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Brief Correspondence

Patterns of Care and Treatment Outcomes in Locoregional Squamous Cell Carcinoma of the Prostate

Ryan J. Hutten, Christopher R. Weil, Jonathan D. Tward, Shane Lloyd, Skyler B. Johnson *

Abstract

Primary squamous cell carcinoma is a rare, aggressive disease with historically poor outcomes and no established treatment guidelines. Case reports are limited but describe multiple treatment approaches. Seeking to identify practice patterns and treatment outcomes, we used the US National Cancer Data Base to identify 66 males with locoregional primary squamous cell carcinoma of the prostate treated with surgery, chemotherapy, and/or radiotherapy between 2004 and 2015. Patients were stratified into treatment groups consisting of local therapy alone ($n = 40$; 61%), local therapy and chemotherapy ($n = 13$; 20%), chemotherapy alone ($n = 7$; 11%), and observation ($n = 6$; 9%). Patients with clinical stage T3–T4 disease were significantly more likely to receive combined chemotherapy and local therapy on multivariable analysis. Median survival was 20 mo for patients treated with local therapy alone, 37 mo with local therapy and chemotherapy, and 11 mo with chemotherapy alone. Overall survival was not significantly different between treatment groups. Despite limitations in sample size, these data suggest that addition of chemotherapy to local therapy is a reasonable treatment approach for select patients.

Patient summary: Squamous cell carcinoma of the prostate is an extremely rare disease. Our review of patterns of care using data from the National Cancer Data Base shows inconsistent use of combined local and systemic therapy. The small sample size for this rare disease limits any conclusions regarding survival differences, but the data suggest that a combination approach using chemotherapy in addition to surgery or radiation is a reasonable treatment option for disease confined to the prostate.

Primary squamous cell carcinoma (SCC) of the prostate is a rare, aggressive form of prostate cancer that accounts for less than 0.5–1% of all new prostate cancer diagnoses. The cellular origin of prostate SCC is not well established; however, potential cells of origin include the prostatic urothelium, the periurethral ducts, basal cells within prostatic acini, and columnar prostatic cells [1,2]. Prostate

SCC has a different presentation to the more common adenocarcinoma, often with normal prostate-specific antigen (PSA), osteolytic rather than osteoblastic metastases, younger age at presentation, and lower urinary tract symptoms (LUTS) including urinary retention [1–4]. Because PSA is often low at diagnosis, cases are often incidentally detected during workup and management of LUTS

Table 1 – Sociodemographic and clinical information for the study patients

	LT alone	LT + CTx	CTx alone	Observation	p value[*]
Patients (n)	40	13	7	6	
Median age, yr (interquartile range)	80 (71–83)	65 (51–79)	76 (62–82)	79 (67–86)	0.26
Race (n)					
White	31	7	6	2	0.22
Black	4	0	0	1	
Hispanic	1	0	1	0	
Other	0	1	0	0	
Insurance status (n)					
Private insurance	7	4	2	0	0.12
Government insurance	32	8	5	4	
Uninsured	0	0	0	1	
Unknown	1	1	0	1	
Facility type (n)					
Other	24	6	4	4	0.80
Academic/research	16	7	3	2	
Charlson comorbidity index (n)					
0	34	10	4	6	0.35
≥1	6	3	3	0	
Clinical T stage (n)					
T1–T2	23	1	4	0	0.01
T3–T4	11	10	3	1	
Nodal status (n)					
Node-negative	8	4	0	0	0.15
Node-positive	6	1	3	0	
No nodal evaluation	24	8	4	6	
Grade (n)					
Well differentiated	3	1	0	1	0.26
Moderately differentiated	11	2	1	1	
Poorly differentiated	19	4	3	3	
Undifferentiated	0	2	0	0	
Pretreatment PSA group (n)					
≤2 ng/ml	10	4	5	0	0.14
2–10 ng/ml	7	4	0	2	
10–20 ng/ml	1	0	0	1	
>20 ng/ml	1	0	0	1	

CTx = chemotherapy; LT = local therapy; PSA = prostate-specific antigen.
[*] Analysis of variance for continuous variables and χ^2 test for categorical variables.

[1,2,4]. There are multiple case reports of primary pure prostate SCC in the literature from 1979 to 2019, treated variably with radiotherapy (RT), androgen deprivation therapy (ADT), platinum and non-platinum chemotherapy regimens, and a wide range of surgeries from transurethral resection of the prostate to pelvic exenteration [1–10]. Median survival (MS) has historically been poor, estimated at approximately 14 mo [6]. Selected reports have demonstrated longer survival with multimodal therapy [6]. To date there is no established guideline for an optimal treatment approach, and no population-level analysis has been reported. Here we report outcomes for patients in the US National Cancer Data Base (NCDB) with primary SCC of the prostate.

Patient data were obtained from the NCDB, which captures data for approximately 70% of new cancer diagnoses in the USA. We queried all male patients with SCC of the prostate diagnosed between 2004 and 2015. Patients were excluded if they had prostate adenocarcinoma or adenosquamous carcinoma, metastases at diagnosis, unknown chemotherapy status, or <3 mo of follow-up after diagnosis to minimize immortal-time bias. A flow diagram of the inclusion and exclusion criteria is shown in Supplementary Figure 1.

Binary variables for the use of surgery, RT, ADT, and chemotherapy were collected. We stratified patients into treatment groups as follows: local therapy (surgery or RT); local therapy and chemotherapy; chemotherapy alone; and observation. Covariates for analysis included age, race, insurance status, facility type, Charlson comorbidity index, clinical T and N stage, grade, and pretreatment PSA. Treatment groups, receipt of chemotherapy, and overall survival (OS) were the primary outcomes of interest.

Patient sociodemographic and clinical features in each treatment group were compared using analysis of variance for continuous variables and a χ^2 test for categorical variables. Statistically significant variables from univariable comparisons were incorporated into a multivariable logistic regression model for receipt of chemotherapy and local therapy. Survival was calculated from the date of diagnosis until date of death from any cause, or censored at the date of last follow-up. OS was estimated using the Kaplan-Meier method and survival differences between treatment groups were evaluated using a log-rank test. Data failed to satisfy the assumption of the Cox proportional hazards model. Therefore, a multivariable Cox proportional hazards model for survival was not included. All statistical analyses were performed in STATA/IC-14

Table 2 – Multivariable logistic regression for receipt of local therapy and chemotherapy

	OR (95% CI)	SE	z	p > z
Age	0.90 (0.82–0.99)	0.04	−2.16	0.03
Facility type				
Other	1.00			
Academic/research program	2.66 (0.32–22.3)	2.88	0.90	0.37
Charlson comorbidity index				
0				
≥1	3.30 (0.42–25.7)	3.46	1.14	0.25
Clinical T stage				
T1–T2	1.00			
T3–T4	46.4 (3.31–649)	62.4	2.85	<0.01
Nodal status				
Node-negative	1.00			
Node-positive	0.23 (0.01–7.78)	0.42	−0.81	0.42
No nodal evaluation	8.86 (0.45–174)	13.45	1.44	0.15

OR = odds ratio; CI = confidence interval; SE = standard error.

(StataCorp. 2015. *Stata Statistical Software: Release 14*. College Station, TX: StataCorp LP).

The median follow-up for the entire cohort was 21.9 mo. The median age of the patients included was 77 yr, and a majority of patients were white (85%) and had Medicare/Medicaid insurance (78%; Table 1). The majority of patients were treated at community centers (58%) rather than academic centers (41%). At diagnosis, 53% of the patients had clinical stage T1–T2 and 47% had stage T3–T4 disease. Some 62% of patients had poorly differentiated or undifferentiated SCC. Of the 22 patients with nodal evaluation, ten were node-positive and 12 were node-negative; however 43 (66%) patients did not have nodal evaluation. Of 37 patients with documented pretreatment PSA, most had low PSA (<2 ng/ml; 51%). Of the 66 patients included, 40 (61%) received local therapy only, 13 (19%) received local therapy and chemotherapy, seven (11%) received chemotherapy alone, and six (9%) received no treatment. Of the 20 patients who received chemotherapy, 13 (65%) received multiagent and five (25%) received single-agent chemotherapy; the type of chemotherapy was unknown for two (10%) patients. Of note, only four patients received ADT. Of the 24 patients who underwent RT, 23 received external beam therapy and one received brachytherapy. Patient characteristics by group are shown in Table 1.

The *p* values for univariable analysis of the association of sociodemographic and clinical factors with treatment group are shown in Table 1. Clinical T stage was the only significant predictor of treatment group on univariable analysis. On multivariable analysis (Table 2), significant predictors for receipt of combined-modality chemotherapy and local therapy were age (odds ratio [OR] 0.90, 95% confidence interval [CI] 0.82–0.99) and clinical stage T3–T4 (OR 46.4, 95% CI 3.31–649).

For the entire cohort, the 1- and 2-yr OS was 68% and 50%, respectively, with MS of 22 mo. The 1- and 2-yr OS and MS were 66%, 48%, and 20 mo for local therapy alone, 100%, 75%, and 37 mo for local therapy combined with chemotherapy, and 29%, 29%, and 11 mo for chemotherapy alone, respectively. OS did not significantly differ between the groups (*p* = 0.42).

To date, this is the largest reported analysis cohort for locoregional SCC of the prostate. Literature pertaining to this rare malignancy has largely been confined to case reports and series. Previously reported treatments from single institutions include mono- and multimodal therapy comprising various combinations of surgery, ADT, RT, and chemotherapy, with a small number reporting longer survival with combined-modality therapy. This report reaffirms that there is no widely accepted standard of care for prostate SCC. The standard of care for other pelvic SCCs, including SCC of the cervix, anus, and vagina, are based around combined-modality therapy including chemotherapy, often with platinum-based chemotherapy regimens. Existing case reports support the use of platinum-based chemotherapy regimens (cisplatin/5-fluorouracil, methotrexate/peplomycin/cisplatin, bleomycin/cisplatin, among others) for SCC of the prostate [2–4].

This study has limitations inherent to the extraction of data for a rare disease from a retrospective national hospital-level database. Specific details of the chemotherapeutic regimens and number of cycles are not available. Unfortunately, owing to the rarity of this disease, prospective or randomized trials to determine the optimal treatment strategy are not feasible. However, this report describes the clinicopathologic characteristics, practice patterns, and clinical outcomes of patients with SCC of the prostate. On the basis of this analysis, and in the absence of prospective data, a multimodal treatment approach that includes chemotherapy remains a reasonable treatment option for appropriately selected patients.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.euros.2020.11.008.

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Department of Radiation Oncology, Huntsman Cancer Hospital, University of Utah, Salt Lake City, Utah

*Corresponding author. Department of Radiation Oncology, University of Utah Huntsman Cancer Institute, 1950 Circle of Hope Drive, Salt Lake City, UT 84112, USA. Tel. +1 801 5812396; Fax: +1 801 5852666.
E-mail address: skyler.johnson@hci.utah.edu (S.B. Johnson).