



The Importance of the Margin of Resection and Use of Radiotherapy in Retroperitoneal Liposarcoma

Michael J. Littau, BA¹; Sujay Kulshrestha, MD²; Corinne Bunn, MD²; Sonya Agnew, MD^{1,2,3}; Patrick Sweigert, MD²; Fred A. Luchette, MD, MSc^{1,2,3}; Marshall S. Baker, MD, MBA^{1,2,3}

¹Loyola University Chicago, Stritch School of Medicine; ²Department of Surgery, Loyola University Medical Center; ³Edward Hines Jr. Veterans Administration Medical Center

Introduction

- More than 50% of all retroperitoneal sarcomas are liposarcomas
- Optimal treatment is margin-negative resection
- Prior studies evaluating the use of radiotherapy (RT) have been underpowered retrospective series including multiple histologies
- Role of RT in these tumors is unclear

Objectives

- Evaluate overall survival benefit of margin-negative resection
- Evaluate overall survival benefit from radiotherapy, in either the adjuvant or neoadjuvant setting
- Identify factors associated with overall survival
- Identify factors associated with use of radiotherapy

Methods

- National Cancer Database (NCDB) 2004 to 2016
- Clinical stage I-III retroperitoneal liposarcoma
- Three size categories: small (< 5cm), intermediate (5-10cm) and large (> 10cm)
- Multivariable logistic regression (MVR) and Cox proportional hazards modelling

Table 1: MVR Predicting Use of Radiotherapy

Characteristic	Neoadjuvant OR (95% CI)	p value	Adjuvant OR (95% CI)	p value
Tumor size (ref = small, < 5cm)				
Intermediate, 5-10cm	1.23 (0.6, 2.73)	0.58	1.7 (1.16, 2.52)	0.01
Large, > 10cm	1.95 (13.07, 4.00)	0.04	0.85 (0.61, 1.23)	0.38
Surgical Margins (ref = R0)				
R1	N/A	N/A	1.94 (1.58, 2.36)	< 0.01
R2	N/A	N/A	1.56 (0.91, 2.56)	0.09
Grade (ref = well differentiated)				
Moderately differentiated	1.35 (0.88, 2.02)	0.16	2.39 (1.81, 3.15)	< 0.01
Poorly differentiated	1.37 (1.01, 1.85)	0.04	2.58 (2.10, 3.17)	< 0.01
Undifferentiated	1.65 (1.17, 2.3)	< 0.01	2.28 (1.75, 2.95)	< 0.01
Hospital Case Volume (ref = < 25%)				
25-50%	1.05 (0.63, 1.77)	0.86	0.81 (0.63, 1.03)	0.08
50-75%	1.81 (1.09, 3.07)	0.03	0.63 (0.52, 0.90)	0.01
> 75%	3.56 (2.09, 6.22)	< 0.01	0.36 (0.26, 0.51)	< 0.01

Table 2: Cox Proportional Hazards Model by Tumor Size

Characteristic	< 5cm HR (95% CI)	p value	5-10cm HR (95% CI)	p value	> 10cm HR (95% CI)	p value
Radiotherapy Sequence (ref = no RT)						
Pre-op RT	1.63 (0.56, 4.79)	0.37	1.08 (0.51, 2.32)	0.84	0.94 (0.73, 1.20)	0.61
Post-op RT	0.53 (0.25, 1.12)	0.10	1.11 (0.78, 1.58)	0.55	0.76 (0.64, 0.90)	< 0.01
Surgical Margins (ref = R0)						
R1	2.29 (1.17, 4.47)	0.02	1.53 (1.06, 2.20)	0.02	1.29 (1.12, 1.50)	< 0.01
R2	5.65 (1.34, 23.74)	0.02	0.75 (0.22, 2.51)	0.64	2.64 (1.96, 3.55)	< 0.01
Grade (ref = well differentiated)						
Moderately differentiated	3.70 (1.62, 8.44)	< 0.01	1.12 (0.61, 2.08)	0.71	1.58 (1.25, 1.98)	< 0.01
Poorly differentiated	3.84 (1.99, 7.39)	< 0.01	2.76 (1.89, 4.03)	< 0.01	3.06 (2.64, 3.55)	< 0.01
Undifferentiated	1.59 (0.64, 3.96)	0.32	2.40 (1.58, 3.66)	< 0.01	2.75 (2.32, 3.26)	< 0.01
Co-morbidity Index (ref = 0)						
1	0.91 (0.45, 1.84)	0.79	1.05 (0.70, 1.58)	0.81	1.18 (1.01, 1.37)	0.03
2	4.58 (1.44, 14.57)	0.01	1.51 (0.79, 2.89)	0.21	1.46 (1.12, 1.88)	< 0.01
3+	22.90 (6.67, 78.55)	< 0.01	3.01 (1.33, 6.84)	0.01	1.96 (1.30, 2.97)	< 0.01
Income Quartile (ref = < 25%)						
25-50%	0.58 (0.22, 1.54)	0.27	0.95 (0.59, 1.54)	0.83	0.86 (0.71, 1.05)	0.15
50-75%	0.64 (0.26, 1.57)	0.33	0.76 (0.46, 1.26)	0.29	0.78 (0.64, 0.95)	0.01
> 75%	0.82 (0.36, 1.85)	0.63	0.66 (0.43, 1.01)	0.05	0.76 (0.63, 0.92)	< 0.01
Age (ref = < 50 years)						
50-70 years	3.18 (0.95, 10.62)	0.06	1.64 (0.87, 3.08)	0.13	1.38 (1.09, 1.75)	0.01
> 70 years	7.19 (1.95, 26.46)	< 0.01	3.56 (1.78, 7.10)	< 0.01	2.70 (2.07, 3.54)	< 0.01

Results

- 4,376 patients met inclusion criteria
 - < 5cm: 265 patients
 - 5-10cm: 594 patients
 - > 10cm: 3,341 patients
- Factors significantly associated with the likelihood of receiving neoadjuvant radiotherapy included: large (> 10cm) tumor size, advanced grade, and hospital case volume (Table 1)
- Factors significantly associated with the likelihood of receiving adjuvant radiotherapy included: intermediate (5-10cm) tumor size, positive resection margins, advanced grade, and hospital case volume (Table 1)
- Factors decreasing likelihood of margin-negative resection include advanced age, advanced grade, and large (> 10cm) tumor size (data not shown, no factors increased the likelihood)
- Factors associated with overall survival included: adjuvant radiotherapy (only for tumors > 10cm), surgical margins, advanced grade, Charlson-Deyo Comorbidity Index, patient income, and advanced age (Table 2)

Conclusions

- Retrospective study design subject to selection and omitted variable biases
- Margin negative resection was associated with improved survival across all tumor size categories
- Adjuvant radiotherapy was associated with improved survival only for large (> 10cm) tumors
- Neoadjuvant radiotherapy was not associated with survival
- Hospitals with a higher case volume were more likely to utilize radiotherapy in the neoadjuvant, rather than adjuvant, setting