Clinicopathologic and survival patterns among prostate carcinosarcoma patients in the U.S.

An analysis of SEER database

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ABSTRACT

INTRODUCTION: Prostatic carcinosarcoma comprises <1% of all prostate neoplasms. The literature on this disease is limited to a few case studies, primarily due to the rarity of this malignancy. We aimed to investigate the demographic, clinical, and histologic factors, prognosis, and survival of prostatic carcinosarcoma.

METHODS: The Surveillance, Epidemiology, and End Results (SEER) database was used to identify patients with prostatic carcinosarcoma from 2000–2018. Demographic and clinical data, including age, race, sex, tumor grade, stage, tumor size, lymph node status, metastasis, and treatment modalities, were recorded.

RESULTS: Patients with prostatic carcinosarcoma had a median age of 72 years at diagnosis, most cases among White individuals (93%). When reported, the histologic grade comprised moderately differentiated (3.3%), poorly differentiated (56.7%), and undifferentiated/anaplastic (40%) subtypes. In patients with reported data, tumor size varied between 2–5 cm (15.8%) and >5 cm (84.2%). Distant metastasis most commonly occurred in the liver (12.5%) and lung (12.5%), followed by the bone (8.3%). The most common treatment performed was surgery with radiation (32.4%). The five-year overall survival was 11.9%.

CONCLUSIONS: Prostatic carcinosarcoma affects men in the seventh decade of life. Regional and distant tumor stage is considered an indicator of survival. Prostate carcinosarcoma is rare; due to its aggressive nature, a deeper understanding, and an improved personalized therapeutic approach are necessary for improving patient outcomes in this challenging arena of oncology.

INTRODUCTION

Most prostate cancers are epithelial in origin. Prostatic carcinosarcoma (also called sarcomatoid carcinoma of the prostate) is an extremely rare but aggressive malignancy, comprising <1% of all prostate tumors. Prostatic carcinosarcoma is a type of acinar adenocarcinoma and is biphasic, exhibiting epithelial and mesenchymal components.[1-3]

Of note, prostatic carcinosarcoma is difficult to detect, as it can progress in the absence of prostate-specific antigen (PSA) elevation.[3] Patients with prostatic carcinosarcoma often have to coexist with adenocarcinoma of the prostate at the time of diagnosis. This rare malignancy is associated with a higher mortality rate than typical prostate adenocarcinomas. Localized disease is associated with favorable outcomes when definitive therapy (e.g., surgery and/or radiation) is offered. Advanced disease confers poor prognosis.[1-3]

This is a descriptive analysis of prostatic carcinosarcoma aiming to provide one of the largest and most-up-to-date database analyses investigating the demographic, clinical, and pathologic factors affecting the prognosis and survival of patients with this rare disease.

METHODS

The National Cancer Institute initiated the Surveillance, Epidemiology, and End Results (SEER) database in 1973. This database contains approximately 28% of U.S. cancer patients. SEER*Stat software (Version 8.4.1)

was used to collect cancer patient data from 2000–2018. The International Classification of Diseases Version 3 (ICD-I-3) was used to collect diagnostics of this subset using the anatomic codes (C61.9), and histologic code 8980/3. Pathologists from different hospitals/sites/registries who have been consulted for histologic analysis of these slides have submitted these codes to the SEER database. Eighteen registries from SEER were then used to extract data and were exported to Statistical Package for Social Sciences (SPSS) version 28.0.0.0 for descriptive analysis.

Data on demographic and clinical factors were collected for this study. These included age, race, sex, tumor grade, stage, tumor size, lymph node status, metastasis, and treatment modalities. The only sites of distant metastases noted on the SEER database are to the liver, lung, brain, and bone. Patients diagnosed with a "death certificate only," "autopsy only," or those deemed "unknown" were excluded from analyses.

SPSS was used for demographics statistics, Cox proportional hazards model regression and survival analysis. Any p-value <0.05 was considered significant.

RESULTS

In this study, 43 cases of prostatic carcinosarcoma were identified over the study period (2000–2018) using the SEER database.

Demographic data and tumor characteristics

The median patient age at diagnosis was 72 years, while the most common age groups were 70–79 (n=14, 32.6%) and ≥80 (n=13, 30.2%). The youngest patient in this cohort was 28 years old. Regarding race, most patients were White (n=40, 93.0%), followed by Black (n=2, 4.7%), and Asian or Pacific Islanders (n=1, 2.3%).

Tumor grades of 13 (30.2%) cases were unknown, while the remaining 30 (69.8%), were known. No cases were well-differentiated (grade I), one (3.3%) was moderately differentiated (grade II), 17 (56.7%) were poorly differentiated (grade III), and 12 (40.0%) were undifferentiated (grade IV). Among patients with reported tumor size, three (15.8%) were 2.1–5.0 cm, 16 (84.2%) were >5.0 cm, and none were ≤2 cm (Table 1).

Metastasis at the time of diagnosis and treatment characteristics

The SEER staging was divided into four categories: localized, regional, distant, and unstaged/unknown. Localized disease refers to a tumor limited to the organ of origin, and regional metastasis refers to the tumor extending

Table 1. Demographic factors and tumor characteristics

Variable (n=191)	Frequency (%)
Age (years)	
1–19	0 (0.0%)
20–29	1 (2.3%)
30–39	0 (0.0%)
40–49	0 (0.0%)
50–59	7 (16.3%)
60–69	8 (18.6%)
70–79	14 (32.6%)
≥80	13 (30.2%)
Race	
White	40 (93.0%)
Black	2 (4.7%)
Asian or Pacific Islander	1 (2.3%)
Grade (n=43)	
Unknown	13 (30.2%)
Known	30 (69.8%)
Grade where known (n=30)	
Well-differentiated – Grade I	0 (0.0%)
Moderately differentiated – Grade II	1 (3.3%)
Poorly differentiated – Grade III	17 (56.7%)
Undifferentiated/Anaplastic – Grade IV	12 (40.0%)
Variable (n=43)	Frequency (%)
Size	
Unknown	24 (55.8%)
Known	19 (44.2%)
Size when known (n=19)	
<2 cm	0 (0.0%)
2–5 cm	3 (15.8%)
>5 cm	16 (84.2%)
Distant metastasis status	
Unknown	19 (44.2%)
Known	24 (55.8%)
Site of metastasis	Frequency (%, when known)
Bone	2 (8.3%)
Brain	0 (0.0%)
Liver	3 (12.5%)
Lung	3 (12.5%)

to nearby organs and/or regional lymph nodes. The distant stage includes cases where the tumor has spread to other organs. In cases with unknown stages, there is no data available to adequately assign the stage (*https://training.seer.cancer.gov/staging/systems/summary/regionalized.html*, accessed on April 7, 2023).

The tumor stage of seven (16.3%) cases was unknown. Most cases were regional (n=15, 34.9%), followed by distant (n=11, 25.6%), and finally localized (n=10, 23.3%) (Figure 1).

Distant metastases status, whether they had metastases to other organs or not, were known in 24 patients (55.8% of overall cases). When metastasis site was known, the most common sites of metastasis were the liver and lungs (both n=3, 12.5%), followed by the bone (n=2, 8.3%). There were no metastases to the brain.

Of the total cases, 34 (79.1%) had an unknown chemotherapy treatment (any systemic therapy). Most cases in this cohort underwent surgery along with radiation (n=12, 32.4%). This was followed by surgery with chemotherapy (n=11, 29.7%). Three (8.1%) cases had chemotherapy only. There were no cases with radiation only. One (2.7%) patient underwent combination therapy (surgery, radiation, and chemotherapy). Five (13.5%) cases did not undergo any treatment (Figure 2).

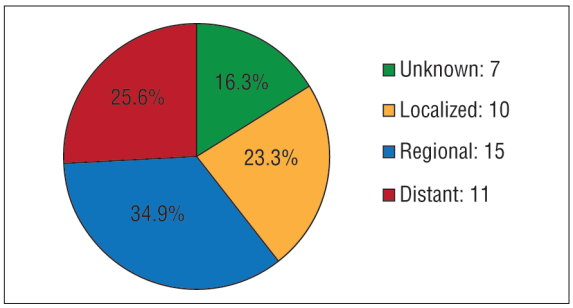

Figure 1. Pie chart of tumor stage.

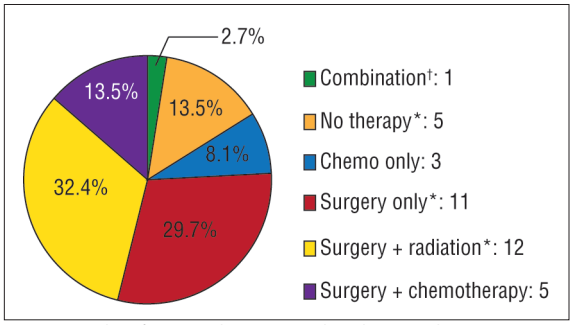

Figure 2. Pie chart of treatment characteristics. *Chemotherapy is unknown. †Combination: Cohort that underwent surgery, radiation, and chemotherapy.

Outcomes and survival analysis by age and race

The overall five-years observed survival was 11.9%, with a 95% confidence interval (CI) of 6.5–17.3. The five-year cause-specific survival (CSS) was 24.8% (95% CI 16.2–33.4) (Figures 3A, 3B).

Age was split into two cohorts: <60 and ≥60 years. Advanced age was not associated with poor survival. Life tables of race could not be performed due to a limited number of cases. Race was not significantly associated with survival.

Life tables of treatment modality could not be performed due to a limited number of cases. There were no significant differences in survival among various treatment modalities.

Survival analysis of clinical factors

Tumor grade and size were not significant predictors of survival; however, stage was significantly associated with survival based on log rank test (p=0.042). Upon univariate analysis, it was revealed that regional stage (hazard ratio [HR] 0.499, 95% CI 0.204–1.208, p=0.127) and distant stage (HR 1.402, 95% CI 0.576–3.413, p=0.456) were not significant predictors of survival.

DISCUSSION

Prostatic carcinosarcoma comprises <1% of all prostate cancers.[3] This study includes 43 patients with prostatic carcinosarcoma. The median age of diagnosis was 72 years, with a higher incidence in men ≥70 years of age (62.8%). This is consistent with previous data, which suggests that prostatic carcinosarcoma is prevalent in the sixth and seventh decades of life.[3,4]

Prostate cancer incidence and mortality rates are higher in African Americans compared to White individuals.[4,5] Given the rarity of prostatic carcinosarcoma, its demographic distribution in race has not been well-established in previous literature. Our analysis demonstrated that the majority of cases were among White patients, with a minority among Black and Asian or Pacific Islander patients.

Existing data demonstrate that larger tumor size is associated with more aggressive disease.[6] Zhou et al reported that in prostate cancer, tumors >10 mm may be more aggressive. In patients where tumor size was known, tumors were either 2–5 cm or >5 cm.

In patients where tumor metastases were known, 34.9% were regional and 25.6% were distant. If metastasis occurred, common locations were the bone, liver, and lung. These findings are consistent with previous literature.[4] Dundore et al reported that in patients with

prostatic carcinosarcoma, all cases exhibited high-grade carcinoma features, with an average Gleason score of 9 (range 7–10), and in all but one patient (out of 21), sarcomas were classified as high-grade. Of the patients with a reported histologic grade in our series, most cases were poorly differentiated and undifferentiated/anaplastic. In our analysis, the overall five-year survival rate was 11.9%. Previous studies report a five-year CSS rate of 41% and a seven-year overall survival of 14%.[4]

Prostate cancer is subclassified based on the 2016 WHO guidelines as glandular neoplasms, urothelial carcinoma, squamous neoplasms, basal cell carcinoma, and neuroendocrine tumors.[2] The histology of prostatic carcinosarcoma is biphasic. The carcinoma portion is usually glandular and acinar, while the sarcoma portion is typically undifferentiated spindle and pleomorphic.[1] In both the sarcomatoid and adenocarcinoma components of prostatic carcinosarcoma, erythroblast transformation-specific (ETS-related) gene (*ERG*) deletion has been identified.[2,3]

Invasive prostatic adenocarcinoma displays abnormal glandular architecture, loss of basal cells, and nuclear atypia with nuclear and nucleolar enlargement. Positive immunostaining for PSA, prostatic acid phosphatase (PAP), protein, and NKX3.1 aid in the diagnosis of metastatic adenocarcinoma.

Intraductal carcinoma demonstrates preservation of basal cells, solid or dense cribriform patterns, and a loose or micropapillary pattern. Intraductal carcinoma is classified as a high-grade and high-stage neoplasm, associated with an aggressive disease course. Ductal adenocarcinoma typically exhibits large glands surrounded by tall pseudostratified columnar cells. Prostatic urothelial carcinoma demonstrates growth within prostatic ducts and acini with solid cylinders.

Urothelial markers, such as thrombomodulin, GATA3, p63, and high molecular weight cytokines can be used to distinguish these cancers from prostatic adenocarcinoma. Squamous and adenosquamous carcinomas of the prostate are remarkably rare, with an average survival of one year. Basal cell carcinomas show adenoid cystic/cribriform patterns of growth. Basal cell carcinoma is associated with Bcl-2 expression and a higher Ki-67 growth index. Neuroendocrine carcinomas of the prostate typically express neuroendocrine markers, including chromogranin, synaptophysin, and CD56.[1,7-14]

In localized prostatic carcinosarcoma, surgery, radiation, or a combination of both revealed a good prognosis and survival. In metastatic prostatic carcinosarcoma, the same options approved for prostate adenocarcinoma are used in widely variable sequences and combinations. While no standard approach exists, endocrine therapy and chemotherapy are the mainstay of systemic treatment. Cytotoxic regimens are derived from those employed in prostate cancer (docetaxel), small cell neuroendocrine carcinoma (carboplatin-etoposide), and sarcoma (doxorubicin), reflecting a lack of well-established protocols. Advanced prostatic carcinosarcoma has a poor prognosis and poor response to therapy.[3,4]

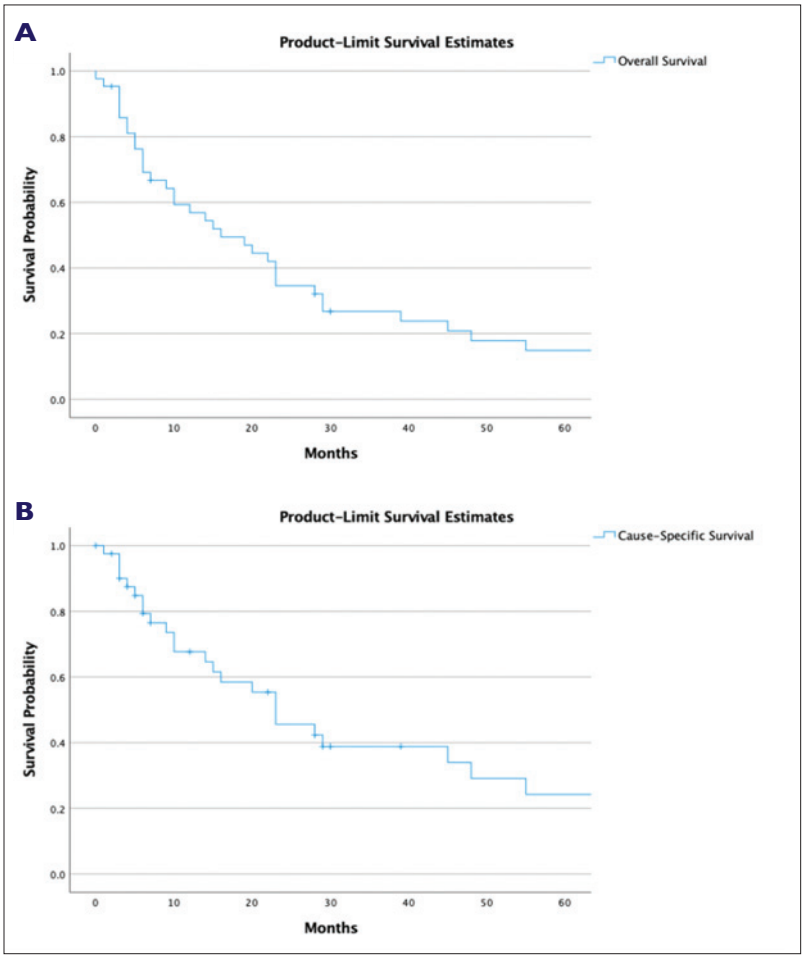

Figure 3. (A) Overall and (B) cause-specific survival.

Limitations

Limitations of our study are related to missing data on tumor grade, size, invasion of lymph nodes or local tissue, presence of distant metastasis, and specific treatments and survival outcomes. The database also did not contain information on mutation profiles, sporadic vs. familial cases, types of chemotherapy used, and granularity on outcomes. Due to the rarity of the disease,

a limited number of patients were assessed. This may lead to decreased power in univariate and multivariate analysis secondary to the limited number of cases in our study.

CONCLUSIONS

Prostatic carcinosarcoma comprises <1% of all prostate neoplasms. Our study is one of the largest to date on this topic. Age, race, tumor size, and tumor grade were not significant predictors of survival, while regional and distant staging was associated with poor survival.

COMPETING INTERESTS: The authors do not report any competing personal or financial interests related to this work.

This paper has been peer reviewed.

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