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Long-term outcomes following post-operative radiotherapy for Stage I/II testicular seminoma – an Australasian single-institution experience

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Abstract

Introduction: The aim of the study is to review the long-term oncological outcomes and adverse effects of post-operative radiotherapy (PORT) for Stage I/II seminoma patients in an Australian radiation treatment centre. **Methods:** This is a retrospective study of 125 patients with Stage I/II seminoma treated with PORT at the Alfred Health Radiation Oncology Service between 1992 and 2013. Patients were linked to the Victorian Cancer Registry to enable confirmation of survival and diagnosis of secondary malignancies (SM). The relapse-free survival (RFS), testicular-cancer-specific survival (TCSS), overall survival (OS) and SM-free survival (SMFS) were estimated with Kaplan–Meier methods. **Results:** The median age at diagnosis was 36 (range 20–62). The median time between diagnosis and PORT was 1.6 months (range: 0.5–4.5). Fifty patients (40%) had PORT to the para-aortic (PA) target alone, while the remaining had PORT to PA and ipsilateral or bilateral iliac lymph nodes. There were no acute adverse effects requiring admission. The median follow-up after PORT was 7.8 years (range = 0.1–19.1). There were two relapses, both of which occurred within 1 year of PORT (estimated 10-year RFS = 98.4%). Five deaths were reported, none of which were testicular cancer-related death (estimated 10-year TCSS = 100%, 10-year OS = 97.3%). There were seven SM (one lower lip cancer, one upper shoulder melanoma, one mesothelioma, two prostate cancer, one acute myeloid leukaemia and one contralateral testicular seminoma) reported in six patients, with estimated 10-year SMFS of 92.9%. **Conclusion:** Our series confirms excellent oncological outcomes among patients with Stage I/II seminoma treated with PORT, with uncommon occurrence of SM.

Introduction

Testicular seminoma is the most common germ cell cancer diagnosed in men. In Australia, the age-standardised incidence rate of seminoma was 3.79 cases/100,000 men, with the peak incidence in men age 30–34.[1] The primary treatment for testicular seminoma involves radical trans-inguinal orchidectomy with ligation of the spermatic cord.

For patients with Stage I seminoma, the options post-operatively include close surveillance, radiotherapy or chemotherapy. Given that seminoma cells are extremely radiosensitive, historically radiotherapy to the para-aortic (PA) and iliac lymph nodes are the standard post-operative treatment for Stage I seminoma patients. Post-operative radiotherapy (PORT) is associated with excellent oncological outcomes, reducing the risk of disease relapse from approximately 15%[2] to less than 5%.[3] However, long-term studies have raised concerns about the late effects of radiation treatment, including the increased risk of second malignancies (SM)[4–6] and cardiovascular diseases.[5,7–10]

This has resulted in a shift to alternative approaches for Stage I seminoma patients, such as surveillance or single-agent chemotherapy. Single-agent post-operative

chemotherapy has emerged as a treatment option for patients, following findings from randomised trials showing non-inferiority of post-operative chemotherapy compared to radiotherapy.[3] However, there is a lack of long-term toxicity data on post-operative single-agent chemotherapy for Stage I seminoma. The other approach is surveillance, particularly for patients who are likely to adhere to a rigorous follow-up protocol for at least 5 years with reservation of radiation treatment for disease relapse.[11]

For Stage IIA and IIB seminoma, PORT remains the current standard of care, with approximately 90% relapse-free survival (RFS) and almost 100% overall survival (OS),[12,13] although chemotherapy, using four cycles of etoposide and cisplatin (EP) or three cycles of bleomycin, etoposide and cisplatin (BEP), is an alternative to radiotherapy.[14] A very recent meta-analysis of 13 studies by Giannatempo et al. suggested a trend in favour of chemotherapy for management of Stage IIB seminoma given the lower incidents of side effects and relapse rate.[15] For stage IIC disease, chemotherapy is the treatment of choice.[12]

We aim to provide additional data to the current literature on the long-term outcomes following postoperative radiotherapy (PORT) for Stage I/II seminoma patients, based on our experience in an Australian radiation treatment centre.

Methods

This is a retrospective study of all patients with histologically confirmed Stage I/II testicular seminoma, who were referred to and subsequently treated with PORT, at the Alfred Health Radiation Oncology Service since its establishment in 1992 through to 2013. Following PORT, all patients were followed up according to the institutional policy, which included 3–6 monthly outpatient follow-up for the first 2 years, with serum marker monitoring, chest X-ray and CT imaging of the abdomen and pelvis, and annual follow-up thereafter for at least 8–10 years. The Alfred Health Radiation Oncology Service maintained a comprehensive departmental database. For patients who had been discharged from the care of the department, patients' most recent disease status (including any recent major medical events such as major surgeries or myocardial infarction) was obtained through contact with the primary care physicians or the medical oncologists on an annual basis.

The primary oncological outcomes of interest are the relapse free survival (RFS), testicular cancer specific survival (TCSS) and overall survival (OS). For TCSS, an event was defined as any death secondary to testicular seminoma due to progressive metastatic disease or acute treatment-related complications, whereas for OS, an event included any reported deaths. The long-term treatment-related side effects of interest are the cardiovascular toxicities (CV), gastrointestinal toxicities (GIT) and second malignancies (SM). The CV events were defined as any documented acute myocardial infarctions, coronary artery bypass grafts, angioplasties, coronary stent insertions, valve replacements or cerebrovascular accidents. GIT events were defined as any endoscopically confirmed peptic ulcer disease or any documented hospital admission with small bowel obstruction following radiation treatment. SM was defined as any biopsy-confirmed malignancies, irrespective of the relation to the field of radiation treatment.

All patient-, tumour-, treatment- and outcome-related data were obtained from the Alfred Health Radiation Oncology Service electronic medical records and database, including a word search for all possible terms that might refer to the outcomes of interest. To ensure consistency and accuracy in data collection, two authors (WLO and LN) reviewed and crosschecked all medical records. In addition, patient identifiers were used to access linked data from the Victorian Cancer Registry (VCR), to enable confirmation of survival data and diagnosis of SM. The VCR links to the Australian Institute of Health and Welfare National Death Index, so patients who had emigrated from Victoria would not be missed as a death if it occurred in Australia. The study was approved by the Alfred Health Ethics Committee (Project No 19/14).

Statistical analyses

The differences in characteristic between Stage I/II seminoma patients were analysed using the Student's t test (or Mann–Whitney U test as appropriate) for continuous variables and the Pearson's chi-squared test for categorical variables. A $P < 0.05$ on a two-sided statistical test is considered statistically significant. The RFS, TCSS, OS and SM free survival (SMFS) were estimated using the Kaplan–Meier methods. The time to event was defined from the date of completion of PORT to the date of outcomes of interest. Patients were censored on the date of last follow-up if they did not experience the outcomes of interest. All statistical analyses were performed using STATA/IC 13 (STATA Corp, College Station, TX).

Results

In all, 169 patients with Stage I/II seminoma were referred to the Alfred Health Radiation Oncology Service and 125 proceeded to have treatment with external beam radiotherapy (EBRT) to the PA nodes or PA nodes and ipsilateral or bilateral iliac lymph nodes. Seventeen patients had chemotherapy and no radiation, four had treatment elsewhere and 23 were put on surveillance and

never received PORT. Of the 125 patients included in our study, 106 (85%) had Stage I seminoma, while the remaining (n = 19, 15%) had Stage II seminoma.

Baseline characteristics

The median age at diagnosis of seminoma was 36 (range = 20–62). Only nine patients (7%) reported a history of undescended testis. Fifty-eight patients (46%) had seminoma involving the right testis. The median tumour size was 40 mm (range: 4–105 mm). Stage II seminoma patients had significantly larger tumour size (median: 53; range: 22–90 mm) compared to Stage I seminoma patients (median: 36; range: 4–105 mm, P = 0.02), and were more likely to have the primary tumour extending beyond the tunica albuginea (i.e. pT2 and above) – 37% in Stage II and 10% in Stage I respectively (P = 0.008) (Table 1).

Two patients had disease relapse on referral for radiotherapy, of which one relapse occurred after 2 years of surveillance, while the other occurred approximately 3 years after adjuvant chemotherapy and was treated with retroperitoneal lymph node dissection before radiation treatment. Two Stage II seminoma patients were referred for radiotherapy due to persistent lymphadenopathy and elevated tumour markers despite post-operative chemotherapy.

Treatment

More than half of the patients (59%) had radiation to the PA plus ipsilateral common iliac lymph nodes (the classic

Table 1. Patient-, tumour- and treatment-related characteristics.

	Stage I (n = 106; 85%)	Stage II (n = 19; 15%)	All (n = 125)
Patient characteristics			
Age at diagnosis, year – median (range)	35 (20–61)	41 (29–62)	36 (20–62)
History of undescended testis – n (%)			
No	100 (94)	16 (84)	116 (93)
Yes	6 (6)	3 (16)	9 (7)
Tumour characteristics			
Laterality – n (%)			
Right	47 (44)	11 (58)	58 (46)
Left	59 (56)	8 (42)	67 (54)
Tumour size – median (range)	36 (4–105)	53 (22–90)	40 (4–105)
Primary tumour – n (%)			
pT1	95 (90)	12 (63)	107 (86)
pT2 (tunica vaginalis involvement)	9 (8)	5 (26)	14 (11)
pT3 (spermatic cord involvement)	2 (2)	2 (11)	4 (3)
Regional lymph nodes – n (%)			
N0	106 (100)	0 (0)	106 (85)
N1	0 (0)	13 (68)	13 (10)
N2	0 (0)	6 (32)	6 (5)
Disease relapse on presentation – n (%)			
No	106 (100)	17 (89)	123 (98)
Yes	0 (0)	2 (11)	2 (1.5)
Treatment details			
Treatment modalities – n (%)			
Orchidectomy + RTx	106 (100)	16 (84)	122 (98)
Orchidectomy + CTx + RTx	0 (0)	2 (11)	2 (1)
Orchidectomy + CTx + RPLND + RTx	0 (0)	1 (5)	1 (1)
Interval between diagnosis (i.e. orchidectomy) and RTx, month – median (range)	1.6 (0.5–9.2)	1.5 (0.7–45)	1.6 (0.5–45)
Treatment field – n (%)			
PA lymph nodes only	43 (41)	7 (37)	50 (40)
PA and ipsilateral common iliac nodes 'hockey-stick'	54 (51)	8 (42)	62 (50)
PA and ipsilateral iliac 'dog-leg'	9 (8)	3 (16)	12 (9)
PA and bilateral iliac nodes	0 (0)	1 (5)	1 (1)
Radiation dose, Gy – median (range)	25 (20–35)	35 (25–40)	25 (20–40)
Number of fractions – median (range)	20 (10–30)	25 (20–28)	20 (10–30)
Follow-up, year – median (range)	8.2 (0.1–19.1)	4.6 (0.9–14.1)	7.8 (0.1–19.1)

RTx, radiotherapy; CTx, chemotherapy; RPLND, retroperitoneal lymph node dissection; PA, para-aortic; Gy, Gray.

'hockey-stick' or 'modified dog-leg' field, with the caudal edge of the field typically at the superior extent of the acetabulum), while one Stage II patient had radiation to bilateral iliac lymph nodes. The remainder of the patients (40%) had radiation administered to the PA target alone. Stage I patients were treated with a median of 25 Gy (range: 20–35 Gy) over a median of 20 fractions (range: 10–30), while Stage II patients were treated to a total median dose of 35 Gy (range: 25–40 Gy) over 25 fractions (range: 20–28). There was no acute adverse reaction requiring hospital admission following radiation treatment.

Outcomes

The patients were followed up for a median of 7.8 years (range = 0.1–19.1). Two patients experienced disease relapse, within 1 year of completion of PORT (Table 2), giving an estimated 10-year RFS of 98.4% (Fig. 1). One Stage II seminoma patient had disease relapse noted on the left superior pubic ramus and ischial tuberosity on CT imaging and bone scan approximately 4 months post-completion of 35 Gy radiotherapy to the PA and ipsilateral iliac lymph nodes. He was subsequently treated with three-cycle BEP chemotherapy and a further 24 Gy radiotherapy to the left ischial and ipsilateral pelvis for the relapse. Six months later, he had another relapse involving the right pulmonary and mediastinal region. He was then treated with second-line salvage chemotherapy (four-cycle paclitaxel, ifosfamide and cisplatin), and has remained disease-free for more than 10 years at last follow-up.

The second relapsed patient presented with Stage I seminoma and was treated with PORT to the PA fields, T11 to L5 inclusive, to a dose of 25 Gy in 15 fractions. At routine follow-up 6 months later, he was noted to have a palpable left iliac fossa mass. This was confirmed radiologically as an 8-cm left iliac nodal mass, extending superiorly to the level of the acetabular roof, outside the treatment field, as well as another PA nodal mass extending inferiorly from the level of left renal hilum, crossing the midline, in or close to the edge of the treatment field. This was proven to be seminoma recurrence on biopsy, and the patient was treated with first-line salvage chemotherapy with three cycles of BEP, with complete radiological response. Three months later, he presented with leg oedema and renal impairment with left hydronephrosis due to an 8-cm nodal recurrence

Table 2. Characteristics and outcomes of patients with disease relapse and second malignancy after postoperative radiotherapy (PORT).

Patient	Date of diagnosis	Tumour characteristics	Treatment details	Site of relapse	Date of relapse	Salvage treatment details	SM	Date of SM diagnosis
1	September 1998	Stage I, pT1, N0	PA + ipsilateral nodes (25 Gy/20#)	–	–	–	Right upper shoulder melanoma	April 2000
							Prostate cancer	June 2009
2	January 2001	Stage I, pT2, N0	PA only (25 Gy/15#)	Ipsilateral pelvic lymph nodes	October 2001	CTx (3xBEP)	AML	February 2010
				Ipsilateral pelvic lymph nodes + mediastinal/right hilar lymph nodes	April 2002	HDCT + autologous BMT + RTx (PA + ipsilateral iliac nodes; 25 Gy/15#)		
3	August 2001	Stage II, pT1, N1	PA + ipsilateral iliac nodes (35 Gy/28#)	Left superior pubic ramus and ischial tuberosity	February 2002	CTx (3xBEP) + RTx (ipsilateral pelvis; 24 Gy/12#)	–	–
				Right hilar pulmonary metastasis	December 2002	CTx (4xTIP)		
4	February 2002	Stage I, pT1, N0	PA + ipsilateral nodes (25 Gy/20#)	–	–	–	Lower lip cancer	March 2003
5	March 2002	Stage I, pT1, N0	PA + ipsilateral nodes (25 Gy/20#)	–	–	–	Prostate cancer	October 2009
6	July 2002	Stage I, pT1, N0	PA only (25 Gy 20#)	–	–	–	Stage I contralateral seminoma	December 2008
7	October 2005	Stage II, pT2, N2	PA + bilateral iliac nodes (35 Gy/28#)	–	–	–	Mesothelioma	October 2008

CTx, chemotherapy; RTx, radiotherapy; BMT, bone marrow transplant; PA, para-aortic lymph nodes; Gy, Gray; BEP, bleomycin, etoposide, and cisplatin; TIP, paclitaxel, ifosfamide, and cisplatin; HDCT, high-dose chemotherapy; SM, second malignancy; AML, acute myeloid leukaemia.

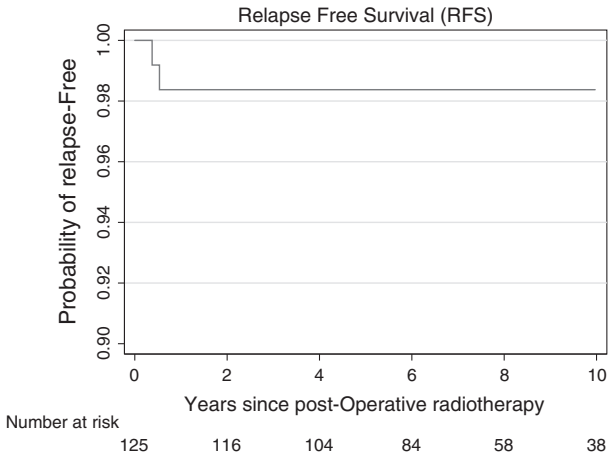

Figure 1. Relapse free survival (RFS) among stage I and II seminoma patients treated with postoperative radiotherapy (PORT).

overlying the psoas muscle as well as new mediastinal nodal involvement. He was treated then with high-dose chemotherapy with autologous bone marrow transplant (BMT) support, again, with complete radiological response. Consolidative radiotherapy was then given to the site of the left iliac node mass (previously radiotherapy naïve) and the left PA mass, L1 to L3 inclusive (overlapping with the original PA strip field); both fields treated to 25 Gy in 15 fractions. There has been no further disease relapse at 13-year follow-up.

At last follow-up, there were five deaths in our cohort, none of which were testicular cancer related, giving an estimated 10-year TCSS of 100% and OS of 97.3% (Fig. 2). There were seven SM (one lower lip cancer, one upper shoulder melanoma, one pulmonary mesothelioma, two prostate cancers, one acute myeloid leukaemia and one contralateral testicular seminoma) diagnosed in six patients at a median of 5.6 years after completion of PORT (range: 0.3–8.9 years) (Table 2), with an estimated 10-year SMFS of 92.9% (Fig. 3). We observed one CV event – a cerebrovascular accident 18 months following completion of PORT in a patient with known ischaemic heart disease and a history of myocardial infarction 10 years prior to PORT. There was also one patient with GIT toxicity (gastroscopy-confirmed peptic ulcer disease) reported during the follow-up period.

Discussion

We report the long-term outcomes of patients with Stage I/II seminoma, treated with PORT in an Australian radiation oncology centre. In our cohort of patients, the 10-year RFS, TCSS and OS were 98.4%, 100% and 97.3% respectively. The excellent oncological outcomes reported in our study are consistent with those reported in the international[16–18] and Australian literature (Table 3).[19–23]

There is a worldwide trend towards decreased utilisation of PORT for Stage I seminoma. Data from the US National Cancer Database showed that the utilisation of PORT for Stage I seminoma dropped from 71% in 2000 to 47% in 2008, with a corresponding rise in the proportion of patients being put on surveillance from 30% in 2000 to 40% in 2008.[24] The most recent European Association of Urology guidelines also do not recommend PORT for Stage I seminoma.[25] However, PORT still has an important role for management of Stage II seminoma.[25] Our reported 98.4% 10-year RFS and 100% TCSS confirms an excellent long-term oncological outcome among patients with Stage I/II seminoma treated with PORT, to limited infra-diaphragmatic fields, and our patients had minimal

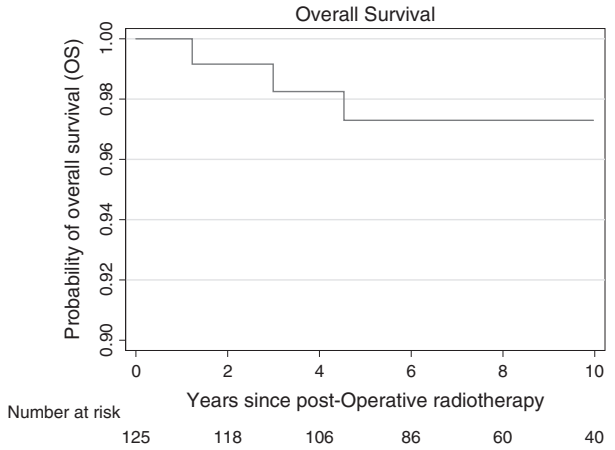

Figure 2. Overall survival (OS) among stage I and II seminoma patients treated with postoperative radiotherapy (PORT).

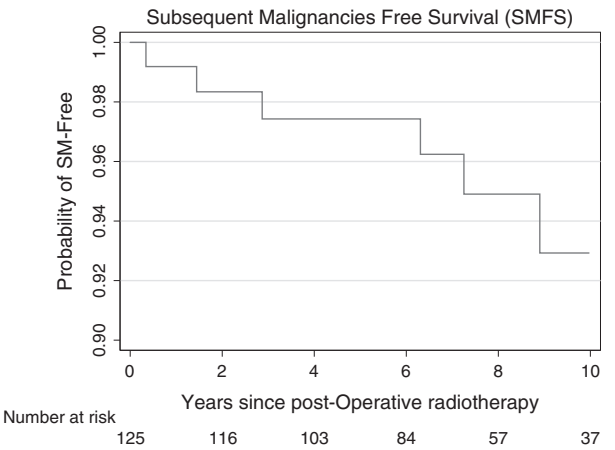

Figure 3. Second malignancy free survival (SMFS) among stage I and II seminoma patients treated with postoperative radiotherapy (PORT).

Table 3. Summary of Australasian studies reporting outcomes of Stages I and II seminoma patients following postoperative radiotherapy (PORT).

Author, year	Hospital	Study period	Disease status	Number of patients	Relapse (crude %)	Relapse-free survival	Mortality (crude %)	Overall survival
Mason et al. (1988)	Queensland Radium Institute, QLD	1968–1985	Stage II	49	7/49 (14%)	–	8/49 (16%)	5-year RFS = 82%
Lindemann et al. (1991)	Westmead Hospital, NSW	1980–1987	Stage I	57	1/57 (1.8%)	–	–	–
			Stage II	14	2/14 (14%)	–	–	–
Yeoh et al. (1993)	Royal Adelaide Hospital, SA	1981–1990	Stage I	69	–	–	3/77 (3.9%)	10-year OS = 96%
			Stage II	8	–	–		10-year OS = 100%
Kearsley et al. (1994)	Royal Brisbane Hospital, QLD	1960–1989	Stage I	270	8/270 (3.7%)	5-year RFS = 95%	11/270 (4.1%)	5-year OS = 97% 10-year OS = 96%
Martin et al., (2010)	Royal Brisbane Hospital, QLD and Alfred Health, VIC	1989–2007	Stage I[1]	18	0/18	100%	0/18	5-year OS = 100%
Current study (2016)	Alfred Health, VIC	1992–2013	Stage I	106	1/106 (0.9%)	10-year RFS = 98%	2/106 (1.9%)	10-year OS = 97%
			Stage II	19	1/19 (5.3%)		3/19 (16%)	

[1]Patients with previous history of cryptochidism.

adverse effects from the radiation in the first decade, serving to remind us that PORT is a valid and effective option for men who cannot, or do not wish to be, managed with surveillance or chemotherapy. PORT has fallen into disfavour because of comparable disease control achieved with single-agent chemotherapy in Stage I disease, and the belief that this will not cause adverse effects in the way PORT did in the decades after treatment – though longer term adverse effects with single-agent chemotherapy are yet to be determined.

In our series, two patients (one Stage I and one Stage II) experienced disease relapse, both of which occurred within 1 year of completion of PORT. One of the patients had Stage 1 seminoma treated with PORT to the PA fields alone, and the pelvic relapse pattern observed in this case is consistent with what is known in the current literature. In the TE10 trial comparing radiation to the PA versus dog-leg field, Fossa et al. reported pelvic relapse in four patients in the PA only treatment arm, and none in the dog-leg field treatment arm.[16] In another series of 199 Stage I seminoma patients treated at the Mayo Clinic with a median follow-up of 13 years, there was only one patient with disease relapse in the pelvic region, who had radiation treatment limited to the PA region only.[26]

We reported seven SMs – pulmonary mesothelioma, melanoma, lower lip cancer, acute myeloid leukaemia, contralateral seminoma and two prostate cancers – in six patients in our series, with a 10-year estimated SMFS of 92.9%. Seminoma patients are at increased risk of SM, particularly at greater than 10 and 20 years after treatment, consequent to the effect of radiotherapy, chemotherapy and possibly shared risk factors in the carcinogenesis pathway.[4,6] In one of the largest multi-national studies of 22,424 seminoma patients with at least 10-year survival in the Nordic countries, Ontario and the US Surveillance, Epidemiology, and End Results (SEER) programme, Travis et al. reported a standardised incidence ratio (SIR) for second solid tumours of 2.0 (95% CI = 1.8–2.2) following radiotherapy alone, and SIR of 3.8 (95% CI = 2.2–6.0) following chemoradiotherapy.[6] Compared to the general population, seminoma survivors have 3.4 times increased risk of pulmonary mesothelioma (95% CI = 1.7–5.9), 1.4 times risk of prostate cancer (95% CI = 1.2–1.6) and 1.8 times risk of malignant melanoma (95% CI = 1.3–2.3).

In a similar international study, comprising data from 13 cancer registries, Richiardi et al. investigated the risk of secondary non-solid tumour and reported an SIR for myeloid leukaemia of 2.4 (95% CI = 1.4–3.8) among 16,603 seminoma patients.[4] In our series, we reported one incident of secondary AML. The patient was treated with high-dose chemotherapy and autologous BMT as well as PORT, adding to his risk of secondary AML. It has been reported in a recent study of the Australasian BMT Recipient Registry that BMT patients have significantly increased risk of AML compared to the general population (SIR = 20.6), and the risk is higher among male patients, those transplanted at a younger age, in the earlier BMT era, or in those with lymphoma or testicular cancer.[27] Multiple earlier studies have also pointed to the introduction of etoposide, with known leukemogenic potential,[28,29] as the main risk factors for development of secondary AML in testicular cancer patients.[30,31] In a matched case–control study of 36 patients with leukaemia and 106 controls, sampled from the same cohort of seminoma survivors in the Nordic/Ontario/SEER study, Travis et al. reported a threefold increased risk of leukaemia with radiotherapy treatment alone, while chemotherapy, either alone or in combination with

radiotherapy, was associated with fivefold increased risk of leukaemia.[32]

We also reported one incident of metachronous contralateral testicular seminoma, diagnosed approximately 6 years after the diagnosis of the first testicular seminoma. The patient had PORT to the PA nodes following the first radical orchidectomy, and was treated with two cycles of carboplatin following the contralateral radical orchidectomy. Testicular cancer patients are well recognised to be at increased risk of developing contralateral testicular seminomas. In the SEER study, Fossa et al. reported 1.9% (95% CI = 1.7–2.1%) in 15-year cumulative risk of metachronous contralateral testicular cancer,[33] while Schaapveld et al. reported a 20-year cumulative risk of 2.2% (95% CI = 1.8–2.8%) in another population-based study in the Netherlands.[34] The development of contralateral testicular cancer, as with undescended testis, is a component of testicular dysgenesis syndrome (TDS) as a result of disruption of embryonal programming and gonadal development.[35] This implies a shared underlying aetiology with the primary testicular cancer, and hence a metachronous contralateral testicular cancer should not be considered as a radiotherapy-induced SM.[36]

We observed one CV event and one GIT event. The CV event is unlikely to be secondary to PORT for seminoma given the short timeframe following PORT, and the patient's known cardiac history. While we acknowledge the possibility of under-reporting CV toxicities given our strict definition of CV toxicities for the study purpose, there is also a lack of consistency in the literature as to what entails CV toxicities following PORT for seminoma. Most studies included coronary artery diseases as a CV toxicity, however others also included congestive heart failure,[10] stroke, transient ischaemic attack and even peripheral vascular disease,[8] while some only reported on CV mortality.[9] In a large population-based study in the Netherlands involving more than 2000 testicular cancer patients, the 20-year actuarial risk of CV toxicities following PORT were reported to be as high as 18%[10]; however, it is important to note the study included patients treated in the 1960s and 1970s – often with larger radiation field, higher radiation dose and frequent use of prophylactic mediastinal irradiation.[10]

The men in our series are relatively young, with an average age of 36 and had a median follow-up of less than 8 years; hence, we might not be surprised by a low incidence (or lack) of CV events observed. Earlier studies have suggested that CV events following cardiac radiotherapy generally become evident beyond approximately 10–15 year follow-up.[8,9] In a single-institution study in the United States, Zagar et al. reported no increased cardiac mortality in the first 15 years follow-up following infra-diaphragmatic PORT for seminoma, but significantly increased cardiac mortality beyond 15 years.[9] Patients may also have had CV events managed at other hospitals, which were not documented in our medical records on follow-up. This is one of our limitations, due to the retrospective nature of this study.

On the other hand, one of the strengths of this study is the accuracy in the definition of survival and SM events since data linkage with the VCR ensures that we have captured all SM and deaths among our cohort of patients. While we could not discount the possibility of patients moving overseas, we believe that the VCR data linkage provides the most accurate available data on SM and deaths.

Conclusion

This study showed high rates of disease control for Stage I/II seminoma patients treated with PORT, and low incidence of SM within the first decade. While the late effects may start to accumulate in the next few decades, our results support the effectiveness and safety of PORT in selected Stage II patients, and in Stage I patients not suited for adjuvant chemotherapy or surveillance.

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Conflict of Interest

The authors declare no conflict of interest.

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