Patterns of Care and Survival Outcomes for Malignant Sex Cord Stromal Testicular Cancer: Results from the National Cancer Data Base

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Purpose: Sex cord stromal tumors of the testis comprise less than 5% of testicular neoplasms. Consequently, data regarding patterns of care and survival are sparse. Using a large national database, we sought to provide a more definitive analysis of outcomes and management of these malignancies.

Materials and Methods: Data were obtained from the National Cancer Data Base. Patients diagnosed from 1998 to 2011 with 2 of the most frequent sex cord stromal tumors of the testis, including Leydig and Sertoli cell tumors, were selected for study. Overall survival estimates were assessed by the Kaplan-Meier method.

Results: Of the 79,120 cases of testicular cancer between 1998 and 2011, 315 (0.39%) were primary malignant Leydig or Sertoli cell tumors. Median patient age was 43 years for both tumors. Of the 315 patients 250 (79%) had malignant Leydig cell tumors and 65 (21%) had malignant Sertoli cell tumors, of which 94% and 78%, respectively, were stage I. Overall survival at 1 and 5 years for stage I Leydig cell tumors was 98% (95% CI 96–100) and 91% (95% CI 85–96), and for stage I Sertoli cell tumors overall survival was 93% (95% CI 83–100) and 77% (95% CI 62–95), respectively ($p = 0.015$). Of patients with stage I Leydig and Sertoli cell tumors 94% and 84%, respectively, received no further treatment following orchiectomy.

Conclusions: Five-year survival estimates of stage I Leydig and Sertoli cell tumors are significantly lower compared to those of stage I germ cell tumors with Sertoli cell tumors significantly worse than Leydig cell tumors. These differences in the survival of sex cord stromal tumors indicate the importance of large databases to evaluate the efficacy of treatment for rare neoplasms.

Key Words: testicular neoplasms, sex cord-gonadal stromal tumors, Sertoli cell tumor, Leydig cell tumor, mortality

Abbreviations and Acronyms

GCT = germ cell tumor

NCDB = National Cancer Data Base

PUF = Participant User File

RPLND = retroperitoneal lymph node dissection

SCST = sex cord stromal tumor

XRT = external beam radiotherapy

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Sex cord stromal tumors account for less than 5% of all adult testicular tumors[1] and approximately 10% are malignant.[2] They arise from the supporting tissues of the testis and include Leydig cell tumors, Sertoli cell tumors and variants, granulosa cell tumors, thecomas and fibromas.[3–6] Although rare, malignant SCSTs present with metastasis approximately 20% of the time. The behavior and prognosis of SCSTs are

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difficult to predict due to the absence of quality outcomes data on these rare malignancies.

While the management of GCTs is standardized, leading to excellent outcomes in excess of 99.7% disease specific survival,[7,8] the same cannot be said for SCSTs. Therefore, the establishment of guidelines for diagnosis and treatment appears to be imperative. Given the lack of data driven recommendations for SCSTs, a variety of therapeutic options have been recommended. They largely parallel the options for GCTs, including up-front radical orchiectomy followed by active surveillance or RPLND for stage I disease. For patients with SCST presenting with more advanced stage disease there is a lack of standardized recommendations and, therefore, the options used usually include RPLND with or without chemotherapy.[9]

To address the lack of information regarding treatments and outcomes of SCSTs we performed a retrospective cohort study using a large national database. We hypothesized that men with stage I SCST would experience outcomes similar to those of men with GCT and have similar patterns of care. We further postulated that men with more advanced stage disease would fare worse compared to their GCT counterparts.

MATERIALS AND METHODS

Data Acquisition, Patient Selection and Variable Definitions

Data were obtained from the NCDB testis cancer PUF. NCDB, a program of ACS (American College of Surgeons), CoC (Commission on Cancer) and the American Cancer Society®, is a nationwide, facility based cancer registry data set that captures more than 70% of all newly diagnosed malignancies in the United States seen annually at more than 1,500 facilities.[10,11]

Using this data set we selected patients diagnosed between 1998 and 2011 with ICD-O-2 and ICD-O-3 codes specific for Leydig cell tumor (8650) or Sertoli cell tumor (8640) testicular cancer. Patients were excluded from study if cancer staging information was unavailable, no portion of treatment was received at the reporting facility or this was not their first or only reported cancer (NCDB sequence number equal to 00 for single malignancy or 01 for primary malignancy). Stage was defined as the value reported for Pathological Stage Group or Clinical Stage Group if pathological stage was not available. Substage groups were collapsed into the corresponding general stage designation, and stages II and III were combined for each histology group due to low counts. Cases with Class of Case code equal to 00 (corresponding to cases diagnosed at but with no treatment received at the facility) were excluded from study.

We evaluated 2 primary end points, including 1) overall survival and 2) reported treatments for each stage of disease with time. The most recent year that data were available for inclusion was 2011 for assessment of treatment trends and 2006 for overall survival. Treatment received within 90 days of diagnosis was coded as primary treatment for all modalities except RPLND, for which timing of the treatment received was unavailable in the database. Therefore, RPLND was the primary treatment if reported. Patients with no primary treatment reported were coded as having received no primary treatment, although they may have received treatment after 90 days.

Statistical Analysis

Overall survival curves by group were estimated by the Kaplan-Meier method with comparisons between groups by log-rank statistics and the HR estimated by Cox proportional hazards regression. R, version 3.1 (https://www.r-project.org/) was used for all remaining analyses.

RESULTS

In the NCDB testicular cancer PUF data set 79,120 cases of testicular cancer were diagnosed between 1998 and 2011. Of these cases 315 were malignant Leydig or Sertoli cell tumors, of which the majority were malignant Leydig cell tumors (fig. 1). Of the 250 patients diagnosed with malignant Leydig cell tumors 234 (94%) had stage I tumors. In comparison, 51 of the 65 Sertoli cell tumors (78%) were stage I.

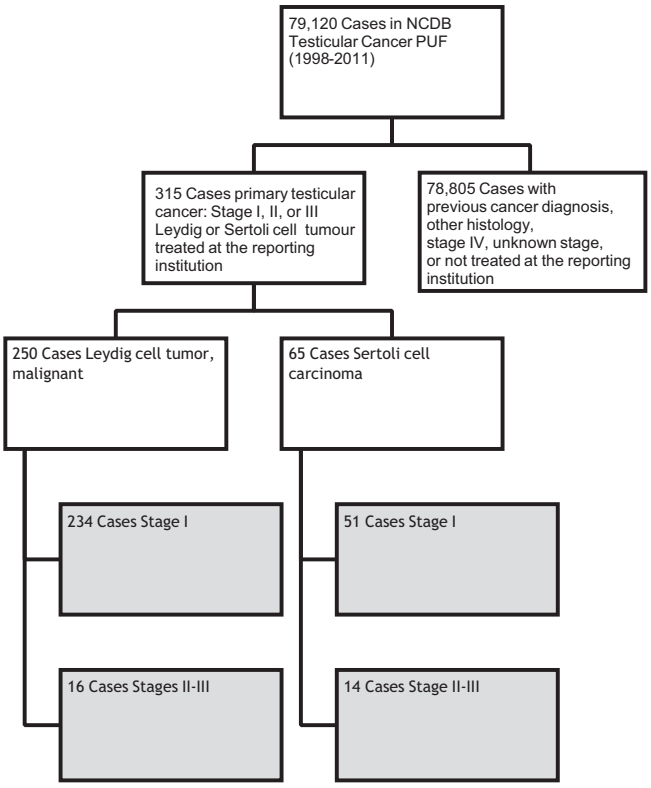

Figure 1. Leydig cell tumor, malignant and Sertoli cell carcinoma cases were selected for analysis from NCDB PUF, excluding those not meeting inclusion criteria.