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Nine-Year Prostate Cancer Survival Differences Between Aggressive Versus Conservative Therapy in Men With Advanced and Metastatic Prostate Cancer

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Abstract

BACKGROUND: To the authors' knowledge, the survival benefit of local therapy in the setting of advanced prostate cancer remains unknown. The authors investigated whether prostate-directed treatment with either surgery or radiotherapy versus conservative treatment in the setting of locally advanced or metastatic disease was associated with improved survival within a cohort of men from the Centers for Disease Control and Prevention's (CDC) Breast and Prostate Cancer Data Quality and Patterns of Care Study (CDC POC-BP).

METHODS: Men diagnosed with locally advanced (cT3-T4 or N+ and M0) or metastatic prostate cancer were identified. The authors compared survival by treatment type, categorized as conservative (androgen deprivation therapy only) versus aggressive (radical prostatectomy or any type of radiotherapy). Nine-year overall survival and prostate cancer-specific survival were estimated using the Kaplan-Meier method. The Cox proportional hazards model was used to determine factors independently associated with 9-year prostate cancer-specific survival.

RESULTS: For men with advanced, nonmetastatic prostate cancer, conservative treatment alone was associated with a 4 times higher likelihood of prostate cancer mortality compared with men treated with surgery (hazard ratio, 4.18; 95% confidence interval, 1.44–12.14). In contrast, no

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AUTHOR CONTRIBUTIONS

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CONFLICT OF INTEREST DISCLOSURES

The authors made no disclosures.

difference was found between conservative versus aggressive treatment after adjusting for covariates for men with metastatic disease. The 9-year prostate cancer-specific survival rate was 27% for those receiving aggressive treatment versus 24% for men undergoing conservative treatment.

CONCLUSIONS: The authors did not observe a survival advantage with local therapy in addition to standard androgen deprivation therapy for men with metastatic prostate cancer. However, the results of the current study did affirm advantages in the setting of locally advanced disease. Aggressive local therapy in the setting of metastatic disease needs to be studied carefully before clinical adoption.

Keywords

advanced; metastatic; prostate cancer; radical prostatectomy; radiotherapy; survival

INTRODUCTION

Patients with metastatic, castration-sensitive prostate cancer traditionally are treated with systemic therapy, primarily in the form of androgen deprivation therapy (ADT). Recent studies have suggested a survival advantage with the addition of cytotoxic chemotherapy with docetaxel, particularly for men with high-volume metastatic disease.[1,2] To our knowledge, the added value of treatment to the primary prostate tumor with either radiotherapy or cytoreductive surgery in the setting of disseminated disease remains unknown. Such a strategy has proven to be beneficial for other malignancies such as renal cell or ovarian carcinoma, and multiple studies using nonrandomized, retrospective data have suggested a possible survival advantage in patients with prostate cancer.[3–7] Positive data from these retrospective studies have supported ongoing randomized trials to study the role of prostate-directed therapy in the face of metastatic disease, but these results must be interpreted cautiously before widespread clinical adoption.

The use of prostate-directed therapy for men with locally advanced, but nonmetastatic, prostate cancer also has been explored. The STAMPEDE (Systemic Therapy in Advancing or Metastatic Prostate Cancer: Evaluation of Drug Efficacy) multiarm trial included men with M0, high-risk, locally advanced, and N+ disease and tested the benefits of radiotherapy in addition to standard ADT. Although both of these groups benefited in terms of progression-free survival with the addition of radiotherapy, with limited follow-up, the effect on disease-specific survival or overall survival (OS) is unknown.[8]

Local treatment to the prostate can be associated with decrements in quality of life (particularly with regard to urinary, bowel, and sexual function), and these risks need to be carefully balanced with any potential survival advantages.[9] In addition, the impact of local treatment within the setting of locally advanced or metastatic disease may vary by mortality risk and therefore any impact must be stratified by clinical or molecular features to determine which men will benefit the most.[10]

We investigated whether prostate-directed treatment with either surgery or radiotherapy versus conservative treatment in the setting of locally advanced or metastatic disease was

associated with improved survival within a cohort of men from the Centers for Disease Control and Prevention's (CDC) Breast and Prostate Cancer Data Quality and Patterns of Care Study (CDC POC-BP). This unique study provided abstracted treatment information for men diagnosed with prostate cancer in 2004 who were identified through population-based cancer registries, and for whom 9-year survival data were obtained.

MATERIALS AND METHODS

The CDC POC-BP study included data from men from 7 states who were diagnosed with prostate cancer in 2004. Data were extracted from population-based cancer registries in each state and supplemented with medical record review. The baseline demographic features assessed included race/ethnicity, neighborhood socioeconomic status (based on census characteristics for patient address at the time of diagnosis), health insurance, and marital status, as categorized in Table 1. Clinical information included stage of disease, prostate-specific antigen (PSA) level, and Gleason score. Comorbidities were measured using the Adult Comorbidity Evaluation-27 (ACE-27), which is a validated instrument associated with survival that is specific to patients with cancer.[11–14] It is based on 26 comorbid conditions with 3 grades of decompensation (or severity) and excludes complications of cancer or its treatment. An overall comorbidity severity score (none, severe, moderate, or mild) was determined by the highest ranking single condition, unless the subject had at least 2 moderate comorbidities in different body systems when the grade was coded as severe. Data regarding the first course of treatment, defined as that given or planned within 6 months of diagnosis, were collected and included surgery (ie, radical prostatectomy [RP]), radiotherapy (including external beam and brachytherapy), and ADT.

As described previously, there were 8232 men with clinically localized disease.[15] Only men diagnosed with locally advanced (cT3-T4 or N+ and M0) (272 men) or metastatic (M1) (314 men) prostate cancer were included in the current analysis. Treatment was categorized as conservative (ADT only) versus aggressive (RP or any type of radiotherapy).

Statistical Analysis

Nine-year OS and prostate cancer-specific survival were estimated using the Kaplan-Meier method. Variables with univariate *P* values <.1 were included in a weighted, multivariate Cox proportional hazards model to determine factors independently associated with 9-year prostate cancer-specific survival. Two states did not provide 9-year survival data, and therefore the 5-year survival data were included. Patients with only a recorded diagnosis year were assigned a midpoint month and day. All analyses were performed using SAS statistical software (version 9.4; SAS Institute Inc, Cary, North Carolina).

RESULTS

The baseline characteristics of the 2 risk groups are shown in Table 1. Among the sociodemographic variables, the 2 groups differed with regard to age at the time of diagnosis, marital status, and insurance coverage. Patients diagnosed with locally advanced prostate cancer were younger than men diagnosed with metastatic cancer, and were more likely to be married and to be covered by private insurance. There were no statistically

significant differences observed between the 2 groups with regard to race/ethnicity, registry region, urban/rural residence, neighborhood socioeconomic status, or comorbidity severity score.

Clinically, the 2 groups differed with regard to PSA and Gleason score, with higher values for both variables noted in the metastatic disease group. The group with metastatic cancer was much more likely to be treated conservatively compared with patients with locally advanced disease (69.7% vs 25.5%). Distributions by stage of disease indicated that the majority of the patients with locally advanced disease had T3N0 disease (74.9%), with 12.7% having N+ disease. The majority of the metastatic cases were either T1 (20.7%) or T2 (34.0%) disease.

Table 2 shows the univariate prostate cancer-specific survival for each variable and the multivariate hazard ratios (HRs) for men with locally advanced prostate cancer, whereas Table 3 shows the same information for the group of patients with metastatic disease. In the patients with locally advanced disease, after adjustment for other variables, prostate cancer-specific survival varied by race, registry region, urban/rural residence, Gleason score, and treatment. It is interesting to note that nonwhite individuals had a lower HR compared with white individuals (HR, 0.33; 95% confidence interval [95% CI], 0.13–0.83), as did those residing in a mixed urban/rural area (vs an urban setting) (HR, 0.39; 95% CI, 0.18–0.84). Gleason score was found to be the greatest predictor of mortality and patients with a high Gleason score (8–10) were nearly 12 times as likely to die of prostate cancer compared with those with a score of 2 to 6 (HR, 11.62; 95% CI, 2.12–63.64), and those receiving conservative treatment were 4 times as likely to die of prostate cancer as those treated with surgery (HR, 4.18; 95% CI, 1.44–12.14). The 9-year prostate cancer-specific survival rate for the conservative treatment group was 67% versus 78% and 89%, respectively, for those receiving radiotherapy and surgery. Figures 1 and 2 illustrate prostate cancer-specific survival by treatment and by Gleason score, respectively, for patients with locally advanced prostate cancer.

Table 3 shows the univariate prostate cancer-specific survival and multivariate HRs for men with metastatic prostate cancer. The only variables found to be associated with survival in the multivariable analysis included marital status (HR for unmarried men, 1.55 [95% CI, 1.03–2.31] vs married men) and Gleason score, for which men with scores of both 7 and 8 to 10 had elevated HRs compared with those with scores of 2 to 6. In contrast to men with locally advanced disease, no difference was found between patients treated with conservative versus aggressive treatment after adjusting for covariates. The 9-year prostate cancer-specific survival rate was 27% for those receiving aggressive treatment (surgery or radiotherapy) versus 24% for men receiving conservative treatment. Figures 3 and 4 illustrate prostate cancer-specific survival by treatment and by Gleason score for this group.

DISCUSSION

To the best of our knowledge, the advantages of aggressive therapy with either surgery or radiotherapy to the prostate gland in men with locally advanced or metastatic prostate cancer are unknown. We noted a clear survival advantage at 9 years with aggressive prostate-

directed therapies in patients with locally advanced or lymph node-positive, nonmetastatic disease versus conservative therapy, with a trend toward an advantage for surgery over radiotherapy. These results are supported by recent data emerging from the multiarm STAMPEDE trial using prostate radiation in addition to ADT in the setting of locally advanced disease over standard ADT alone.[8] In contrast, in the metastatic setting, we did not find a prostate cancer-specific survival advantage over systemic ADT alone with 9 years of follow-up and 30% of the cohort receiving some form of aggressive therapy. Other studies have addressed this question in larger cohorts, although with more limited follow-up compared with the current study.

Prospective, randomized data exist that demonstrate a survival advantage with prostate-directed radiotherapy in addition to ADT compared with ADT alone in men with locally advanced and clinically lymph node-positive disease.[16] Inclusion criteria for this international/intergroup trial included men with locally advanced disease (clinical T3 or T4, N0 or NX, or M0 disease) or clinically organ-confined tumors with either a PSA level >40 ng/ mL or both clinical T2 disease and a PSA concentration of >20 ng/mL. After a median follow-up of 8 years, the addition of prostate radiotherapy improved the OS rate by 8% (HR, 0.7; 95% CI, 0.57–0.85).[17] Within the STAMPEDE randomized trial, subgroup analysis similarly demonstrated failure-free survival advantages with the addition of prostate radiotherapy to standard ADT in men with high-risk M0 and N+M0 prostate cancer.[8] A more recent study of European men with very high-risk prostate cancer and clinical features concerning for metastatic disease (PSA >50 ng/mL) compared the survival outcomes of men treated with prostate-directed therapy (either prostatectomy or radiotherapy) with ADT with those of men treated with ADT alone. Using a retrospective design, the authors demonstrated a substantial cancer-specific survival advantage with the addition of local therapy (HR, 2.87; 95% CI, 2.16–3.82).[18]

In the face of metastatic disease, the treatment advantages of local therapy are not as clear, with no definitive level 1 evidence. However, positive results from several retrospective series have prompted the design and implementation of clinical trials with prostate-directed surgery or radiotherapy within this setting. Several authors have studied data from the Surveillance, Epidemiology, and End Results registry to compare survival outcomes for men with metastatic prostate cancer treated with or with-out local therapy.[5,10,19,20] Culp et al demonstrated improved 5-year OS in men receiving either RP or prostate brachytherapy in the face of metastatic disease (HR, 0.35; 95% CI, 0.30–0.41 [P<.01]).[5] Satkunasivam et al demonstrated prostate cancer-specific morality risk reductions of 52% and 62%, respectively, with the use of RP and radiotherapy in men with metastatic disease after a median follow-up of 20 months.[6]

A separate analysis using Surveillance, Epidemiology, and End Results data demonstrated that these survival advantages for men with metastatic disease may be sensitive to baseline biologic risk. When the baseline cancer-specific mortality rate was >50% based on the Cox proportional hazards model with clinical criteria, no advantages were noted with the addition of local therapy to ADT.[10] We controlled for these factors in the current analysis and also found no advantage for local therapy.

Loppenberg et al used propensity score matching to study a cohort of 15,501 patients with metastatic prostate cancer from the National Cancer Data Base from 2004 to 2012.[7] Patients who received local therapy were found to have improved OS at 3 years compared with those treated with ADT alone (69% vs 54%; P<.001). This analysis also demonstrated lower survival advantages with local therapy as the predicted mortality rate increased to >72%. In the metastatic setting, the data from the current study demonstrated clear survival differences by baseline mortality risk, primarily based on Gleason score. Evolving data have suggested that true Gleason score 6 prostate cancer does not have metastatic potential.[21] Although we did find men with Gleason score 6 prostate cancer at baseline in the metastatic disease cohort, we were not able to perform a contemporary pathologic review and many of these cases would likely be upgraded based on changes to Gleason scoring after the International Society of Urological Pathology report of 2005.[22] In addition, baseline risk in the current study was based on biopsy Gleason score and higher-grade tumors within the prostate may be missed after standard 12-needle core prostate biopsy.[23] Despite these limitations, we noted clear survival heterogeneity by Gleason score in men presenting with metastatic disease, and therefore any survival advantages offered by local therapy need to be studied within this context. The data set in the current study was not large enough to study survival advantages stratified by disease risk.

The current study was limited by the nonrandomized approach to treatment selection. We attempted to adjust for important baseline variables associated with treatment category, including comorbidity; however, we were unable to adjust for potential unrecognized confounding variables that may have been associated with treatment choice and survival, which may bias the results. For example, healthier men with advanced but lower volume tumors, which may lead to longer survival, may be more likely to undergo aggressive therapy (RP or radiotherapy) compared with ADT alone. We also do not know the indications for treatment to the prostate in this population, nor do we have any information regarding subsequent therapies received by this cohort. In addition, we were unable to perform a centralized, contemporary pathologic review of the prostate specimens.

Conclusions

Metastatic prostate cancer is a heterogeneous disease. To our knowledge, the survival advantages offered by local therapy in the face of distant metastases remain unknown for patients with prostate cancer. In the current study, we did not observe a survival advantage with either radiotherapy or surgery in addition to standard ADT in the setting of metastatic disease. However, the current study findings did affirm the advantages of these therapies in the locally advanced setting. For men with metastatic prostate cancer, this needs to be studied carefully before clinical adoption, especially to identify subgroups of men who will benefit the most from an aggressive approach. In addition, any advantages must be interpreted within the setting of improved survival with additional systemic agents including docetaxel and more recently abiraterone, both of which have demonstrated dramatic survival advantages when given in the castrate-sensitive state.

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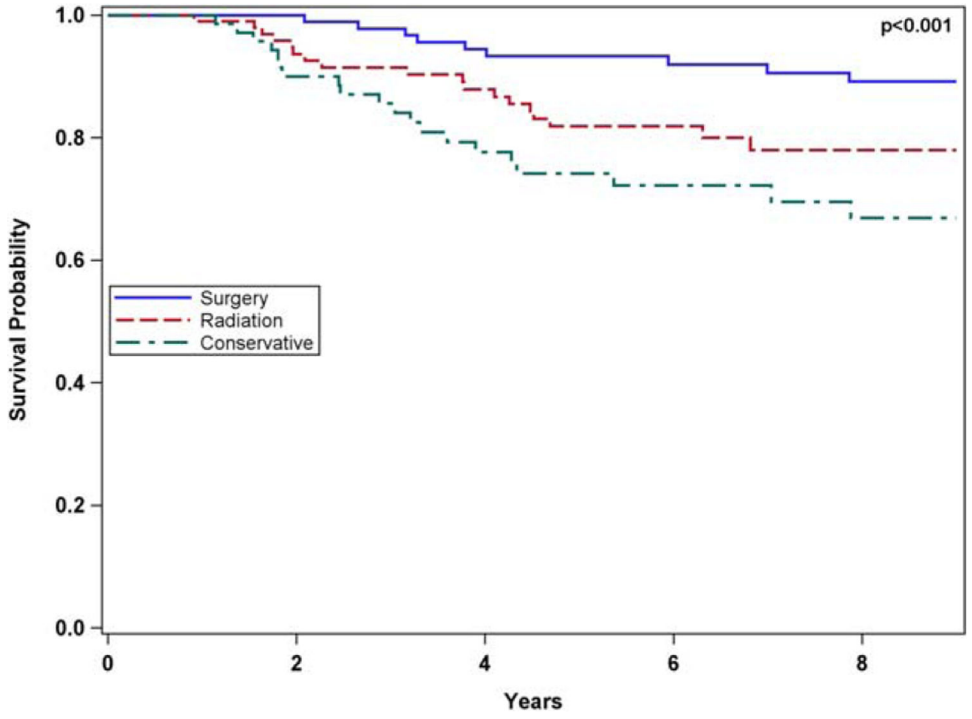

Figure 1.

Prostate cancer-specific survival by treatment in patients with locally advanced prostate cancer.

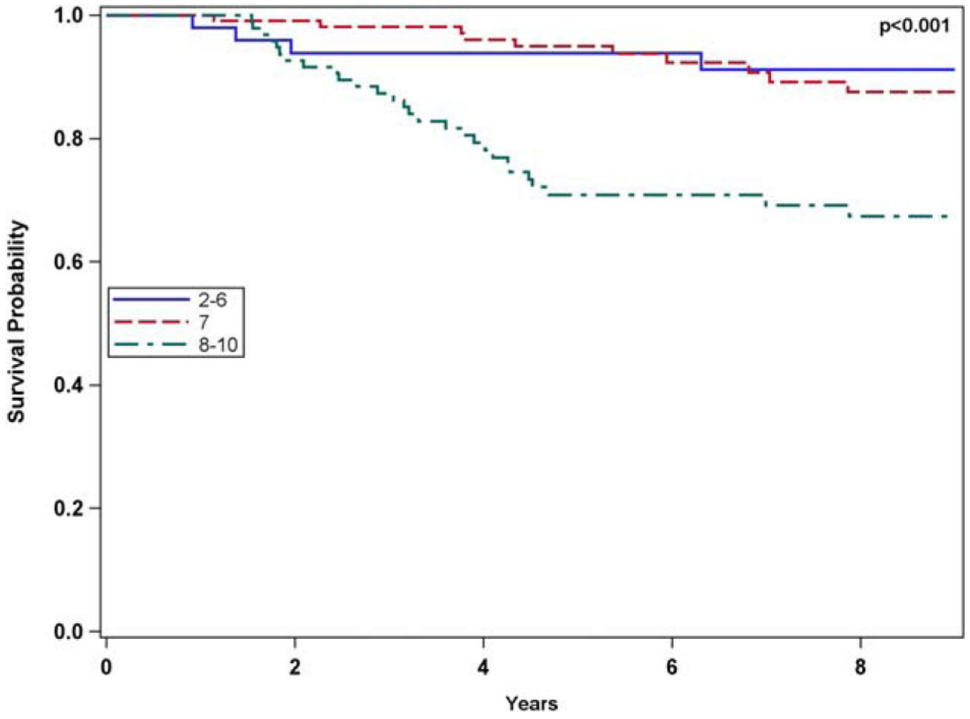

Figure 2.
Prostate cancer-specific survival by Gleason score in patients with locally advanced prostate cancer.

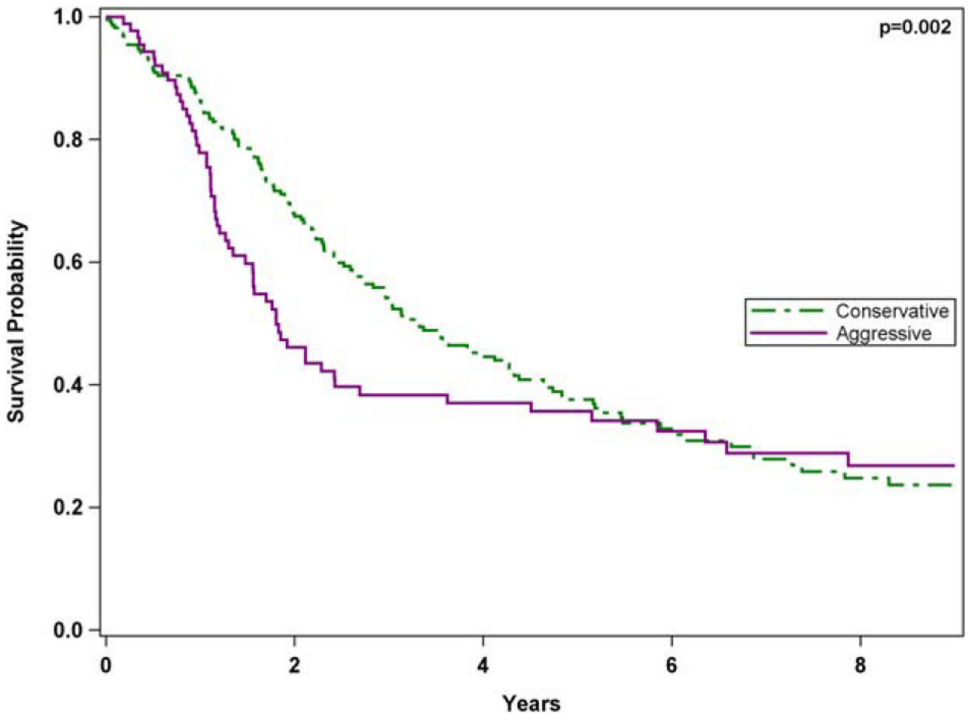

Figure 3.
Prostate cancer-specific survival by treatment in patients with metastatic prostate cancer.

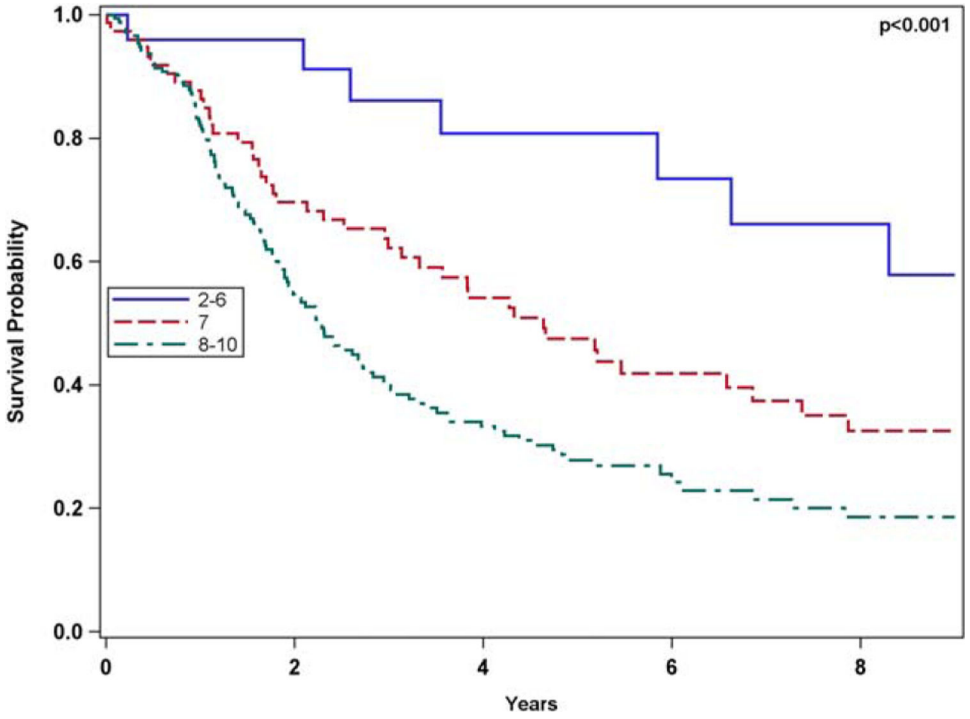

Figure 4.
Prostate cancer-specific survival by Gleason score in patients with metastatic prostate cancer.

TABLE 1.

Patient Demographic and Clinical Characteristics

Variable	Locally Advanced No. (%)	Metastatic No. (%)	*P*
Total	272 (100.0)	314 (100.0)	
Age at diagnosis, y			.033
<60	70 (25.8)	58 (18.8)	
60–69	97 (34.0)	98 (27.4)	
70	105 (40.2)	158 (53.7)	
Race			.40
White	146 (71.0)	155 (65.2)	
Black	97 (21.8)	124(26.0)	
Hispanic	19 (5.0)	26 (7.0)	
Other	10 (2.2)	9 (1.8)	
Marital status			<.001
Married	184 (72.1)	172 (54.5)	
Not married	88 (27.9)	142 (45.5)	
Insurance			.011
Private	130 (51.1)	108 (35.8)	
Public	127 (42.2)	185 (57.6)	
None	15 (6.7)	21 (6.6)	
Registry region			.34
1	38 (20.6)	56 (23.4)	
2	73 (24.2)	69 (17.0)	
3	7 (3.7)	18 (7.4)	
4	67 (13.8)	65 (10.7)	
5	23 (10.2)	32 (11.0)	
6	33 (16.9)	41 (21.0)	
7	31 (10.6)	33 (9.5)	
Urban/rural residence			.17
Urban	103 (41.5)	160 (50.9)	
Rural	44 (13.6)	54 (18.2)	
Mixed	124 (45.0)	99 (30.9)	
SES			.72
Low	60 (18.7)	98 (22.0)	
Middle	68 (25.8)	73 (25.5)	
High	143 (55.5)	142 (52.5)	
Comorbidity severity			.065
None	79 (30.1)	84 (25.0)	
Mild	139 (50.4)	135 (42.7)	
Moderate/severe	42 (14.0)	71 (24.0)	
Unknown	12 (5.6)	24 (8.2)	
PSA, ng/mL			<.001

Variable	Locally Advanced No. (%)	Metastatic No. (%)	*P*
≤10	98 (37.0)	39 (13.4)	
>10	165 (63.0)	262 (86.6)	
Gleason score			<.001
2–6	50 (20.0)	25 (9.4)	
7	114 (39.6)	75 (26.3)	
8–10	102 (40.4)	179 (64.3)	
Treatment group			<.001
Conservative	74 (25.5)	222 (69.7)	
Surgery	97 (31.3)	14 (4.2)	
Radiotherapy	101 (43.1)	78 (26.1)	
T and N categories			.001
Tx-T0N0	0	26 (10.0)	
T1N0	0	61 (20.7)	
T2N0	0	107 (34.0)	
T3N0	207 (74.9)	23 (5.4)	
T4N0	30 (12.3)	44 (11.8)	
Tx-T0N1	1 (0.2)	8 (4.5)	
T1N1	12 (3.5)	4 (1.6)	
T2N1	9 (3.9)	13 (4.9)	
T3N1	11 (4.7)	9 (2.2)	
T4N1	2 (0.4)	19 (4.9)	

Abbreviations: PSA, prostate-specific antigen; SES, socioeconomic status.

TABLE 2.

Nine-Year OS, Prostate Cancer-Specific Survival, and Multivariate HRs for Men With Locally Advanced Prostate Cancer

		OS		Prostate Cancer-Specific Survival			
Variable	**No.**	**No. of Events**	**9-Year OS, %**	**No. of Prostate Events**	**9-Year Prostate Cancer-Specific Survival, %**	**Univariate *P***	**Multivariate HR (95% CI)**
Age at diagnosis, y						.86	
<60	70	19	71 ± 5.6	13	80 ± 5.1		
60–69	97	42	54 ± 5.3	17	79 ± 4.7		
≥70	105	64	36 ± 4.9	17	81 ± 4.1		
Race						.094	
White	146	72	48 ± 4.3	29	77 ± 3.9		1.00
Nonwhite	126	53	55 ± 4.7	18	82 ± 3.9		0.33 (0.13–0.83)
Marital status						.051	
Married	184	77	55 ± 3.8	31	8.0 ± 3.2		1.00
Not married	88	48	43 ± 5.5	16	76 ± 5.4		0.84 (0.41–1.70)
Insurance						.21	
Private	130	48	61 ± 4.4	23	79 ± 4.0		
Public	127	68	43 ± 4.6	21	81 ± 3.8		
None/unknown	15	9	26 ± 14.5	3	78 ± 11.1		
Registry region						<.001	
1	38	19	50 ± 8.1	6	81 ± 7.0		1.00
2	73	28	62 ± 5.7	13	80 ± 5.0		3.82 (1.21–12.06)
3	7	2	71 ± 17.1	0	100		0
4	67	34	49 ± 6.1	8	86 ± 4.5		1.88 (0.50–7.08)
5	23	12	52 ± 10.4[a]	6	70 ± 10.6[b]		1.32 (0.27–6.58)
6	33	12	70 ± 8.0[a]	5	84 ± 6.6[b]		2.11 (0.56–7.90)
7	31	18	42 ± 8.9	9	66 ± 9.4		2.22 (0.66–7.43)
Urban/rural residence						<.001	
Urban	103	50	49 ± 5.1	22	75 ± 4.7		1.00
Rural	44	23	45 ± 7.9	8	77 ± 7.3		0.78 (0.33–1.87)
Mixed	124	51	56 ± 4.7	17	84 ± 3.7		0.39 (0.18–0.84)
SES						<.001	

		OS		Prostate Cancer-Specific Survival			
Variable	**No.**	**No. of Events**	**9-Year OS, %**	**No. of Prostate Events**	**9-Year Prostate Cancer-Specific Survival, %**	**Univariate *P***	**Multivariate HR (95% CI)**
Low	60	26	56 ± 6.5	6	87 ± 4.8		1.00
Middle	68	29	55 ± 6.3	12	80 ± 5.3		1.52 (0.50–4.64)
High	143	69	48 ± 4.4	29	76 ± 4.0		1.97 (0.64–6.11)
Comorbidity severity						.31	
None	79	35	55 ± 5.7	13	81 ± 4.8		
Mild	139	61	54 ± 4.4	25	79 ± 3.8		
Moderate/severe	42	20	42 ± 9.0	6	77 ± 8.8		
Unknown	12	9	25 ± 12.5	3	70 ± 14.7		
PSA, ng/mL						<.001	
≤10	98	37	60 ± 5.1	10	88 ± 3.5		1.00
>10	165	85	45 ± 4.1	35	74 ± 4.0		2.38 (0.92–6.17)
Gleason score						<.001	
2–6	50	15	68 ± 6.8	4	91 ± 4.3		1.00
7	114	47	55 ± 4.9	10	88 ± 3.8		2.64 (0.52–13.42)
8–10	102	58	41 ± 5.1	28	67 ± 5.2		11.62 (2.12–63.64)
Treatment group						<.001	
Conservative	74	45	37 ± 5.8	20	67 ± 6.4		4.18 (1.44–12.14)
Surgery	97	27	71 ± 4.8	9	89 ± 3.4		1.00
Radiotherapy	101	53	43 ± 5.3	18	78 ± 4.8		1.59 (0.62–4.12)

Abbreviations: 95% CI, 95% confidence interval; HR, hazard ratio; OS, overall survival; PSA, prostate-specific antigen; SES, socioeconomic status.

[a]OS at 5 years.

[b]Prostate cancer-specific survival at 5 years.

TABLE 3.

Nine-Year OS, Prostate Cancer-Specific Survival, and Multivariate HRs for Men With Metastatic Prostate Cancer

		OS		Prostate Cancer-Specific Survival			
Variable	**No.**	**No. of Events**	**9-Year OS, %**	**No. of Prostate Events**	**9-Year Prostate Cancer-Specific Survival, %**	**Univariate *P***	**Multivariate HR (95% CI)**
Age at diagnosis, y						.24	
<60	58	41	29 ± 6.0	36	35 ± 6.6		
60–69	98	77	17 ± 4.3	67	20 ± 5.0		
≤70	158	142	9 ± 2.4	89	24 ± 4.7		
Race						.079	
White	155	126	15 ± 3.3	89	25 ± 4.7		1.00
Nonwhite	159	134	15 ± 2.9	103	25 ± 4.0		0.93 (0.55–1.58)
Marital status						<.001	
Married	172	139	16 ± 3.0	104	25 ± 4.1		1.00
Not married	142	121	13 ± 3.0	88	26 ± 4.5		1.55 (1.03–2.31)
Insurance						<.001	
Private	108	88	15 ± 3.8	72	20 ± 4.7		1.00
Public	185	160	12 ± 2.5	111	26 ± 4.1		1.07 (0.68–1.66)
None/unknown	21	12	43 ± 10.8	9	52 ± 11.6		0.41 (0.15–1.12)
Registry region						.014	
1	56	40	29 ± 6.0	31	38 ± 7.0		1.00
2	69	62	10 ± 3.6	49	18 ± 5.4		1.21 (0.72–2.02)
3	18	14	22 ± 9.8	10	39 ± 12.2		0.75 (0.29–1.92)
4	65	60	8 ± 3.3	44	17 ± 6.0		1.25 (0.73–2.15)
5	32	23	28 ± 7.9[a]	16	42 ± 9.8[b]		0.71 (0.30–1.66)
6	41	31	27 ± 6.9[a]	22	39 ± 8.6[b]		0.88 (0.41–1.89)
7	33	30	9 ± 5.0	20	18 ± 8.9		1.36 (0.57–3.25)
Urban/rural residence						<.001	
Urban	160	134	15 ± 2.9	101	25 ± 4.0		1.00
Rural	54	44	8 ± 4.9	28	19 ± 10.4		0.76 (0.37–1.54)
Mixed	99	82	15 ± 3.9	63	22 ± 5.2		1.26 (0.80–1.97)
SES						.001	
Low	98	88	10 ± 3.0	66	21 ± 5.1		1.00
Middle	73	59	17 ± 4.7	43	27 ± 6.3		0.77 (0.39–1.51)
High	142	113	17 ± 3.5	83	26 ± 4.8		0.79 (0.44–1.40)
Comorbidity severity						<.001	
None	84	67	17 ± 4.5	54	25 ± 5.7		1.00
Mild	135	115	13 ± 3.1	88	21 ± 4.2		1.04 (0.65–1.68)
Moderate/severe	71	62	11 ± 3.9	37	29 ± 7.9		0.76 (0.42–1.38)
Unknown	24	16	31 ± 10.0	13	39 ± 11.4		0.48 (0.17–1.30)

		OS		Prostate Cancer-Specific Survival			
Variable	**No.**	**No. of Events**	**9-Year OS, %**	**No. of Prostate Events**	**9-Year Prostate Cancer-Specific Survival, %**	**Univariate *P***	**Multivariate HR (95% CI)**
PSA, ng/mL						<.001	
≤10	39	28	23 ± 7.5	20	34 ± 9.4		1.00
>10	262	220	14 ± 2.3	164	24 ± 3.3		1.67 (0.95–2.94)
Gleason score						<.001	
2–6	25	16	33 ± 9.9	7	58 ± 12.9		1.00
7	75	58	21 ± 4.9	43	33 ± 6.4		3.05 (1.13–8.24)
8–10	179	153	12 ± 2.7	119	19 ± 3.8		5.39 (2.13–13.65)
Treatment group						.002	
Conservative	222	185	14 ± 2.5	134	24 ± 3.7		0.81 (0.50–1.30)
Aggressive	92	75	17 ± 4.1	58	27 ± 5.3		1.00

Abbreviations: 95% CI, 95% confidence interval; HR, hazard ratio; OS, overall survival; PSA, prostate-specific antigen; SES, socioeconomic status.

[a]OS at 5 years.

[b]Prostate cancer-specific survival at 5 years.