Clinical Oncology xxx (2016) 1–9

Contents lists available at ScienceDirect

Clinical Oncology

journal homepage: www.clinicaloncologyonline.net

Original Article

Stage II Testicular Seminoma: Patterns of Care and Survival by Treatment Strategy☆

S.M. Glaser *, J.A. Vargo *, G.K. Balasubramani †, S. Beriwal *

* Department of Radiation Oncology, University of Pittsburgh Cancer Institute, Pittsburgh, PA, USA
† Department of Epidemiology, School of Public Health, University of Pittsburgh, Pittsburgh, PA, USA

Received 19 November 2015; received in revised form 28 January 2016; accepted 2 February 2016

Abstract

Aims: Stage II testicular seminoma is highly curable with radiotherapy or multi-agent chemotherapy (MACT). These modalities have not been compared in a randomised manner.

Materials and methods: Using the US National Cancer Data Base, we identified 2437 stage II seminoma patients (IIA = 960, IIB = 812, IIC = 665) treated with orchiectomy and either radiotherapy or MACT from 1998 to 2012. Factors affecting treatment modality (radiotherapy versus MACT) were studied using multivariable logistic regression. Propensity scores for treatment selection were incorporated into multivariable Cox regression analyses of overall survival.

Results: The median follow-up was 65 months (interquartile range 34–106). Rates of radiotherapy utilisation were: IIA = 78.1%, IIB = 54.4%, IIC = 4.2%. Rates of MACT utilisation were: IIA = 21.9%, IIB = 45.6%, IIC = 95.8%. For both IIA and IIB patients, later year of diagnosis, academic treatment facility and pathological confirmation of lymph node positivity were associated with increased utilisation of MACT. Also predictive for preferential utilisation of MACT were comorbidity score ≥ 1 and non-private insurance for IIA patients and T stage ≥ 2 for IIB patients. For IIA patients, survival was improved with radiotherapy compared with MACT with a 5 year survival of 99.0% (95% confidence interval 98.2–99.8) versus 93.0% (95% confidence interval 89.0–97.0). This advantage persisted on propensity-adjusted multivariate analysis (hazard ratio 0.28; 95% confidence interval 0.09–0.86; $P = 0.027$). For IIB patients, 5 year survival was 95.2% (95% confidence interval 92.8–97.6) for radiotherapy and 92.4% (95% confidence interval 89.2–95.6) for MACT (Log-rank $P = 0.041$), with no significant difference on multivariable analysis.

Conclusions: Radiotherapy is associated with improved survival over MACT for IIA patients, with no significant survival difference for IIB patients.

Key words: Chemotherapy; NCDB; patterns of care; radiotherapy; stage II; testicular seminoma

Introduction

Testicular seminoma is the most common solid tumour in men in their third or fourth decade of life, with about 70–80% diagnosed with stage I disease, 15–20% with stage II disease and less than 5% with more disseminated disease [1,2]. As this represents the most curable solid malignancy, recent efforts have focused on decreasing toxicity related to treatment, with active surveillance becoming the preferred treatment strategy after radical orchiectomy for stage I disease. Radiotherapy was historically the preferred treatment for stage II patients. For those with stage IIA–IIB disease (nodal disease ≤5 cm) treatment with radiotherapy has resulted in relapse-free survival rates of 90–95% and disease-specific survival approaching 100%, as even the rare patients suffering with relapse are highly salvageable with chemotherapy [3–6]. However, relapse rates for stage IIC disease (nodal disease >5 cm) treated with radiotherapy have been reported to be 25–55% [3,4,7], with most relapses being distant. Although, studies of more extensive radiotherapy fields lowered rates of relapse for stage IIC patients (10–20%), such treatment is no longer standard due to concerns of toxicity and the efficacy of chemotherapy [8,9]. Indeed, chemotherapy has been evaluated as an alternative to radiotherapy, with similar appearing efficacy

☆ Data have been submitted in abstract format to the 35th annual meeting of the European Society of Radiotherapy and Oncology, Turin, Italy.

Author for correspondence: S. Beriwal, Magee Womens Hospital of UPMC (Radiation-Oncology), 300 Halket St, Pittsburgh, PA 15213, USA. Tel: +1-412-641-4600; Fax: +1-412-641-6601.
E-mail address: beriwals@upmc.edu (S. Beriwal).

http://dx.doi.org/10.1016/j.clon.2016.02.008
0936-6555/

in those with non-bulky disease and improved outcomes in those with stage IIC disease [2,10,11].

There is little controversy as to the preferred role of chemotherapy for those with stage IIC disease [7,10–12]. However, for patients with non-bulky nodal disease, significant controversy as to ideal treatment exists [11]. Radiotherapy and chemotherapy have never been prospectively compared for stage II seminoma. This controversy is reflected in consensus national guidelines with the National Comprehensive Cancer Network recommending radiotherapy as the preferred treatment for stage IIA, whereas European Association of Urology (EAU) guidelines equally allow for radiotherapy or chemotherapy. Both guidelines are equivocal for stage IIB and recommend chemotherapy for stage IIC. Other treatment strategies for stage II seminoma, such as single-agent carboplatin, have been shown to be inferior [13] or remain investigational, as is the case with combination carboplatin plus radiotherapy [14,15].

Due to the rarity of stage II seminoma, a sufficiently powered randomised trial comparing radiotherapy with chemotherapy is unlikely to be completed. Given the paucity of level I evidence and shifting treatment paradigms, we sought to analyse factors predicative for the utilisation of radiotherapy versus multi-agent chemotherapy (MACT) and corresponding overall survival among stage II seminoma patients on a national level using a hospital-based registry.

Materials and Methods

Data Source

Using de-identified data exempt from Institutional Review Board oversight, we queried the US National Cancer Data Base (NCDB) of testicular cancer patients from 1998 to 2012. The NCDB is a joint project of the American Cancer Society and the Commission on Cancer of the American College of Surgeons. It is a nationwide, facility-based, tumour surveillance data set that encompasses more than 1500 hospitals and captures 70% of all newly diagnosed malignancies in the USA [16,17]. The American College of Surgeons has executed a Business Associate Agreement that includes a data use agreement with each of its Commission on Cancer accredited hospitals.

Patient Selection

Of the 80 385 patients in the original NCDB testicular cancer database, 2437 stage II seminoma patients who had undergone orchiectomy followed by either MACT or radiotherapy within 3 months of diagnosis were identified, as summarised in the CONSORT diagram (Figure S1). All patients were newly diagnosed between 1 January 1998 and 31 December 2012. All patients were between the ages of 18 and 90 years.

Table 1
Baseline characteristics ($n = 2437$)

Baseline characteristics	*n* (%)
Sociodemographic factors	
Year of diagnosis	
1998–2001	618 (25.4)
2002–2005	643 (26.4)
2006–2009	656 (26.9)
2010–2012	520 (21.3)
Age	
< 40 years	1350 (55.4)
≥ 40 years	1087 (44.6)
Charlson-Deyo comorbidity score	
0	1565 (64.2)
≥1	103 (4.2)
Unknown	769 (31.6)
Race	
White	2264 (92.9)
Non-White	142 (5.8)
Unknown	31 (1.3)
Insurance status	
Private	1791 (73.5)
Government	315 (12.9)
None	271 (11.1)
Unknown	60 (2.5)
Residential setting	
Metropolitan	2001 (82.1)
Urban	358 (14.7)
Unknown	78 (3.2)
Median income (residential area)	
<$38 000	337 (14.1)
$38 000–47 999	518 (21.6)
$48 000–62 999	690 (28.8)
≥ $63 000	849 (35.5)
Unknown	43 (1.8)
% without high school degree (residential area)	
< 7%	676 (27.7)
7–12.9%	816 (33.5)
13–20.9%	559 (22.9)
≥ 21%	346 (14.2)
Unknown	40 (1.6)
Distance from facility to residence	
< 10 miles	1292 (53.0)
≥ 10 miles	1108 (45.5)
Unknown	37 (1.5)
Facility type	
Community/comprehensive community	1600 (65.7)
Academic/research	834 (34.2)
Unknown	3 (0.1)
Facility location	
Northeast	516 (21.2)
South	691 (28.4)
Midwest	771 (31.6)
West	459 (18.8)
Facility volume	
< 5 cases	1190 (48.8)
≥ 5 cases	1247 (51.2)
Pathological factors	
T stage	
1	1353 (55.5)
2	745 (30.6)
≥ 3	210 (8.6)
Unknown	129 (5.3)

Please cite this article in press as: Glaser SM, et al., Stage II Testicular Seminoma: Patterns of Care and Survival by Treatment Strategy, Clinical Oncology (2016), http://dx.doi.org/10.1016/j.clon.2016.02.008