Patterns of care and survival outcomes for adolescent and young adult patients with testicular seminoma in the United States: A National Cancer Database analysis

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Summary

Introduction
Testicular germ cell tumors (GCTs) are the most common solid tumor among adolescent and young adult (AYA) males. AYA patients with GCTs most typically have non-seminoma compared with seminoma, and accordingly there are fewer data reported on the AYA experience with testicular seminoma.

Objective
To evaluate national trends in postoperative treatment and overall survival (OS) outcomes in testicular seminoma by age group, specifically comparing AYAs with older adults.

Study design
The National Cancer Data Base (NCDB) was queried for patients with testicular seminoma diagnosed between 2004 and 2012, who underwent orchiectomy followed by observation or adjuvant therapy (chemotherapy, radiation (RT), or both). Patients were grouped by age: AYA (15—39 years), adults between 40 and 55 years, and adults >55 years. Overall survival (OS) was presented using Kaplan—Meier curves and groups compared via a log-rank test. Univariate (UVA) and multivariate (MVA) analyses were performed using Cox proportional hazards regression models. Binary multiple logistic regression identified differences in variables by age category.

Results
Of the total 22,361 patients the majority were AYAs (12,880, 57.6%), followed by adults 40—55 years (8,022, 35.9%), and >55 years (1,459, 6.5%). Unadjusted 5-year OS was significantly better for AYAs versus adults 40—55 years and >55 years (98.0%, 96.4%, 87.7%; $p < 0.001$), as was 10-year OS (96.1%, 91.8%, 71.3% respectively; $p < 0.001$). The Table shows that on a MVA, OS was significantly better for AYAs versus adults 40—55 years and adults >55 years. AYA patients were also more commonly treated at centers with greater clinical volume. Additionally, AYA patients were less likely to present with metastatic disease. Accordingly, AYA patients were less likely to undergo retroperitoneal lymph node dissection (OR 0.81; $p = 0.001$) and were less often managed with adjuvant therapy including chemotherapy (OR 0.91; $p = 0.027$), RT (OR 0.93; $p = 0.025$), or both (OR 0.68; $p = 0.020$).

Discussion
AYA patients with testicular seminoma present with earlier stage disease and in the clinical Stage I setting are more often are managed with active surveillance following orchiectomy when compared with older adults in this population-based analysis. Among AYA patients, OS was modestly better when compared with adults 40—55 years and significantly better when compared with adults >55 years.

Conclusion
Our objective to describe the patterns of care and survival outcomes for AYA patients with testicular seminoma in the USA was met by reviewing this large national dataset. These results may inform future guidelines for management of AYA seminoma.

Table

Cox regression for predictors of overall survival (OS) for testicular seminoma

Variable	Univariate			Multivariate		
	HR	95% CI	p	HR	95% CI	p
Age, years						
15—39	1			1		
40—55	1.81	1.53—2.14	<0.001	1.80	1.52—2.13	<0.001
>55	6.13	5.06—7.44	<0.001	4.26	3.47—5.23	<0.001

Logistic regression for variables associated with adolescent young adults (AYAs) compared with older adults

Variable	Univariate			Multivariate		
	OR	95% CI	p	OR	95% CI	p
Facility case volume, tertiles						
Low	1			1		
Middle	1.13	1.06—1.21	<0.001	1.14	1.07—1.21	<0.001
Upper	1.18	1.10—1.26	<0.001	1.17	1.09—1.25	<0.001
Stage						
I	1			1		
II	0.82	0.75—0.89	<0.001	0.86	0.78—0.95	0.002
III	0.69	0.61—0.78	<0.001	0.72	0.64—0.83	<0.001

Introduction

Although testicular cancer constitutes only approximately 1% of new cancer diagnoses among men [1], it is the most common solid malignancy among male adolescents and young adults (AYA) [2,3]. Survival outcomes are typically excellent among this group of patients, with 5-year survival exceeding 90% [4]; however, the growing incidence of testicular cancer [3] exposes increasing numbers of patients to the potentially toxic effects of curative therapy. In terms of the types of testicular cancer, these are almost all germ cell tumors and the vast majority of testicular germ cell tumors in this AYA population are non-seminomatous germ cell tumors (NSGCT). As a result, comparatively little is known about seminomas in this AYA group. While a recent population-based analysis characterized survival outcomes and patterns of care among adolescents and adults with NSGCT [5], gaps remain in our understanding of AYA patients with seminoma.

AYA patients face challenges distinct from those confronting younger or older cancer patients beyond biological factors [6], including access to care [7], psychosocial support [8], and underrepresentation in clinical trials [9]. These differences prompted the National Cancer Institute to convene a Progress Review Group in 2006 with a goal of advancing cancer care among AYA [10]. The past decade has seen tremendous progress in our understanding of cancer in this unique group [11], including the formulation of AYA-specific guidelines to guide care [12]. A 2013 workshop identified a particular need to characterize the epidemiology and patterns of care for cancers afflicting AYA and specifically identified the National Cancer Database (NCDB) as a valuable resource for this purpose [13]. We therefore aimed to describe national trends in management and survival among AYA with testicular seminoma in the NCDB. We hypothesized that similar to AYAs with NSGCT, AYA patients with testicular seminoma experience improved survival compared with older adult patients.

Material and methods

Data source and patient selection

The NCDB is a joint project of the Commission on Cancer of the American College of Surgeons and the American Cancer Society [14]. It is a hospital-based registry that represents 70% of all cancer cases in the USA, drawing data from more than 1500 commission-accredited cancer programs. The data used in the study are derived from a de-identified NCDB file. The American College of Surgeons and the Commission on Cancer have not verified and are not responsible for the analytic or statistical methodology employed, or the conclusions drawn from these data.

We identified 26,694 pediatric and adult patients with seminoma of the testis (C62.0-C62.9) diagnosed between 2004 and 2012 with known follow-up and survival outcomes. Seminoma patients were selected from histologic codes based on International Classification of Disease for Oncology (third edition) histology code (ICD-O-3): 9061 (seminoma, not otherwise specified (NOS)) and 9062 (seminoma, anaplastic). Cases treated with palliative intent ($n = 52$), patients younger than 15 years ($n = 15$), and those with anaplastic

histology ($n = 205$) were removed. Next, those with unknown modality of treatment among surgery, radiation, or chemotherapy ($n = 3572$) were removed. Lastly, patients who did not receive primary surgery were excluded ($n = 489$). Primary surgery included local or partial excision of the entire testicle ($n = 79$), excision of testicle ($n = 21,533$), orchiectomy ($n = 720$), or surgery NOS ($n = 29$).

Patient demographics and treatment variables

Potentially relevant patient and treatment characteristics were included. Age was analyzed as a categorical variable and defined as AYAs (15—39 years), adults 40—55 years, and adults >55 years old. Race was categorized as white, African-American, other, and unknown. Insurance status was defined by the NCDB and included not insured, private insurance/managed care, government-based (Medicaid, Medicare, other government), and unknown. Patient comorbidities were categorized as 0, 1, or ≥ 2 according to Charlson-Deyo comorbidity scores [15]. Overall stage was based on the American Joint Committee on Cancer staging guidelines based on corresponding year of diagnosis [16]. Adjuvant radiation (aRT) was coded as external beam radiation. Retroperitoneal lymph node dissection (RPLND) and adjuvant chemotherapy (aCT) were analyzed as binary (yes/no). Based on the frequency of occurrence of the facility unique identification code in the entire NCDB-derived testicular cancer dataset, we categorized each facility by tertiles as low-volume, intermediate-volume, and high-volume. In this group, the median institutional volume of cases of testicular seminoma was 31 (range 1—335). The thresholds that defined the tertiles were: low volume = 1—22, intermediate-volume = 23—45, and high-volume ≥ 46.

Comparison with general population

To further explore the influence of age on overall survival, we segmented our seminoma population from the NCDB into 5-year cohorts by age at diagnosis and compared their 5-year survival against the 5-year expected survival of the general population from the Surveillance, Epidemiology, and End Results (SEER) database.

Statistical analysis

Statistical analyses were performed using SPSS V23.0 (SPSS Inc., Chicago, IL, USA). Pearson chi-square tests were used to assess associations between categorical variables and age category. Multiple binary logistic regression models were used to assess the association between patient and treatment characteristics between AYA and adult (≥ 40 years) patients, including receipt of RPLND, aRT, aCT, and adjuvant combined modality therapy (aCMT) consisting of both aRT and aCT. The Hosmer—Lemeshow test was used to check for the goodness-of-fit of the regression models. Of note, an OR greater than 1 indicates that this variable was more common in the AYA population than in adults ≥ 40 years. Conversely, an OR less than 1 indicates that this variable was more common in the population of adults ≥ 40 years. OS was then examined using the Kaplan—Meier method. Univariate survival analysis (UVA) was performed with the log-rank test,