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UROLOGICAL ONCOLOGY

Contemporary analysis of epididymal tumors using a national database

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Introduction Epididymal tumors are rare malignancies with sparse research available to guide recommendations. We sought to characterize malignant epididymal tumors in the United States using population level data.

Material and methods The Surveillance, Epidemiology, and End-Results database was queried for patients diagnosed with malignant epididymal tumors between 1975–2016. International classification of disease for oncology code C63.0 was used to identify population with disease of interest. Primary objective was to characterize patient demographics, disease characteristics, and management. Secondary objectives included overall and cancer-specific survival (CSS) utilizing Kaplan-Meier (KM) analysis.

Results A total of 66 cases of malignant epididymal tumors were identified during the study period. The cohort was largely white (84.8%), with a mean age of diagnosis of 46.9 years old. The predominant histology consisted of rhabdomyosarcoma 26%, leiomyosarcoma 23%, liposarcoma 17%, adenocarcinoma 9%, and malignant fibrous histiocytoma 5%. During histopathological assessment, 21.1% of tumors were classified as high-grade while 71.2% exhibited sarcomatoid elements. Majority of patients presented with localized disease (68.2%), whereas regional (18.2%) and distant (13.2%) disease was less frequently discovered. All patients were diagnosed by surgical therapy consisting of radical epididymectomy (39.4%), partial epididymectomy (27.3%) or 'unknown surgery' (33.3%). Meanwhile, 15.2% and 34.8% received radiation and chemotherapy, respectively. KM analysis revealed an 84.9% CSS at 5-years. Over 60% of documented cases have arisen since 2000, with 3.0% of the cohort diagnosed in 2016, increased from 1.5% of the diagnoses in 1975.

Conclusions Malignant epididymal tumors are exceedingly rare and typically present with localized disease. Surgical excision is associated with an estimated 85% CSS at 5-years.

Key Words: epididymis ‹› sarcoma ‹› clinical practice pattern ‹› survival

INTRODUCTION

Epididymal tumors, both benign and malignant, are rare neoplasms that constitute a larger group of paratesticular tumors. With early descriptions by Evans in 1943 and Golden and Ash in 1945, epididymal tumors have since made up 5% of all intrascrotal tumors and 0.03% of all male cancers [1–4]. Anatomically, epididymal tumors arise within the paratesticular region inside the scrotum, which is embryologically derived from a heterogeneous mixture of epithelium and mesothelium that also gives rise to tissues of the spermatic cord, testicular tunics, and vestigial remnants [4]. The etiology of epididymal tumors remains unclear due to its limited prevalence; however, it has been postulated that this is a reflection of the antitumorigenic environment within the epididymis optimized for spermatozoa development [3].

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Often presenting with scrotal swelling or mass formation, malignant epididymal tumor distinction amongst testicular and other paratesticular neoplasms is difficult pre-operatively. This necessitates appropriate diagnosis to occur intra or post-operatively [5]. Consequently, treatment of epididymal neoplasms has not been standardized, and is limited to en bloc excision via radical orchiectomy or epididymectomy once intraoperative findings suggest malignancy [6]. If there are indications of metastasis, it is further recommended to undergo retroperitoneal lymph node dissection, although this data is based on very limited series [7]. Defined by case reports and literature reviews, the current scope of knowledge on epididymal tumors is narrow [2, 8–14]. To bridge this gap, we queried the Surveillance, Epidemiology, and End Results (SEER) database to evaluate and characterize demographics, disease characteristics, and management for patients with malignant epididymal tumors diagnosed between 1975–2016.

MATERIAL AND METHODS

The SEER Program provides information on cancer statistics and is supported by the Surveillance Research Program in the National Cancer Institute's Division of Cancer Control and Population Sciences. The chosen dataset spans 18 regions across the United States and represents 27.8% of the population. [15] We queried this dataset for patients with cancer located at the epididymis as evidence by International Classification of Disease (ICD) code 63.0. We identified 66 patients who met our inclusion criteria. Patients in whom this was not their first malignancy were excluded. Also, patients without proper ICD classification confirming the tumor is of epididymal origin, patients with incomplete data, and those not included in the SEER database were excluded. Patients with testicular or other local tumors involving the epididymis were not considered as they would have a different ICD code for primary site. Demographic and clinical variables collected from the population of interest included patient age, race, marital status, and SEER stage. SEER stage was categorized as localized, regional or distant. Tumor characteristics and treatment outcomes included histologic type, tumor grade, presence of sarcomatoid variant, surgical intervention, administration of radiation and/or chemotherapy, length of follow-up, cancer-specific survival (CSS) and overall survival (OS).

Descriptive analysis was performed for the entire cohort and categorized by histology and survival outcomes. Kaplan-Meier analysis was performed for cancer specific and overall survival outcome. We utilized SPSS v24 (New York, United States) for all analyses. Our primary outcome was a descriptive analysis with a secondary outcomes of overall and cancer-specific survival.

RESULTS

A total of 66 cases of malignant epididymal tumors were identified during the 1975–2016 study period. Patient demographics including age, race, insurance type, marital status, and SEER stage are described in Table 1. The cohort consisted predominantly of Caucasians (84.8%) with a mean age of diagnosis of 46.9 years of age. Extent of disease as classified by the SEER staging system demonstrated 68.2% of tumors to be localized, 18.2% regional, and 13.6% distant.

Table 1. *Patient demographics and clinical tumor characteristics*

Variable	All (n = 66)
Mean age (years ±SD)	46.9 ±21.6
Race	
White	56 (84.8%)
Black	4 (6.1%)
Other	6 (9.1%)
Insurance	
Unknown	44 (66.7%)
Insured	20 (30.3%)
Medicaid	2 (3.0%)
Marital status	
Single	20 (30.3%)
Married	41 (62.1%)
Widowed	1 (1.5%)
Divorced	2 (3.0%)
Unknown	2 (3.0%)
SEER stage	
Localized	45 (68.2%)
Regional	12 (18.2%)
Distant	9 (13.6%)
High-grade	14 (21.2%)
Sarcomatoid variant	47 (71.2%)
Surgery type	
Unknown	22 (33.3%)
Partial epididymectomy	18 (27.3%)
Radical epididymectomy	26 (39.4%)
Radiation	10 (15.2%)
Chemotherapy	23 (34.8%)
Length of follow-up (months ±SD)	128.6 ±93.2
Death	
Cancer-specific	23 (34.8%)
Adenocarcinoma	8 (12.1%)
Leiomyosarcoma	1 (12.5%)
Liposarcoma	2 (25.0%)
Malignant fibrous histiocytoma	1 (12.5%)
Sex cord gonadal stromal	1 (12.5%)
Unclassified	1 (12.5%)

SEER – Surveillance, Epidemiology, and End-Results

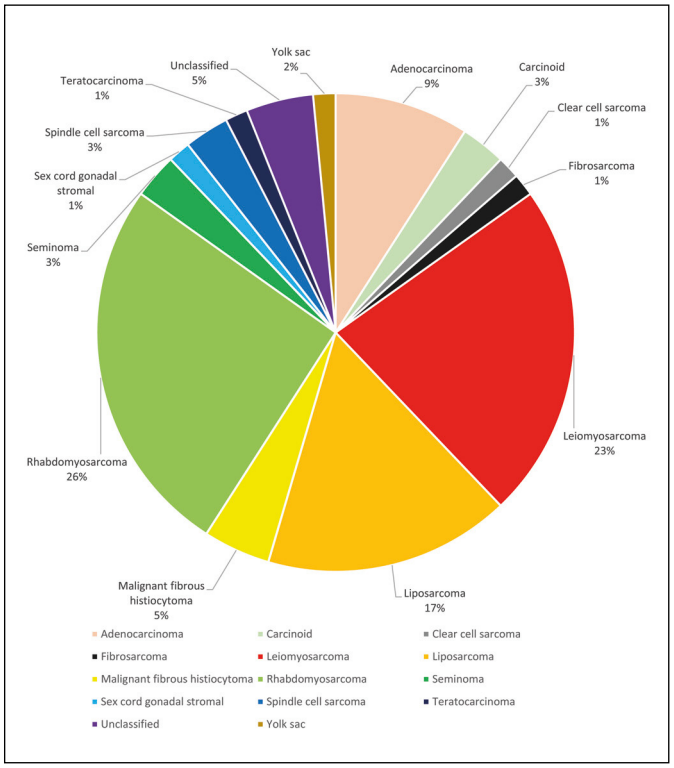

Figure 1. *Histology of epididymal tumors.*

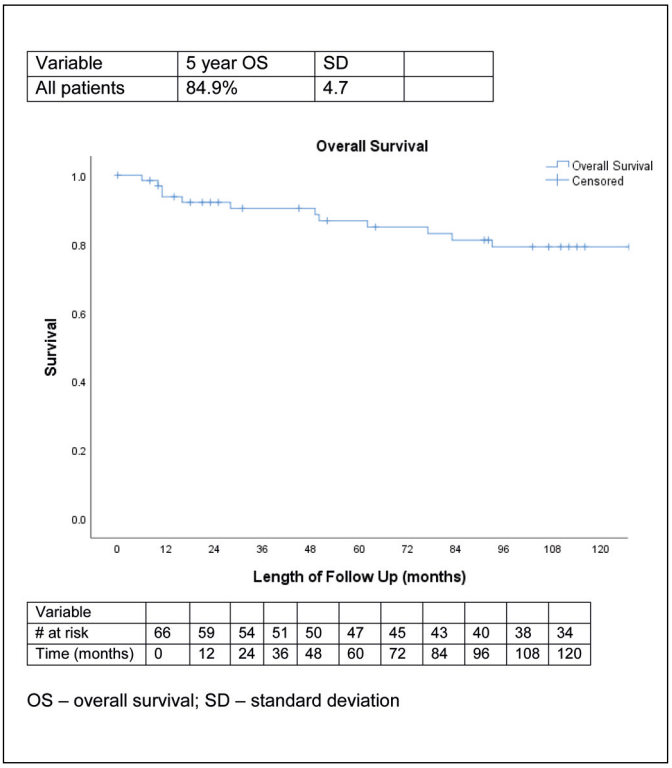

Figure 2. *Kaplan-Meier curve for overall survival.*

Peri and post-operative outcomes including histological sub-type, surgery type, post-operative radiation, post-operative chemotherapy, length of follow-up, and death are also reported in Table 1. Therapy for epididymal cancer in this cohort consisted of radical epididymectomy (39.4%), unknown surgery (33.3%), and partial epididymectomy (27.3%). Histologically, epididymal tumor subtypes consisted of sarcomatoid variants including rhabdomyosarcoma (25.8%), leiomyosarcoma (22.7%), liposarcoma (16.7%), and others (34.8%) as demonstrated in Figure 1. The other categories include adenocarcinoma, carcinoid, clear cell carcinoma, fibrosarcoma, malignant fibrous histiocytoma, seminoma, sex cord gonadal stromal, spindle cell sarcoma, teratocarcinoma, unclassified, and yolk sac histological subtypes. Histopathologic assessment determined 21.1% of tumors were high-grade, with 71.2% displaying sarcomatoid features. Post-operatively, 10 patients (15.2%) and 23 patients (34.8%) received radiation or chemotherapy, respectively.

Kaplan-Meier survival analyses are summarized in Figures 2 and 3. In the cases identified, 43 patients (65%) survived by the end of the studied time period. The estimated 5-year overall survival (OS) and cancer-specific survival (CSS) rate was 84.9% and 91% respectively. Mean follow-up for all patients was 128.6 months. Of patients suffering cancer-specific

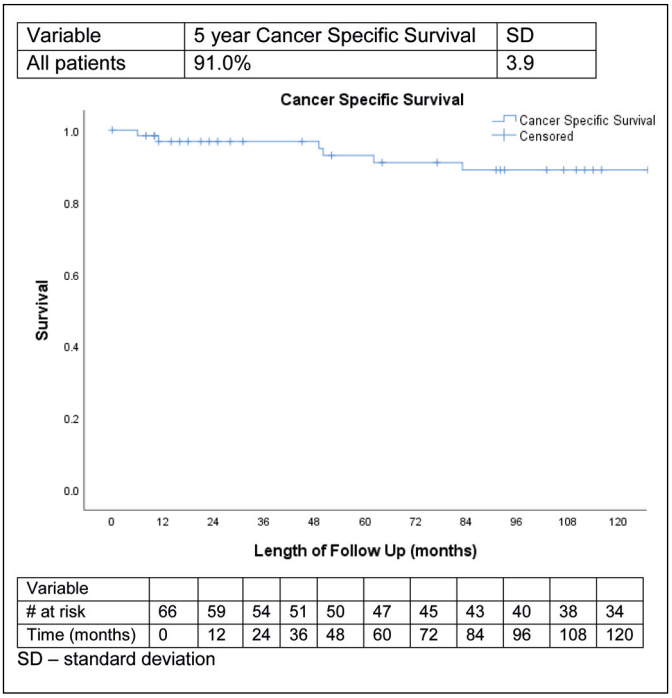

Figure 3. *Kaplan-Meier curve for cancer-specific survival.*

death, 25% had leiomyosarcoma, 25% had an unclassified histology, and the remaining 50% had adenocarcinoma, liposarcoma, sex cord stromal tumor,

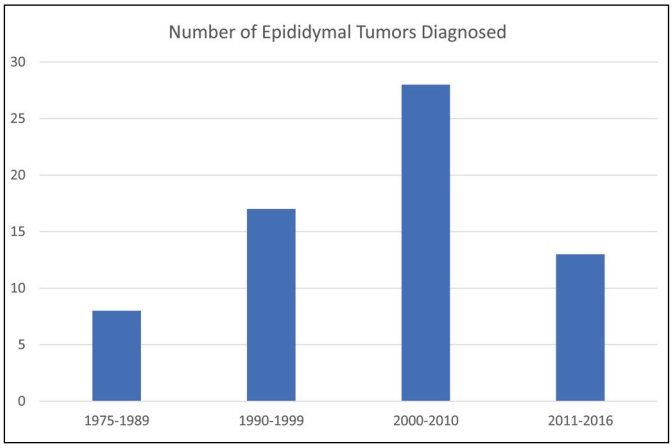

Figure 4. *Number of epididymal tumors diagnosed.*

or malignant fibrous histiocytoma. The diagnosis and time association is presented in Figure 4.

DISCUSSION

Comprising 5% of all intrascrotal malignancies and 0.03% of all male cancers, epididymal cancer is a rare paratesticular malignancy that is embryologically derived from the epithelial and mesothelial region inside the scrotum [1–4]. As a result of its rarity, the current breadth of knowledge on this topic is minimal and limited to case reports and literature reviews. To our knowledge, there has been no literature published describing patient demographics, disease characteristics, or management of epididymal cancer at a population-level to date. Understanding the disease pattern and determinants of epididymal cancer is critical as it will set the stage for improvement of patient counseling and allow for the development of standardized management guidelines. Furthermore, delineation of these characteristics will help guide future researchers in constructing study designs focused on improving patient outcomes.

The literature on epididymal malignancies is scarce. In an oncological study conducted by Yeung et al., the authors proposed the low incidence of epididymal malignancy may be a by-product of the epididymis's anti-tumorigenic environment which exhibits anti-oxidative factors, tumor suppressors, strong immune-surveillance, and aversion of angiogenesis. Using data from the China Hospital Knowledge Database (CHKD) from 1979–2010, their study also demonstrated that epididymal tumors were found to occur unilaterally or bilaterally in post-pubescent individuals with a mean age group of 30–40 years. A majority of cases identified, 82% of the 328 cases in the Asian survey and 67% of the 257 cases in the Western survey (New York only) were of benign histology [3]. Despite this study offering important clinical data on epididymal tumors, the external validity is limited as only Dhaka, Ireland, and New York cancer registries were queried.

To help bridge this epidemiological gap in knowledge, our study identified 66 cases of epididymal tumors in the United States (US) using the SEER data registry which represents nearly 28% of the US population and includes New York. Interestingly, over 60% of the cases were documented after the year 2000 with 3% of cases after 2016. Alongside descriptive data on patient characteristics and clinical outcomes, our data is the first to demonstrate the estimated 5-year CSS rate among the US cohort, which was 91% with an estimated 5-year OS rate of 84.9%. This favorable CSS is most likely a reflection of the low grade classification associated with the majority of these cases (78.7%) in combination with the various treatments modalities offered to these patients (ie, surgical, radiation, chemotherapy). Despite the use of a comprehensive database such as SEER, the relative rarity of epididymal malignancy has limited our study to a small sample size with a heterogenous mixture of characteristics (ie, histological findings, varying treatments) that prevents any compelling conclusions to be made regarding determinants of cancer specific deaths.

Amongst the rare epididymal neoplasms, the number of benign tumors reported exceed malignant ones 3 to 1 [16]. According to a recent literature review by Graham et al., adenocarcinomas represents a majority of benign epididymal tumors with a total number of 25 cases in English literature [17]. This finding was shared by Yeung et al., as their study reported adenomatoid tumors to be the most common amongst both the Asian (55%) and Western (73%) surveys belonging to this histological subtype. However, both of these studies are an inaccurate representation of the true US histological distribution. The study conducted by Graham et al. reports on every case published in English, but includes cases from outside the US. Meanwhile, the Western survey cohort in the study conducted by Yeung et al., considers New York as a representative sample of the US. In contrast, our study utilized the SEER database which is more representative of the cancer incidence and survival in the US. We found that the three most common histological subtypes were rhabdomyosarcoma (17%), leiomyosarcoma (15%), and liposarcoma (11%). Adenocarcinoma accounted for only 9% of all cases.

Our retrospective study has several limitations which are inherent to its design, of which include a small sample size, sample bias, and unmeasured confounding variables. Given the low number

of cases of epididymal malignancies, any calculations evaluating the prevalence of this disease could be inaccurate and therefore were not performed. Moreover, the specific database within SEER system used to perform our analysis is not capable of being analyzed for prevalence as per the SEER*Stat program. Also, as a large database review, the study is vulnerable to inaccurate coding while appropriate AJCC staging is not available. Inaccurate coding could lead to misclassification of the origin of the tumor which could inflate or artificially decrease our population of interest. In light of the limited knowledge available regarding epididymal malignancies, our study is the first to assess patient and tumor characteristics at a population level and is therefore a beneficial addition to the current literature.

CONCLUSIONS

Epididymal malignancy is a rare and histologically diverse disease. Treatment with surgical excision, radiation and/or chemotherapy results in a 91% estimated 5-year CSS.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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