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Epidemiology and survival outcome of adult kidney, bladder, and prostate rhabdomyosarcoma: A SEER database analysis

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Abstract

Rhabdomyosarcoma (RMS) is rare in adulthood, accounting for 2%–5% of adult soft tissue tumors, and less than 20% occur in genitourinary organs. Given its rarity, survival data on adult kidney, bladder, and prostate RMSs is limited. In this population-based analysis, we performed an analysis of all adult RMS cases reported in Surveillance, Epidemiology, and End Results (SEER) database to understand prognostic factors among kidney, bladder, and prostate RMS. A query of the SEER database was performed from 1973 to 2016 for patients >18 of age with RMS. The final cohort consisted of 14 kidney, 35 bladder, and 21 prostate RMS cases in the adult population. Demographic, treatment, and survival data were obtained. Analysis was performed using Fisher's exact test, survival analysis, and model. The median (range) age of diagnosis for adult bladder RMS was 65 years old (19–84) compared to 52.5 (28–68) and 42 (19–87) for kidney and prostate ($p = 0.007$). About 78.6% of patients underwent surgical intervention. Five-year overall survival (OS) for adult kidney, bladder, and prostate RMS are 17.1% (2.9–41.6%), 22.2% (9.4–38.4%), and 33.0 (12.8–55.0%), respectively. OS was not statistically associated with primary site ($p = 0.209$). On multivariable analysis, compared to adult bladder RMS, kidney RMS had a higher incidence of mortality (HR: 2.16, 95% CI 1.03–4.53, $p = 0.041$). Incidence of mortality from prostate RMS was not significantly different from bladder RMS (HR: 0.70, 95% CI 0.30–1.65, $p = 0.411$). Extent of disease (HR: 5.17, 95% CI 2.09–12.79, $p < 0.001$) and older age (HR 1.03, 95% CI 1.01–1.04, $p = 0.002$) were adverse prognostic factors for OS. Overall survival at 5 years for adult kidney, bladder, and prostate RMS is poor. Localized disease and younger age are prognostic factors for improved outcomes in adult RMS. Hence, early diagnosis and intervention appear paramount to improved survival for this rare malignancy in adulthood.

Keywords

Rhabdomyosarcoma, kidney, bladder, prostate, survival outcome, epidemiology, incidence, Surveillance, Epidemiology, and End Results (SEER)

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Introduction

Soft tissue tumors are a heterogeneous collection of mesenchymal masses that occur throughout the lifespan. Benign sarcomas, including lipoma, fibroma, and leiomyoma, occur more commonly than malignancy sarcomas.[1] In the genitourinary tract, leiomyosarcomas and liposarcomas are the most prominent histological subtypes.[2] A prevalent tumor of childhood and adolescence, rhabdomyosarcoma

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(RMS) is exceedingly rare in adulthood, accounting for 2%–5% of adult soft tissue tumors.[3] Of the adult reports of RMS, less than 20% occur in the genitourinary organs, a higher rate than in the pediatric RMS cases.[4] With multimodality treatment, survival has greatly improved for pediatric RMS with noted cure rates as high as 70%–90%.[5–7] In contrast, overall survival rate for adult RMS is 27%, significantly lower than pediatric RMS, illustrating the disparity in treatment advances and disease pathogenesis between these age groups.[4]

Current understanding and recommendations for adult-onset urinary tract RMS is based on the paucity of case reports and series in literature. Of adult sarcomas, RMS has the poorest prognosis and primary sarcomas of the kidney and prostate are prognostic of worse outcomes.[8] Frequently, kidney, bladder, and prostate RMS are diagnosed in late stage in adulthood because of nonspecific symptoms and rapid pathogenesis.[9,10] Due to the rarity of adult kidney, bladder, and prostate RMS, information regarding the epidemiology and survival outcomes of these disease sites are limited in literature. Furthermore, with significantly improved outcomes in pediatric RMS, more investigation is necessary to better characterize urinary tract RMS. In this population-based study, we performed an analysis of all adult RMS cases reported in the Surveillance, Epidemiology, and End Results (SEER) databased to understand survival differences between kidney, bladder, and prostate RMS.

Materials and methods

Surveillance, Epidemiology, and End Results Database

The Surveillance, Epidemiology, and End Results (SEER) is a United States population database containing information on cancer incidence and survival (ww.seer.cancer.gov). This cancer registry collects and publishes cancer incidence and survival data from 20 population-based cancer registries encompassing approximately 34.6% of the United States population. The database was initially developed on January 1, 1973 in the states of Connecticut, Iowa, New Mexico, Utah, Hawaii, and metropolitan areas of Detroit and San Francisco-Oakland. In the years following, the database was expanded to include New York, Kentucky, Louisiana, and Southern California. The SEER database contains several demographic and clinicopathologic parameters, including race/ethnicity, age of cancer diagnosis, primary tumor site, tumor morphology, stage at diagnosis, treatment course, and survival status.[11] This comprehensive registry serves as a valuable tool to perform descriptive analyses of rare malignancies.[12]

Data extraction algorithm

The SEER program was utilized to identify all reported cases of primary kidney, bladder, and prostate diagnosed between 1973 and 2016. The inclusion criteria were set with the following parameters: AYA Site Recode/WHO 2008 for rhabdomyosarcoma and anatomic primary sites of kidney (C64.9), bladder (C67.0–67.9), and prostate (61.9). This generated a case list of 245 patients. We excluded patients under the age of 19. We used the SEER summary staging to analyze malignant progression. Specifically, local disease represented tumor presence without extension beyond the designated organ, and regional disease signified tumor extension to adjacent organs and/or regional lymph nodes. Individuals with distant metastasis were classified as having distant disease.

Statistical analysis

Patient characteristics were compared via a descriptive statistical analysis. Patient numbers and percentages were provided for categorical characteristics. Median values and ranges were calculated for continuous characteristics. Fisher's exact test and Chi-square test were conducted to calculate p-values for categorical variables, while Kruskal-Wallis test was employed to calculate p-values for continuous variables. The probabilities of overall survival were estimated via the Kaplan-Meier method. The differences between cohorts were analyzed using a log-rank test. The median follow-up time were calculated with a reverse Kaplan-Meier method, and the differences between groups were assessed via a log-rank test. Multivariable Cox proportional hazards model was performed using a stepwise model selection procedure to estimate adjusted hazard ratios for factors associated with overall survival. All covariates were first included in the univariable analysis, and only covariates with p-value < 0.1 were entered in the multivariable Cox model, and a p-value < 0.05 was considered to indicate statistical significance.

Results

Patient characteristics

From 1973 to 2016, 70 adult patients were extracted from the SEER program database: 14 kidney, 35 bladder, and 21 prostate RMS. Table 1 outlines the patient characteristics for kidney, bladder, and prostate RMS. About 50% (7) of kidney RMS were males compared to 68.6% (24) of bladder RMS. The majority of cases were reported in white, non-Hispanic patients. The median (range) age of diagnosis for adult bladder RMS was 65 (19–84) compared to 52.5 (28–68) and 42 (19–87) for kidney and prostate ($p = 0.007$). Four kidney (28.6%), eight bladder (22.9%), and three (14.3%) prostate cases were reported with localized disease at presentation. Five kidney (35.7%), 14 bladder (40.0%), and three (14.3%) prostate cases were reported with regional disease at presentation. Four kidney (28.6%), nine bladder (25.7%), and six (28.6%) prostate cases were reported with distant disease at presentation. There was no

Table 1. Patient characteristics for bladder, kidney, and prostate rhabdomyosarcoma.

Characteristic	Urinary				*p*-value
	Overall (*n* = 70)	Bladder (*n* = 35)	Kidney (*n* = 14)	Prostate (*n* = 21)	
Sex, *n* (%)					
Female	18 (25.7)	11 (31.4)	7 (50.0)	0 (0.0)	<0.001
Male	52 (74.3)	24 (68.6)	7 (50.0)	21 (100.0)	
Race, *n* (%)					
White	62 (88.6)	32 (91.4)	12 (85.7)	18 (85.7)	0.553
Black	2 (2.9)	1 (2.9)	1 (7.1)	0 (0.0)	
Other	6 (8.6)	2 (5.7)	1 (7.1)	3 (14.3)	
Ethnicity, *n* (%)					
Hispanic	12 (17.1)	5 (14.3)	4 (28.6)	3 (14.3)	0.415
Non-hispanic	58 (82.9)	30 (85.7)	10 (71.4)	18 (85.7)	
Extent of disease, *n* (%)					
Distant	19 (27.1)	9 (25.7)	4 (28.6)	6 (28.6)	0.069
Regional	22 (31.4)	14 (40.0)	5 (35.7)	3 (14.3)	
Localized	15 (21.4)	8 (22.9)	4 (28.6)	3 (14.3)	
Unstaged	14 (20.0)	4 (11.4)	1 (7.1)	9 (42.9)	
Surgery, *n* (%)					
Yes	55 (78.6)	30 (85.7)	11 (78.6)	14 (66.7)	0.218
No	15 (21.4)	5 (14.3)	3 (21.4)	7 (33.3)	
Radiation, *n* (%)					
Yes	17 (24.3)	6 (17.1)	3 (21.4)	8 (38.1)	0.233
No	53 (75.7)	29 (82.9)	11 (78.6)	13 (61.9)	
Chemotherapy, *n* (%)					
Yes	33 (47.1)	13 (37.1)	5 (35.7)	15 (71.4)	0.032
No	37 (52.9)	22 (62.9)	9 (64.3)	6 (28.6)	
Age					
Median (Range)	55 (19–87)	65 (19–84)	52.5 (28–68)	42 (19–87)	0.007

significant difference in extent of disease upon presentation for these various RMS diagnoses ($p = 0.069$). The majority of patients (78.6%) underwent surgical intervention. Of the cohort, only 17 patients (five kidney, three bladder, and eight prostate) pursued radiation therapy. For bladder and kidney RMS, 37.1% and 35.7% of patients, respectively completed chemotherapy treatment compared to 71.4% of prostate RMS patients ($p = 0.032$).

Outcome data

One-year and 5-year overall survival (OS) for adult kidney, bladder, and prostate RMS are 34.3% (95% CI: 11.6–58.7%) and 17.1% (2.9–41.6%), 50.9% (33.3–66.0%) and 22.2% (9.4–38.4%), and 76.2% (51.9–89.3%) and 33.0 (12.8–55.0%), respectively. Table 2 and Figure 1 demonstrate the Kaplan-Meier estimates for overall survival for adult kidney, bladder, and prostate RMS. Overall survival is not statistically different for adult kidney, bladder, and prostate RMS (Table 2; $p = 0.209$).

Table 3 shows univariate and multivariate analyses for overall survival for adult kidney, bladder, and prostate RMS. In univariate analysis, primary site for adult RMS was not associated with worse outcomes (kidney vs bladder: HR 1.3, 95% CI 0.69–2.65, $p = 0.380$; prostate vs bladder: HR 0.68, 95% CI 0.35–1.34, $p = 0.70$). In multivariable analysis, compared to adult bladder RMS, kidney RMS tended to have a higher incidence of mortality (Table 3; HR: 2.16, 95% CI 1.03–4.53, $p = 0.041$). Prostate RMS had a lower risk of death compared to bladder RMS (Table 3; HR: 0.70, 95% CI 0.30–1.65, $p = 0.411$). Extent of disease was observed as an adverse prognostic factor for OS, with distant stage associated with a higher incidence of death compared to localized (Table 3; HR: 5.17, 95% CI 2.09–12.79, $p < 0.001$). In regard to therapeutic treatment, no surgical intervention was associated with worse survival compared to these with intervention (Table 3; HR 2.06, 95% CI 1.06–3.99, $p = 0.032$). Patients with no chemotherapy intervention were noted to be an adverse prognostic factor for OS (Table 3; HR: 1.78, 95% CI 1.02–3.10, $p = 0.042$).

Discussion

Adult primary RMS of the kidney, bladder, and prostate are exceedingly rare. The paucity of these cases limits our understanding of adult RMS on a population level. A few institutions have published single-centered experiences with primary soft tissue tumors in the genitourinary tract,

Table 2. Kaplan-Meier survival estimates for bladder, kidney, and prostate rhabdomyosarcoma.

KM estimates	Urinary ($n=70$)						
	Bladder ($n=35$)		Kidney ($n=14$)		Prostate ($n=21$)		p-value
	%	95% CI	%	95% CI	%	95% CI	
Overall survival							
1 year	50.9	33.3–66.0	34.3	11.6–58.7	76.2	51.9–89.3	0.209
2 years	37.0	20.8–53.3	34.3	11.6–58.7	41.3	20.1–61.4	
5 years	22.2	9.4–38.4	17.1	2.9–41.6	33.0	12.8–55.0	
10 years	22.2	9.4–38.4	8.6	0.5–31.5	33.0	12.8–55.0	
Median follow-up, months	113		–		83		0.535

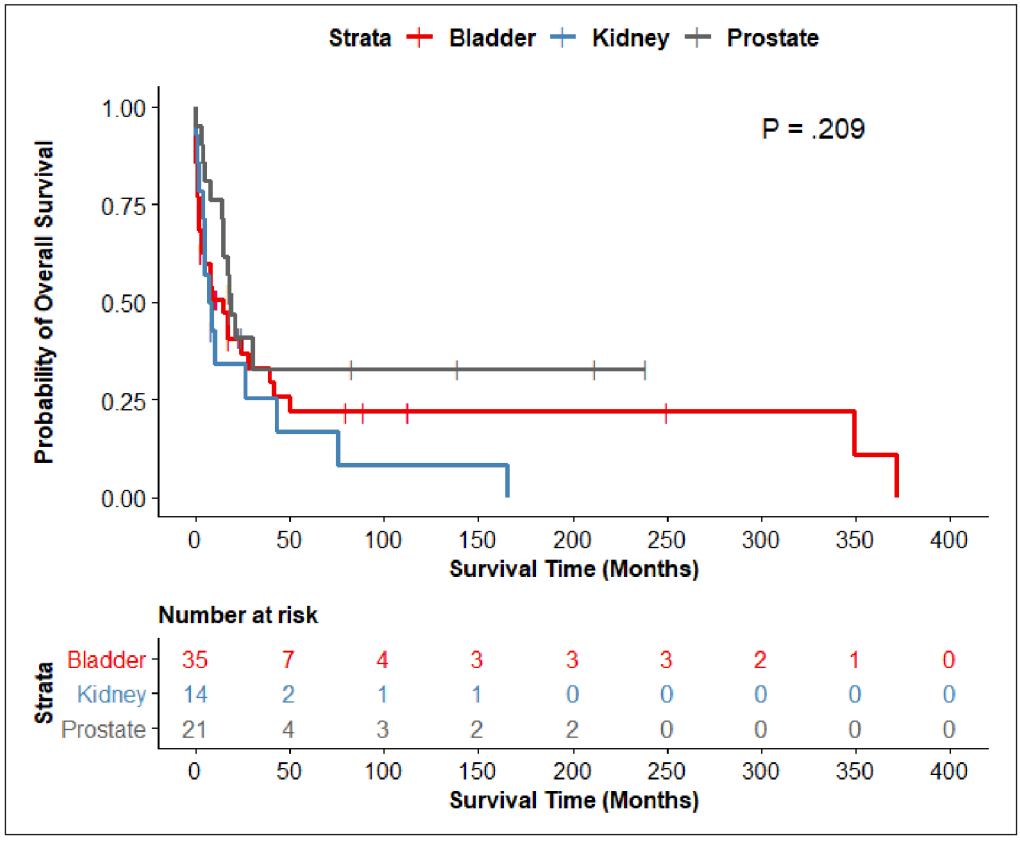

Figure 1. Overall survival for bladder, kidney, and prostate rhabdomyosarcoma.

but these analyses are severely underrepresented by RMS subtypes. The study by Dotan et al. Shared their institutional experience with urologic sarcomas of which only 13 RMS cases were reported in the kidney, bladder, and prostate.[8] In a larger series by Wang et al., only 17 of 119 sarcomas cases were attributed to RMS.[2] Hence, a major limitation of these previous studies is the generalization of survival data to adult urinary tract RMS. In this study, we determined the OS for adult kidney, bladder, and prostate RMS and prognostic factors for OS. To our knowledge, this is the largest sarcoma study to purely analyze adult urinary tract RMS and report OS rates and prognostic data for this rare malignancy.

Using the SEER program database, we identified 70 reports of primary adult RMS of the kidney, bladder, and prostate. Bladder RMS tends to present later in adulthood (median age of 65) compared to kidney and prostate (52.5 and 42, respectively). Although not statistically significant, a larger portion of bladder RMS are diagnosed in regional or distance disease compared to prostate and kidney RMS. It may be possible that presenting symptoms occur later in life and subsequently, diagnosed in later staged disease. Compared to pediatric RMS, prognosis is significantly impacted by age with worse outcomes for aged and geriatric patients.[4] In concordance, our univariate and multivariate analysis also suggested that age is a prognostic factor

Table 3. Univariate and multivariate cox model for overall survival.

Organ system: urinary ($n = 70$)						
Variable	Univariable analysis			Multivariable analysis		
	HR	95% CI	*p*-value	HR	95% CI	*p*-value
Organ						
Kidney versus bladder	1.35	0.69–2.65	0.380	2.16	1.03–4.53	0.041
Prostate versus bladder	0.68	0.35–1.34	0.268	0.70	0.30–1.65	0.411
Age	1.03	1.01–1.04	<0.001	1.03	1.01–1.04	0.002
Extent of disease						
Distant versus localized	3.38	1.46–7.82	0.005	5.17	2.09–12.79	<0.001
Regional versus localized	1.50	0.66–3.43	0.337	1.59	0.66–3.80	0.300
Unstaged versus localized	2.09	0.84–5.20	0.111	3.29	1.13–9.63	0.030
Sex						
Female versus male	0.91	0.49–1.72	0.778			
Chemotherapy						
No versus yes	1.78	1.02–3.10	0.042			
Surgery						
No versus yes	2.06	1.06–3.99	0.032			
Ethnicity						
Hispanic versus non-hispanic	1.67	0.80–3.49	0.175			
Race						
Black versus white	3.23	0.76–13.68	0.111			
Other versus white	0.31	0.08–1.28	0.104			
Radiation						
No versus yes	1.81	0.93–3.54	0.081			

for OS for adult kidney, bladder, and prostate RMS. Interestingly, in regard to tumor invasion, metastasis, regional lymph node involvement, and histologic subtype, age at diagnosis is an independent predictor of outcome for all RMS.[3,13]

Five-year OS for adult kidney, bladder, and prostate RMS are 17.1% (2.9%–41.6%), 22.2% (9.4%–38.4%), and 33.0 (12.8%–55.0%), respectively. Generally, adults diagnosed with renal RMS tend to have a higher rate of mortality compared to bladder and prostate. This may be due to the cellular origins of primary renal RMS. In literature, it is theorized that these high-grade neoplasms differentiate from underlying renal cancers such as sarcomatoid renal cell carcinoma, metastatic carcinoma, metastatic melanoma, and rhabdoid tumors.[14] Because of its rarity, limited data is available to better understand the pathogenesis of this aggressive RMS. Moreover, poor outcome for these sarcomas is most likely multifactorial, including biological differences in adult and pediatric RMS and ineffective treatment modalities. In a study by Bergamaschi et al, adaptation of pediatric-type strategies of RMS were relatively effective for adult RMS but was not enough to achieve the results noted in children. Furthermore, they noted that issues in compliance and the aggressive biology of adult RMS may play a role in varying outcome based on age groups.[15]

On univariate analysis, we demonstrate that extent of disease is associated with OS for adult urinary tract RMS. Overall, 27.1% and 31.4% of adult urinary tract RMS in our cohort presented with distant and regional disease, respectively. Interestingly, the proportion of patients diagnosed with localized, regional, and distance disease at presentation is similar to all pediatric RMS suggesting that adults may not present with later stage urinary tract RMS.[4] This fact may provide insight about the importance of proper clinical and surgical management for adult RMS cases. It appears that adult kidney, bladder, and prostate RMS do not present more frequently with locally advanced or metastatic disease compared to pediatric counterparts, suggesting that other factors in the clinical course may play a role in poor outcomes.

Based on the Children's Oncology Group protocol, a combination of surgery, chemotherapy, and radiotherapy is utilized to manage pediatric RMS and frequently, adopted by oncology to treat adult RMS.[16] In our cohort, surgical intervention and chemotherapy improved OS for adult kidney, bladder, and prostate RMS. Of the 70 patients, 78.6% underwent surgical management for primary tumor. Significantly more adults with prostate RMS completed chemotherapy compared to those with kidney or bladder diseases (74.1% vs 37.1% and 35.7%, respectively). In literature, there is a paucity of successful reports of neoadjuvant chemotherapy and adjuvant radiotherapy for adult RMS.[17,18] From 1989 to 2009, Wang et al. published a case series of 25 adult soft tissue prostate tumors (six were RMS)

demonstrating that chemotherapy did not improve overall survival.[19] Given our findings, it is plausible that specific subtypes of soft tissue tumors in the prostate, like RMS, may be responsive to chemotherapy. Furthermore, it may be possible that prostate RMS presents with inoperable or significant tumor burden, thus requiring further medical management compared to renal and bladder. Nevertheless, coordination of care with pediatric and adult oncologists is crucial to develop specific clinical and biological research to improve treatment options for adult urinary tract RMS.

There are several limitations to this study, including the inherent bias with retrospective studies. Due to the low incidence rates of adult RMS, the sample size of this study was relatively small. Complete data regarding tumor size, histologic characteristics and use of systemic therapy was not available on SEER database. Previous papers have noted about the concern about heterogeneous cohorts as a limitation of soft tissue tumor studies.[15] However, by controlling for adult and organic specific RMS, we present data that is more homogenous and population specific. In all, this represents the largest population-based and survival study available on kidney, bladder, and prostate RMS in adulthood.

Conclusion

Overall survival for adult kidney, bladder, and prostate RMS is poor. Adult cases of kidney RMS generally have a worse OS compared to bladder and prostate. Age of diagnosis and extent of disease are associated with worse outcomes. Surgical intervention and chemotherapy were shown to have prognostic value for OS. Hence, early diagnosis and intervention are paramount to improve survival for this rare malignancy in adulthood.

Author contributions

SRP collected data, drafted the manuscript, and researched the current literature. CPH assisted with data collection. JH performed statistical analysis. NEA drafted the manuscript. JTK, KEG, PEC, and SBR supervised the project and provided critical review on several manuscript drafts.

Declaration of conflicting interest

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Ethical approval

Ethical approval for use of the SEER database was obtained from the SEER Database Group.

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