PAPER 6

How do the outcomes of radiation associated pelvic and sacral bone sarcomas compare to primary osteosarcomas following surgical resection?

Alexander L. Lazarides, MD,[1,2] Zachary DC Burke, MD,[1] Manit Gundavda, MD,[1] Rostislav Novak MD PhD, [1] Michelle Ghert MD,[3] David A Wilson MD,[4] Peter Rose MD,[5] Philip Wong MD [6], Anthony G. Griffin MSc,[1] Peter C Ferguson MD,[1] Jay S Wunder, MD, MSc[1], Matthew Houdek MD,[5*] Kim Tsoi, MD, PhD[1*]

1. University of Toronto Musculoskeletal Oncology Unit, Mount Sinai Hospital, Division of Orthopaedic Surgery, Department of Surgery, University of Toronto, Toronto, ON, Canada
2. Sarcoma Department, Moffitt Cancer Center, Tampa, FL
3. Musculoskeletal Oncology Unit, McMaster University, Hamilton, ON, Canada
4. Department of Orthopaedic Surgery, Dalhousie University, Halifax, NS, Canada
5. Department of Orthopaedic Surgery, Mayo Clinic, Rochester, MN, USA
6. Department of Radiation Oncology, University of Toronto, Toronto, ON, Canada

*Co-Senior Authors

Background:

Radiation associated sarcoma of the pelvis and/ or sacrum (RASB) is a rare but challenging disease process associated with a poor prognosis. To date, series are limited by small patient numbers; data to inform prognosis and the optimal management for these patients is needed. The purpose of the current study is to examine a patient population from tertiary sarcoma centers in North America that frequently treat RASB to analyze treatment outcomes. We hypothesized that patients with RASB would have worse oncologic and surgical outcomes than patients diagnosed with primary osteosarcoma or spindle cell sarcoma of the pelvis (POPS).

Methods:

This was a retrospective, multi-institution, comparative cohort analysis. We reviewed all surgically treated patients diagnosed with a localized radiation-associated pelvic and sacral bone sarcoma between January 1st, 1985, and January 1st, 2020. Radiation-associated sarcomas were defined as a histologically-confirmed bone sarcoma of the pelvis in a previously irradiated field with a minimum 3-year interval between radiation for the primary tumor and the sarcoma diagnosis. The tumor histology was required to be unique from the original cancer diagnosis. We also identified a comparison group during the same time interval that included all patients diagnosed with a localized, primary pelvic and/ or sacral osteosarcoma or spindle cell sarcoma of bone since they would be eligible for treatment with osteosarcoma-type chemotherapy. We only included patients who underwent surgical resection with curative intent and, for survivors, had at least 12 months follow-up. Exclusion criteria included non-operative treatment,

palliative surgical treatment, metastases at diagnosis and soft tissue sarcomas invading bone. The primary outcome measure was disease-specific survival (DSS) following surgical resection.

Results:

There were 35 patients with localized radiation associated sarcoma of the bony pelvis and/or sacrum (RASB) and 73 patients with primary localized osteosarcoma or spindle cell sarcoma of the pelvis and/or sacrum (POPS) and treated with surgical resection. Patients with RASB were older than those with POPS (52 years vs. 37 years, **p<0.001**). Patients with RASB were less likely to receive chemotherapy (71% for RISB vs. 90% for POPS, **p=0.01**), though there was no difference in utilization of perioperative radiation (p=0.51). Patients with RASB were more likely to receive dual agent chemotherapy (41%) while patients with POPS were most commonly treated with three agents (i.e. high-dose methotrexate, Adriamycin, cisplatin; 54%) **(p<0.001)**. For the patients that began chemotherapy, those with RASB were less likely to receive five or more treatment cycles than patients with POPS (31% vs 69%, **p=0.009**).

There was no difference in the rate of limb salvage between patients with RASB (78%) or POPS (68%). There was also no difference in the rate of margin positive surgery (19% vs. 14%) or surgical complications (78% vs 65%) between patients with RASB and POPS.

16% of patients with RASB died in the perioperative period (within 90 days of surgery) as compared to 4% with POPS (**p= 0.03**). Five- year DSS (31% vs. 54% **p=0.02**) was worse for patients with RASB vs. POPS. When controlling for chemotherapy use, however, RASB was no longer associated with worse 5-year survival (HR 1.4 [0.77-2.55], p=0.27). Only 20% of patients with a RASB remained alive and disease free after 3 years. For patients undergoing surgical resection of localized disease, there was no difference in 5-year local recurrence free survival (LRFS) or metastasis free survival (MFS) for patients with RASB vs. POPS. Patients with a RASB who developed a local recurrence, though, had worse 5-year DSS than those with POPS (0% vs. 33%, **p=0.013)**.

Discussion:

POPS and RASB involving the pelvis and sacrum present challenging disease processes and their oncologic outcomes are similarly poor. However, the data presented here shows that perioperative mortality and disease specific survival for patients with RASB is even worse than for patients with POPS. While surgery can result in a favorable curative outcome for a small subset of patients, surgical treatment is fraught with complications. As such, careful counseling is necessary to reach a patient-centered decision regarding the suitability and feasibility of proceeding with surgical treatment of these tumors.

Table 1. Patient, tumor, and treatment differences between radiation associated sarcoma of the pelvis and sacrum and primary osteosarcoma/ spindle cell sarcoma

	Radiation Associated Sarcoma of Pelvis (n=35)	**Primary Osteosarcoma/ Spindle Cell Sarcoma of Pelvis (n=73)**	
	n (%)	**n (%)**	**p-value**[#]
Median Age (years)	57 (14-84)	38 (12-81)	**<0.001**
Gender			
Male	21 (58)	42 (58)	0.94
Female	15 (42)	31 (42)	
Location			
Pelvis	19 (54)	50 (68)	**<0.001**
Sacrum	15 (43)	10 (14)	
Combined	1 (3)	13 (18)	
Median Tumor Size	9 (3-20)	11 (3-28)	0.1
Grade			0.27
Intermediate	4 (12)	4 (6)	
High/ undifferentiated	30 (88)	68 (94)	
Chemotherapy			**0.011**
Yes	25 (71)	66 (90)	
No	10 (29)	7 (10)	
Radiotherapy			0.51
Yes	6 (17)	9 (12)	
No	29 (83)	64 (88)	
Type of Surgery			0.16
Limb Salvage	28 (80)	49 (67)	
Amputation	7 (20)	24 (33)	
Type of Closure			0.18

Primary	34 (97)	66 (90)	
Flap	1 (3)	7 (10)	
Margin Status			0.35
Positive	6 (18)	8 (11)	
Negative	28 (82)	65 (89)	
Complications			0.28
Yes	29 (78)	55 (65)	
No	8 (22)	39 (35)	
Perioperative Death within 90 days of Surgery			**0.03**
Yes	6 (17)	3 (4)	
No	29 (83)	70 (96)	
Median time to local recurrence (months)	5 (3- 21.1)	14 (2- 200)	0.07
Median time to metastasis (months)	8 (3.5- 52.1)	11 (3- 141)	0.69
Median time to death (months)	11 (0-50)	13 (0-57.3)	0.53

#Significance was denoted for $p<0.05$

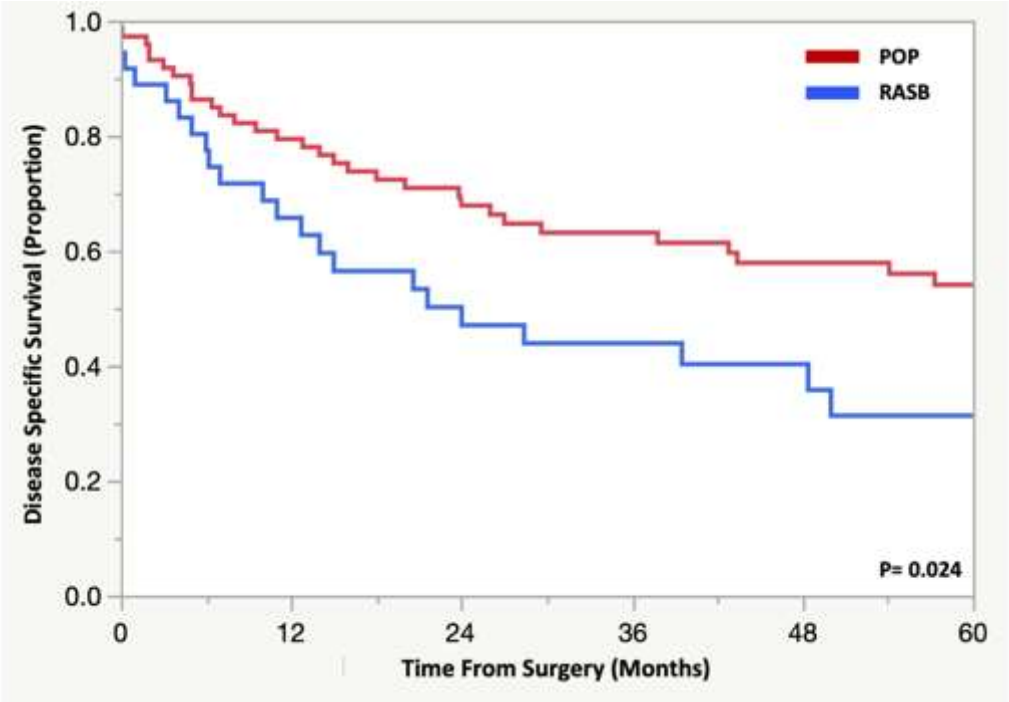

Figure 1. Kaplan Meier analysis for overall disease specific survival between a) patients with a radiation associated sarcoma of the pelvis/ sacrum and a primary osteosarcoma or spindle cell sarcoma. Kaplan Meier analysis for disease specific survival between patients with a radiation associated sarcoma of the pelvis/sacrum and a primary osteosarcoma or spindle cell sarcoma.