initiation within 5 years of the diagnosis. Significant predictors of secondary treatment were age younger than 65 years and elevated serum PSA at diagnosis. Neither race, extraprostatic stage cT3 disease nor higher total Gleason score was a significant predictor of treatment.

Conclusions: Men who elect initial watchful waiting for prostate cancer tend to be older, have lower serum PSA and more favorable disease characteristics than those who seek treatment. PSA at diagnosis is the dominant factor for predicting secondary treatment.

KEY WORDS: prostate, prostate-specific antigen, prostatic neoplasms

Prostate cancer is the most commonly diagnosed cancer in American men and the second leading cause of cancer related death.[1] The optimal management of prostate cancer remains controversial. To date no consensus exists on the best form of treatment for any disease stage.

Given the protracted natural history of prostate cancer and the advanced age at diagnosis in many patients, initial surveillance or watchful waiting remains an important treatment option for those newly diagnosed with the disease. Retrospective series indicate that watchful waiting may achieve a long-term survival outcome similar to that of other treatment modalities, especially in older men with well or moderately differentiated, low stage prostate cancer. Moreover, such a favorable outcome may be achieved without any associated treatment related morbidity.[2–4] With widespread prostate specific antigen (PSA) screening in all age groups considerable stage migration has occurred and increased numbers of patients may be candidates for watchful waiting as the primary therapy for prostate cancer.

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To date information on the outcome of patients electing watchful waiting is limited since it has generally been derived from experiences at single institutions.[5] We describe national trends in the use of watchful waiting as primary therapy for prostate cancer. Specifically the demographic and clinical profile of men who elected surveillance as the initial management of prostate cancer was assessed, as were the incidence and predictors of secondary prostate cancer treatment.

MATERIALS AND METHODS

We analyzed data on patients with prostate cancer enrolled in the Cancer of the Prostate Strategic Urological Research Endeavor (CaPSURE) database who elected watchful waiting as the initial form of therapy. CaPSURE is a longitudinal, observational database of patients with prostate cancer recruited through a network of urologists at 29 community and academic urology practice sites distributed regionally throughout the United States. At each practice site men with biopsy proved prostate cancer are invited to join the study in a consecutive fashion as they present for outpatient care. Subjects may be enrolled in the database despite a considerable interval since the initial diagnosis.

At enrollment extensive clinical and demographic information is recorded based on the existing medical record. These

TABLE 1. *Comparison of patients who elected watchful waiting and those who underwent immediate treatment*

No. Pts.	No. Watchful Waiting (%)	No. Immediate Treatment (%)	p Value (chi-square test)
Total No.	329	4,129	
Age (mean 73.7, median 75.1):			0.001
Younger than 65	38 (11.6)	1,499 (36.7)	
65–74	125 (38.0)	1,937 (47.4)	
75 or Older	166 (50.5)	651 (15.9)	
Race:			0.001
White	302 (92.6)	3,478 (84.6)	
Black	19 (5.8)	484 (11.8)	
Other	5 (1.5)	151 (3.7)	
Median yr. diagnosis	329 (1994)	4,098 (1994)	
Clinical T stage at diagnosis:			0.001
cTX	2 (1.6)	107 (2.6)	
cT1	143 (43.6)	864 (20.9)	
cT2	170 (53.8)	2,750 (66.6)	
cT3–cT4	13 (4.0)	409 (9.9)	
PSA at diagnosis (mean 12.3, median 7.4):			0.001
0.0–4.0	53 (18.6)	363 (9.8)	
4.1–10.0	139 (48.8)	1,654 (44.6)	
10.1–20.0	62 (21.8)	861 (23.2)	
20.1 or Greater	31 (10.9)	823 (22.4)	
Gleason score at diagnosis (mean 4.8, median 5):			0.001
2–6	249 (86.2)	2,514 (67.2)	
7	31 (10.7)	771 (20.6)	
8–10	9 (3.1)	454 (12.1)	
Risk of disease:			0.001
Low	67 (20.4)	296 (7.3)	
Intermediate	177 (54.0)	1,836 (45.3)	
High	84 (25.6)	1,917 (47.4)	
Death:	23	230	0.003*
Related to prostate Ca	3 (13.0)	60 (26.1)	
Related to other Ca	1 (4.3)	24 (10.4)	
Other causes	16 (69.6)	83 (36.1)	
Unknown causes	3 (13.0)	63 (27.4)	

* Other causes versus remaining 3 groups.

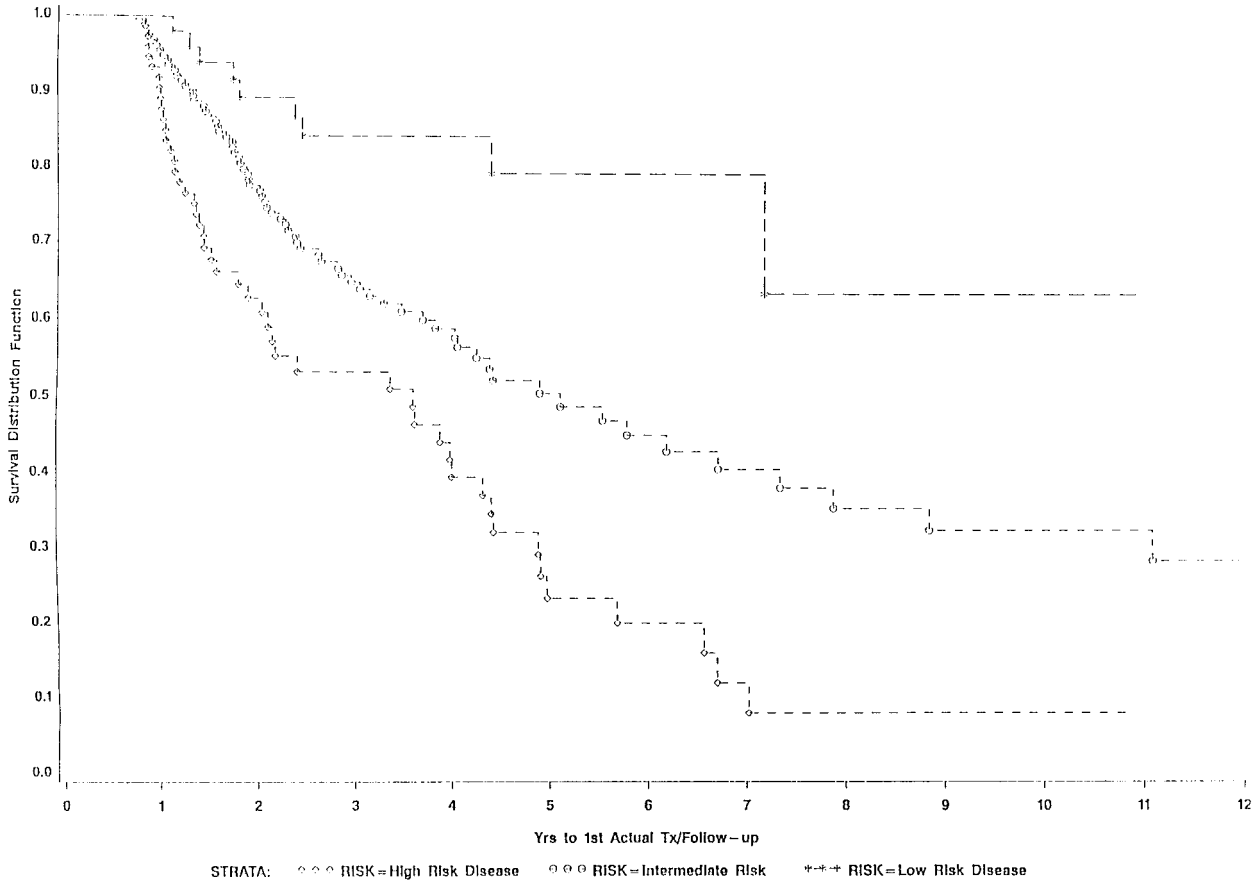

FIG. 1. Kaplan-Meier event-free treatment survival curve stratified by disease risk

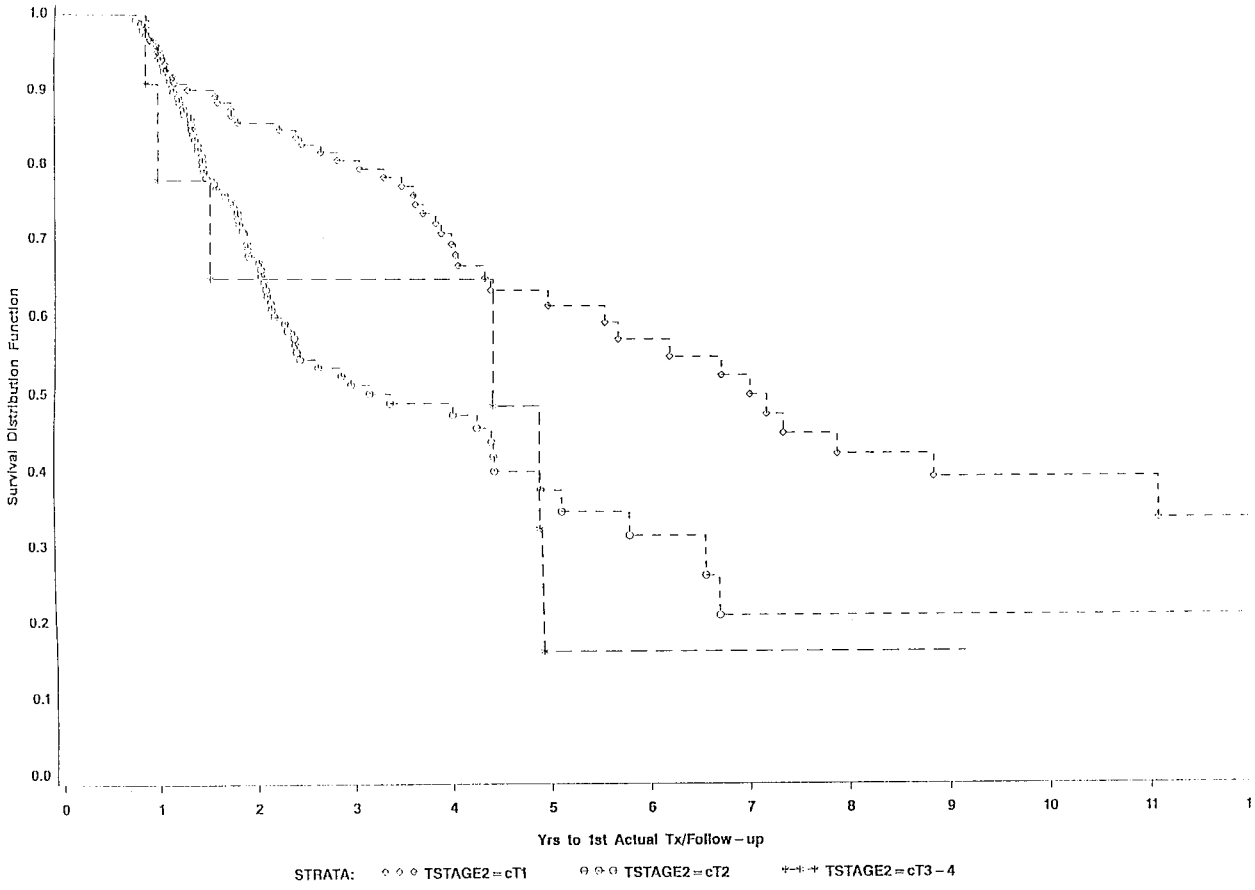

FIG. 2. Kaplan-Meier event-free survival curve stratified by T stage at diagnosis

data include the type of primary treatment given as well as patient age, cancer stage, tumor grade and initial serum PSA. Additional data are recorded prospectively at each office visit after the baseline visit, including new procedures, treatments and diagnostic tests. Hospital discharge summaries are obtained for all hospitalizations reported, and all international classification of diseases, version 9 diagnoses and procedures are abstracted. Patients are followed in the database until death or study withdrawal. Institutional review board approval for the study is obtained at each clinical site and patient informed consent for participation is required for data collection. Additional details of the project methodology have been published previously.[6]

Men who elected watchful waiting as the initial treatment option are the subjects of our study. Patients were excluded from analysis if they started therapy within 9 months of the prostate cancer diagnosis or elected watchful waiting more than 9 months after the diagnosis. Demographics and clinical characteristics of the watchful waiting group were compared to those of all others with prostate cancer in the CaPSURE database using the chi-square test statistic. To define the risk profiles of patients in the database high, intermediate or low disease risk categories were assigned based on clinical T stage, serum PSA at diagnosis and biopsy Gleason score. High risk tumors were defined as Gleason score 7 or greater, serum PSA greater than 15 ng./ml. or stage T3 or greater disease. Low risk cancer was defined as stage T1 or T2aN0M0 disease, Gleason score 6 or less with no Gleason 4 or 5 components and serum PSA less than 5 ng./ml. The intermediate risk category included all remaining cases.

Freedom from event (treatment) curves in the watchful waiting group were calculated using the Kaplan-Meier method. After adjusting for patient age, race, PSA at diagnosis, clinical T stage and total Gleason score, the multivariate Cox proportional hazards regression model was used to assess the predictors of treatment initiation in the watchful waiting group. A time dependent Cox model was also constructed to model the time dependent covariates of PSA before treatment and change in PSA or clinical stage during watchful waiting.

RESULTS

Of 4,459 patients enrolled in the CaPSURE database 471 (10.6%) elected watchful waiting as the initial form of cancer treatment. Mean and median followup in these cases was 3.06 and 2.25 years, respectively (range 0 to 25) after diagnosis. Of the 471 men 79 started therapy within 9 months of diagnosis, while an additional 63 elected watchful waiting 9 months or more after the initial diagnosis. Such patients were excluded from current analysis because the former group likely included those who simply deferred initial treatment and the latter likely included those who were indecisive regarding any form of therapy for prostate cancer. Since we evaluated only cases in which the clinical course most closely represented the natural history of watchful waiting, 329 (8.2% of the overall CaPSURE cohort) form the basis of our study.

Mean and median age of these patients was 73.6 and 75.08 years, respectively (range 44.16 to 87.17). PSA at diagnosis was recorded in 285 of the 329 cases (87%) at enrollment. Mean and median serum PSA was 12.29 and 7.4 ng./ml., respectively. Mean and median Gleason score documented in 289 cases (88%) was 4.8 and 5, respectively. Disease was clinical stage T1 in 143 patients (43.9%), stage T2 in 170 (52.1%) and stage T3 to T4 in 13 (4%). Of the patients 92.6%

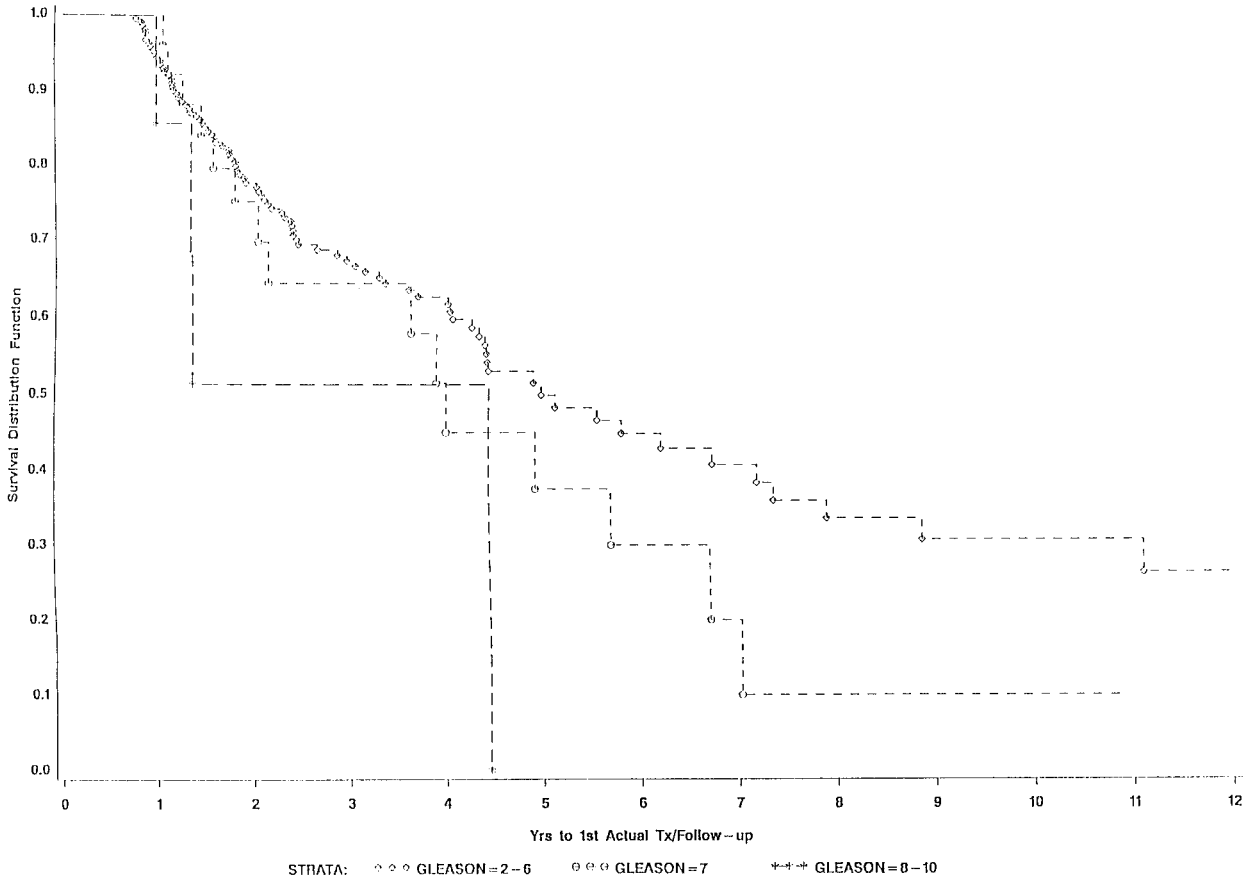

FIG. 3. Kaplan-Meier event-free survival curve stratified by clinical Gleason score at diagnosis

were white and 5.8% black. Disease was low, moderate and high risk in 20.4%, 54% and 25.6%, respectively, of those for whom complete information was available on serum PSA, clinical T stage and Gleason score. There were significant differences in CaPSURE patients who elected initial surveillance and those who underwent other forms of prostate cancer treatment (table 1). Men who elected watchful waiting were significantly older, had significantly lower stage and grade disease, and significantly lower serum PSA values at diagnosis than other patients.

According to death certificate data 23 men (7%) on watchful waiting died during the study period. Prostate cancer was the cause of death in only 3 of the 23 patients (13%). Of the 3 men 2 who had been assigned to the high risk disease category due to a PSA of greater than 20 ng./ml. at diagnosis died of prostate cancer, and 1 who was considered at intermediate risk died 15 years after diagnosis.

Of the patients on watchful waiting 39% received secondary cancer treatment during followup. Figures 1 to 5 show Kaplan-Meier estimates of freedom from treatment. The risk of secondary treatment 5 years after diagnosis in the watchful waiting cohort was 52.5%. The risk of secondary treatment after definitive local therapy in the CaPSURE database has been previously reported.[7]

Univariate analysis demonstrated that PSA at diagnosis was the dominant factor for predicting secondary treatment (fig. 4 and table 2). Table 3 shows the multivariate Cox proportional hazards model assessing predictors of secondary treatment. As in univariate analysis, PSA at diagnosis was the most important factor for predicting initiation of secondary treatment (table 3). In addition, patient age was an important predictor of secondary treatment in the multivariate model since patients older than 65 years were less likely to receive secondary treatment compared to those younger than 65 years. In addition, men with clinical stage T2 disease were more likely to undergo secondary treatment than those with clinical stage T1 disease ($p = 0.0153$). Neither race, extraprostatic stage cT3 disease extension nor higher total Gleason score was a significant predictor of secondary treatment.

We also performed a Cox regression analysis of time dependent covariates, including PSA before treatment and change in PSA or disease stage during watchful waiting. Since patients were enrolled in the database prospectively at diagnosis as well as after diagnosis and treatment, time dependent data were not complete for each patient. For instance, a baseline serum PSA and at least 1 followup value were available in 163 of the 329 cases analyzed. Median increase in PSA in patients who received secondary treatment was 6.2 ng./ml. and median ratio (final/initial PSA) was 1.82 ng./ml. In those who remained on watchful waiting serum PSA was stable (median change 0 ng./ml.). Up staging was uncommon, occurring in only 3% of treated patients and 4% of those who remained on watchful waiting.

The ratio of increasing serum PSA from baseline was a significant predictor of secondary treatment by the Cox regression model. The hazards ratio for the change in serum PSA was 1.99 (confidence interval 1.18 to 3.35). Therefore, for each factor serum PSA increased from baseline, the risk of treatment approximately doubled compared to when serum PSA remained stable with time. For example, a ratio of 2, calculated as the most recent/baseline PSA, indicates almost 2-fold (1.99) the risk of treatment compared to a ratio of 1. Furthermore, a ratio of 3 indicates a 1.99-fold greater risk than a ratio of 2. Of the 128 patients with secondary treatment 86 (67%) underwent androgen deprivation therapy with nilutamide, bicalutamide, diethylstilbestrol, flutamide, leuprolide, finasteride and goserelin (table 4). External beam

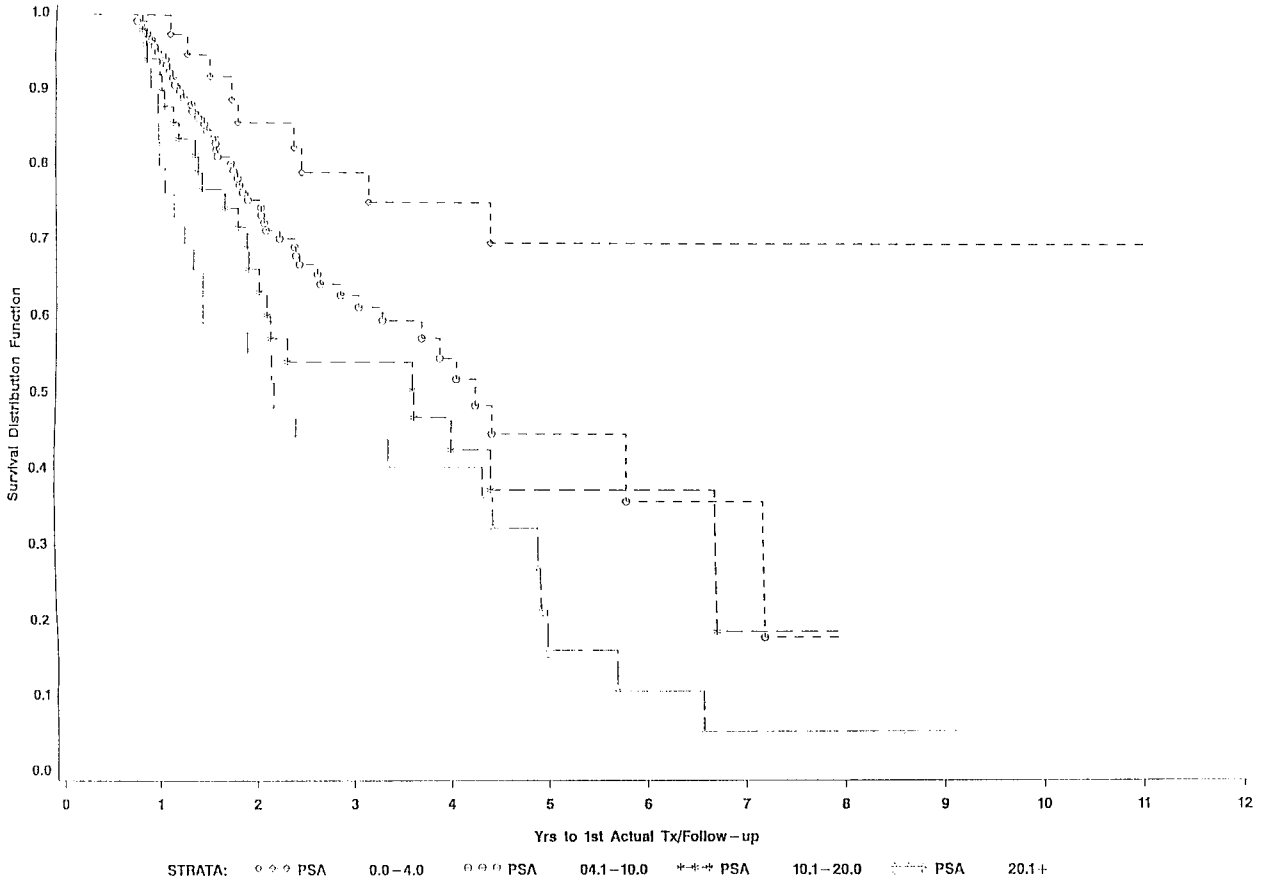

FIG. 4. Kaplan-Meier event-free survival curve stratified by PSA at diagnosis

radiation therapy, radical prostatectomy, orchiectomy and cryosurgery were done in 22 (17%), 14 (11%), 4 (3%) and 2 (1.5%) cases, respectively.

DISCUSSION

The optimal management of prostate cancer remains controversial because no consensus yet exists on the best form of treatment for any stage disease. Steinberg et al proposed that watchful waiting is the best treatment option in men with well or moderately differentiated, low volume prostate cancer and a life expectancy of less than 10 years.[8] However, to our knowledge little information is available on the outcome, such as secondary treatment and cause specific mortality, of contemporary patients treated in this fashion in the United States and no randomized trials have been done directly comparing observation to any definitive local treatment modality available for those with prostate cancer. While the prostate cancer versus observation trial comparing radical prostatectomy with expectant management is randomized, the results of this trial will not be available for some time.[9] Until such information becomes available physicians seeking data on watchful waiting must rely on nonrandomized retrospective studies, of which most were performed outside of the United States.

Many previous series of watchful waiting analyzed the overall survival rate of patients electing such treatment. Johansson et al reported the disease specific outcome of 642 patients diagnosed with prostate cancer in Sweden.[2] Of the 300 men with localized prostate cancer 223 received no initial therapy, followed by delayed treatment for symptomatic progression. A total of 77 patients received initial external beam radiation, androgen deprivation or radical prostatectomy. The corrected 15-year survival rate was similar in the immediate and delayed treatment groups, and only 11% of patients died of prostate cancer. Men with poorly differentiated disease had the highest death rate from prostate cancer (56%) compared to those with well (7%) or moderately (16%) differentiated disease. Similarly, Albertsen et al evaluated 451 men with clinically localized prostate cancer identified from the Connecticut tumor registry.[4] Patients received no treatment, or immediate or delayed androgen deprivation therapy at disease progression and were followed an average of 15.5 years after diagnosis. Albertsen et al observed that age adjusted survival of men with Gleason score 2 to 4 tumors was similar to that of the general population. However, those with Gleason score 5 to 7 and 8 to 10 tumors had a 4 to 5 and 6 to 8-year loss of life expectancy, respectively, compared to that of the general population without prostate cancer. In a more recent series of the Connecticut tumor registry Albertsen et al evaluated the probability of death within 15 years of diagnosis in men 55 to 74 years old treated conservatively for clinically localized prostate cancer.[10] As in previous studies, tumor grade was the most important predictor of death from prostate cancer in patients treated with initial surveillance.

In contrast to previous studies of men on watchful waiting, we determined the demographic and clinical profiles of those who elected watchful waiting as the initial management of prostate cancer. Moreover, we determined the incidence and predictors of secondary treatment in these patients. The cases analyzed in our series represent a large national sample of prostate cancer cases recruited from various urology practice sites distributed throughout the United States. Clinical sites were selected to represent a wide variety of practice settings, including managed care, fee for service practices and university based teaching hospitals. Broad geographic representation is included. Thus, the CaPSURE database

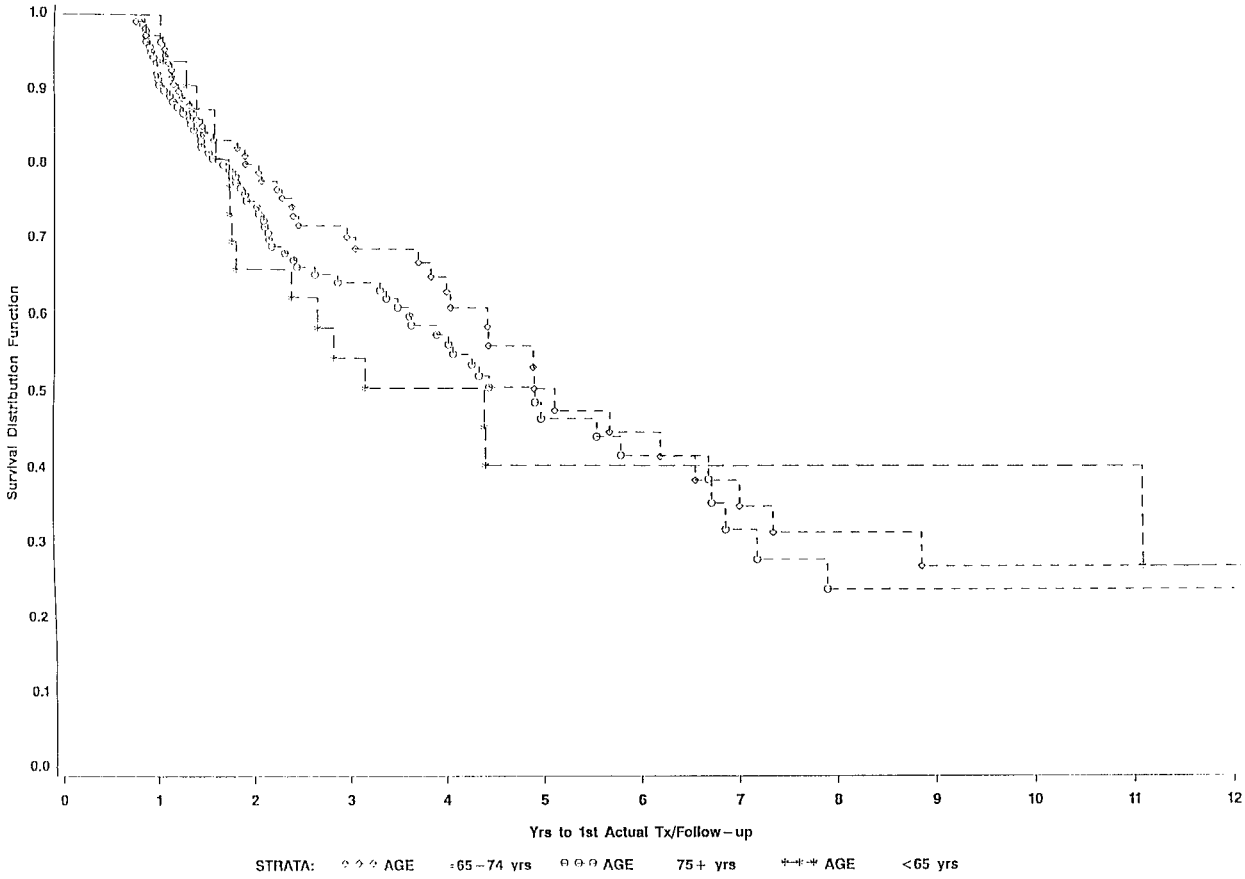

FIG. 5. Kaplan-Meier event-free survival curve stratified by patient age

TABLE 2. *Kaplan-Meier estimates of the risk of secondary treatment*

	Freedom From Secondary Treatment			p Value (log rank test)
	No. Pts.	% 2 Yrs. ± SE	% 5 Yrs. ± SE	
All watchful waiting pts.	329	76.1 ± 2.6	47.5 ± 3.9	
Age:				
Younger than 65	38	66.1 ± 8.8	40.6 ± 10.0	
65–74	125	80.1 ± 3.9	50.6 ± 6.7	0.5484 vs. younger than 65
75 or Older	166	75.1 ± 3.8	46.8 ± 5.4	0.9075 vs. younger than 65
Race:				0.4416
White	302	75.6 ± 2.7	47.5 ± 4.0	
Black	19	83.3 ± 10.8	33.3 ± 18.8	
Clinical T stage at diagnosis:				
CT1	143	85.9 ± 3.2	61.6 ± 5.4	
CT2	170	67.9 ± 4.0	37.6 ± 5.5	0.0001 vs. pT1
CT3–T4	13	64.9 ± 16.7	16.2 ± 14.7	0.0657 vs. pT1
PSA at diagnosis (ng./ml.):				
0–4.0	53	85.8 ± 5.9	69.9 ± 8.9	
4.1–10.0	139	75.5 ± 4.1	44.9 ± 7.1	0.016 vs. 0–4.0
10.1–20.0	62	66.4 ± 7.2	37.4 ± 9.1	0.0028 vs. 0–4.0
20.1 and Greater	31	55.2 ± 9.3	16.2 ± 8.0	0.0001 vs. 0–4.0
Clinical Gleason score at diagnosis:				
2–6	249	77.7 ± 2.9	50.0 ± 4.6	
7	31	75.2 ± 8.8	37.6 ± 12.0	0.1898 vs. 2–6
8–10	9	51.4 ± 20.4		0.0850 vs. 2–6
Risk of disease:				
Low	67	89.4 ± 4.5	79.4 ± 7.1	
Intermediate	177	77.7 ± 3.4	50.6 ± 4.9	0.0032 vs. low
High	84	62.8 ± 5.8	23.3 ± 6.5	0.0001 vs. low

may provide a realistic view of how prostate cancer is managed nationwide, providing important information with respect to disease specific outcomes associated with various forms of prostate cancer treatment.

We noted that men who elected watchful waiting tended to be older, and have lower baseline PSA and more favorable disease characteristics than those who chose definitive therapy. Compared to others in the CaPSURE database fewer patients in the watchful waiting group died of prostate cancer than of other causes. Such an outcome may have been expected since the majority of patients who elected watchful waiting had favorable disease characteristics and were older at diagnosis. Of our study population 39% underwent secondary cancer treatment within the followup period with the likelihood of secondary cancer treatment reaching 52.5% at 5 years after prostate cancer diagnosis.

This rate of secondary cancer treatment is somewhat higher than previously reported in patients treated with

TABLE 3. *Cox proportional hazards model for predictors of secondary treatment*

Risk of Secondary Treatment	No. Pts.	Unadjusted Estimates			Adjusted Estimates		
		Hazards Ratio	95% CI	p Value	Hazards Ratio	95% CI	p Value
Age:	329						
65–74 vs. younger than 65		0.866	0.493–1.519	0.6148	0.374	0.179–0.784	0.0091
75 or Older vs. younger than 65		1.041	0.607–1.786	0.8834	0.336	0.166–0.679	0.0024
Clinical T stage at diagnosis:	326						
cT2 vs. cT1		2.222	1.520–3.248	0.0001	1.833	1.123–2.992	0.0153
cT3–cT4 vs. cT1		2.305	0.982–5.410	0.0550	1.149	0.440–3.002	0.7769
PSA at diagnosis (ng./ml.):	285						
4.1–10.0 vs. 0–4.0		2.400	1.172–4.916	0.0167	3.064	1.352–6.944	0.0073
10.1–20.0 vs. 0–4.0		3.122	1.448–6.730	0.0037	3.680	1.544–8.769	0.0033
20.1 or Greater vs. 0–4.0		4.693	2.178–10.112	0.0001	6.864	2.587–18.202	0.0001
Clinical Gleason score at diagnosis:	289						
7 vs. 2–6		1.438	0.831–2.488	0.1946	1.082	0.570–2.053	0.8090
8–10 vs. 2–6		2.459	0.898–6.735	0.0800	1.179	0.395–3.515	0.7681
Risk of disease:	328						
Intermediate vs. low		2.749	1.372–5.508	0.0043			
High vs. low		5.335	2.612–10.895	0.0001			
19 Black vs. 302 white + 5 other pts.	326	1.353	0.630–2.907	0.4385	1.220	0.451–3.302	0.6948

TABLE 4. *Type of secondary treatment*

	No. Pts. (%)
Androgen deprivation therapy	86 (67.2)
External beam radiation therapy	22 (17.2)
Radical prostatectomy	14 (10.9)
Orchiectomy	4 (3.1)
Cryosurgery	2 (1.6)
Total	128 (100)

watchful waiting.[11,12] It is also higher than that reported after definitive local therapy. Grossfeld et al provided rates of secondary treatment after definitive local therapy using similar data from the CaPSURE database.[7] Of 1,894 CaPSURE patients treated with radical prostatectomy, external beam radiation or cryosurgery 22% underwent secondary cancer treatment within a mean of 3 years after the initial therapy. Lu-Yao[13] and Fowler[14] et al also reported rates of secondary treatment after radical prostatectomy, including 16% within 2 years, 22% within 3 years and up to 35% within 5 years of surgery.

It was also interesting that the most common form of secondary treatment in our series was androgen deprivation therapy followed by external beam radiation therapy. Patients were much less likely (16%) to choose surgical intervention as secondary treatment. This finding may be due to the advanced age of the population that initially elected watchful waiting, limited life expectancy due to competing co-morbid conditions or patient preference against surgical intervention.

While we did not determine why patients in the database elected watchful waiting, it is likely that a number of factors influenced this decision, including patient preference and physician recommendation. McLaren et al followed 113 men who chose watchful waiting after referral to the British Columbia Cancer Agency.[12] Reasons for choosing watchful waiting included patient preference in 37% of cases, physician recommendation in 42%, decreased life expectancy in 19% and contraindication to radiotherapy in 2%. Mazur and Hickman counseled 140 veterans at an outpatient medical clinic regarding radical prostatectomy and watchful waiting as treatment options for prostate cancer.[15] Patients were then asked which option they would prefer if they were diagnosed with prostate cancer and why they elected that specific treatment option. Of the patients interviewed 53% stated that they would prefer surgical treatment over watchful waiting, including 92% who reported that the possibility of complete tumor removal was the strongest factor influencing the decision. In contrast, 42% of the men stated that they would prefer observation as the initial disease treatment, of whom 80% reported that the possibility of complications was the strongest factor influencing the decision. Older patients in their study were significantly more likely to prefer observation rather than surgical intervention. Overall health status was not significantly associated with patient preference.

Physician preference may also be important for determining which patients are offered watchful waiting and how patients perceive treatment options. The finding that those who elected watchful waiting in our series had more favorable disease characteristics is to be expected because the literature supports watchful waiting in such patients.[3,4] In addition, co-morbidity may have had an impact on such decisions. The recent national survey of urologists and primary care physicians of Fowler et al revealed that two-thirds of physicians considered watchful waiting appropriate in patients with less than 10 years of life expectancy.[16]

While we did not assess why patients underwent secondary cancer treatment, it is notable that such treatment was given more frequently to those with higher serum PSA and those who were younger at diagnosis. Moreover, patients in whom serum PSA changed with time were more likely to undergo secondary treatment compared to those in whom serum PSA remained stable. Such results may reflect the tendency toward definitive treatment of younger patients with prostate cancer as well as the impact of serial PSA testing on medical resource use. McLaren et al evaluated the predictive value of initial PSA and PSA doubling time on clinical behavior in cases of early untreated prostate cancer.[12] They demonstrated that while PSA doubling time was a strong predictor of clinical tumor progression by digital rectal examination, initial PSA was the only significant predictor of time to secondary treatment. It is also interesting that cancer stage was not associated with secondary treatment in our study and migration to higher stage disease was uncommon, occurring in only 3% of those who received secondary treatment. In addition, tumor grade was not associated with secondary treatment, although grade appears to be the most important predictor of cause specific survival in patients on watchful waiting.[10] Thus, our data suggest that for patients on watchful waiting physicians rely on serum PSA as a surrogate marker of disease progression in a similar fashion to that after definitive local treatment with radical prostatectomy or radiation therapy.

Our study has limitations. Although the database represents a national population of patients from various practice settings, serial PSA data were available for only 163 of the 329 patients (49.5%) studied. Since men were enrolled in the database prospectively at diagnosis, and after diagnosis and treatment, time dependent information was incomplete for many patients. Those with similar disease characteristics were not randomized to other treatment options, making it

impossible to compare disease specific outcomes in watchful waiting versus other forms of initial treatment. In addition, the rationale for the initial election of watchful waiting and secondary treatment was not known. Nevertheless, our study provides considerable insight into the natural history of patients selected for watchful waiting in this country. Such information may be important to patients, physicians and other health care professionals who counsel patients on the various treatment options available for prostate cancer.

CONCLUSIONS

Men who elect initial watchful waiting for prostate cancer tend to be older, and have lower serum PSA and more favorable disease characteristics than those who seek definitive local therapy. A low percent of such men died of prostate cancer in our study. Eventual treatment was given in 52% of cases within 5 years of prostate cancer diagnosis. Patients who were younger and had higher serum PSA at diagnosis were significantly more likely to undergo secondary treatment, as were those in whom serum PSA increased during observation. The most common form of secondary treatment was androgen deprivation therapy, followed by external beam radiation therapy and radical prostatectomy.

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EDITORIAL COMMENT

The appropriate treatment of newly diagnosed prostate cancer continues to pose a dilemma for patients and clinicians. In younger patients with high grade disease the risk of disease progression and possible death from prostate cancer are sufficiently high to justify the potential risk of complications associated with radical surgery or radiation therapy. These men rarely elect watchful waiting. Older men, especially those with relatively low grade disease, have a much more difficult decision. Are the risks associated with treatment balanced by the potential gain in longevity or quality of life? In the absence of data from randomized trials patients must turn to case series reports.

These authors provide us with new information concerning this important group of men. Using information available from the CaPSURE database they convincingly demonstrated that men electing watchful waiting are older than those seeking treatment after the diagnosis of prostate cancer. While median followup is only 2.3 years, 23 patients died of various causes but only 3 died of prostate cancer. At least 2 patients had serum PSA that many would regard as too high to reflect localized disease. The remaining patient was diagnosed more than 15 years ago and before the advent of PSA testing. None of these patients would likely have benefited from aggressive local therapy. Thus, we may assume that they made the correct decision regarding treatment selection.

A surprising 39% of these men underwent secondary cancer therapy because of increasing serum PSA or concern regarding disease progression. Will these secondary treatments improve clinical outcomes? In the absence of randomized trials we will probably not know. Physicians are usually quick to recommend treatment for cancer. No matter what the outcome they claim a benefit for the patient. If disease progresses, they have done everything possible. If it does not progress, they assume that they have cured the patient. Simply watching a patient is much more difficult. If disease progresses, the physician has failed regardless of whether the tumor was curable. If the disease does not progress, the patient assumes that he did not need physician input.

The true value of this patient cohort will become evident during the next several years. Although we may not be able to control for the differences between men who seek secondary therapy and those who do not, we will determine whether they fare as well as patients who elect radical surgery or radiation therapy. With more information concerning clinical outcomes, especially in men who choose to forgo treatment, we will be better able to guide our patients to select a clinical course that is most appropriate for their particular condition.

Peter C. Albertsen
Department of Urology
University of Connecticut Health Center
Farmington, Connecticut