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Recurrence patterns after resection of retroperitoneal sarcomas: An eight-institution study from the US Sarcoma Collaborative

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Abstract

Background and Objectives: Resection of primary retroperitoneal sarcomas (RPS) has a high incidence of recurrence. This study aims to identify patterns of recurrence and its impact on overall survival.

Methods: Adult patients with primary retroperitoneal soft tissue sarcomas who underwent resection in 2000–2016 at eight institutions of the US Sarcoma Collaborative were evaluated.

Results: Four hundred and ninety-eight patients were analyzed, with 56.2% (280 of 498) having recurrences. There were 433 recurrences (1–8) in 280 patients with 126 (25.3%) being locoregional, 82 (16.5%) distant, and 72 (14.5%) both locoregional and distant. Multivariate analyses revealed the following: Patient age $P = .0002$, tumor grade ($P = .02$), local recurrence (P

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CONFLICT OF INTERESTS

The authors declare that there is no conflict of interests.

DATA ACCESSIBILITY

Data are available upon request from the author.

= .0003) and distant recurrence ($P < .0001$) were predictors of disease-specific survival. The 1-, 3-, and 5-year survival rate for patients who recurred vs not was 89.6% (standard error [SE] 1.9) vs 93.5% (1.8), 66.0% (3.2) vs 88.4% (2.6), and 51.8% (3.6) vs 83.9% (3.3), respectively, $P < .0001$. Median survival was 5.3 years for the recurrence vs 11.3+ years for the no recurrence group ($P < .0001$). Median survival from the time of recurrence was 2.5 years.

Conclusions: Recurrence after resection of RPS occurs in more than half of patients independently of resection status or perioperative chemotherapy and is equally distributed between locoregional and distant sites. Recurrence is primarily related to tumor biology and is associated with a significant decrease in overall survival.

Keywords

distant relapse; local relapse; overall survival; predictors

1 | INTRODUCTION

Retroperitoneal sarcomas (RPS) are a rare and heterogeneous group of solid tumors. Complete surgical resection is the cornerstone of management. Multiple studies have documented a significant risk of recurrence, even after obtaining negative margins, ranging from local, distant or combined recurrence (CR) and such relapses have been shown to significantly worsen survival.^{1,2}

Sarcomas represent a diagnostic and therapeutic challenge in surgical pathology with more than 100 different subtypes and variable tumor biology amongst each histiotype. Given their rare nature and pathologic variability, mainly select large single-institution studies (eg, MSKCC, MDACC, Milan group) or multi-institutional collaboratives have investigated certain fundamental questions regarding their management.^{3,4} There is significant debate regarding the ideal surgical management, compartmental or simple resection with negative margins to achieve long-term, recurrence-free survival (RFS).⁵ The role of radiation therapy or chemotherapy, either in the neoadjuvant or adjuvant setting, has not been definitively characterized in terms of its implications in disease recurrence and ultimately survival.^{6,7}

The current study aims to identify patterns of recurrence, its impact on survival as well as predictors of locoregional and distant recurrence (DR) using the United States Sarcoma Collaborative (USSC) database which represents a data set from eight large experienced centers.

2 | MATERIALS AND METHODS

All patients with RPS that underwent surgical resection from January 2000 to April 2016 in the USSC were retrospectively reviewed. This Collaborative is compiled of eight high-volume academic centers and it was approved by each respective Institutional Review Board (Wake Forest University, Winston-Salem, NC; Winship Cancer Institute, Emory University, Atlanta, GA; Stanford University, Palo Alto, CA; The Ohio State University, Columbus, OH; Medical College of Wisconsin, Milwaukee, WI; University of Chicago, Chicago, IL; Washington University, St. Louis, MO; University of Wisconsin, Madison, WI). Patients

with desmoid tumors, multifocal or metastatic disease at presentation, palliative intent resection, or incomplete survival data were excluded. Patients who developed recurrent disease were analyzed and grouped into a local recurrence (LR), DR, and, CR subgroup based on the pattern of recurrence.

Demographic and clinicopathologic characteristics were analyzed including age, sex, race, functional status, tumor size, histologic types, tumor grade, presence of necrosis, lymphovascular invasion, adjacent organ involvement, and lymph node involvement.

Histopathologic type, TNM grade according to 7th edition American Joint Committee on Cancer (AJCC) staging system, French Federation of Cancer Centers Sarcoma Group (FNCLCC) grade were documented.^{8,9} A combined grade variable was utilized and classified all tumors coded as high-grade, G3, or G2 as high-grade; all tumors coded as low-grade, G1, or both low-grade and G2 as low-grade. On the basis of the histopathology-specific grading guidelines in the 7th and 8th editions of the AJCC Staging Manuals, missing grades for certain subtypes were automatically given high-grade (eg, dedifferentiated liposarcoma) or low-grade (eg, well-differentiated liposarcoma) designations. The completeness of resection was classified as microscopically complete (R0), microscopically incomplete (R1), and macroscopically incomplete (R2).

2.1 | Statistical analysis

The primary outcomes included disease-specific survival (DSS; defined as time from diagnosis to date of death as a result of disease), time to LR (defined as time from date of surgery to date of first LR for patients with complete resections only), and time to DR or CR (defined as time from date of diagnosis to date of first DR or CR). Patients who died of disease without a date of recurrence were considered to have recurred at the midway point between the dates of surgery and death. Proportional hazards regression models were created first for univariate analyses; multivariable models were created and included all variables significant at $P < .20$ in single variable models. Hazard ratios and corresponding 95% confidence intervals were calculated for all variables where $P < .10$. Statistical significance was assumed for all variables with $P < .05$. The Kaplan-Meier method was used to estimate survival and recurrence-free time. SAS (version 9.4; Cary, NC) was used for all analyses.

3 | RESULTS

3.1 | Basic clinicopathologic characteristics

Four hundred ninety-eight RPS patients were included in this study, 218 (43.8%) had no recurrence and 280 (56.2%) patients had 433 recurrences, ranging from one to eight recurrences per patient. Of those, 201 (46.4%) were LR, 92 (21.2%) DR and 140 (32.3%) CR. There was no significant difference in median age (59.8 vs 60.2; $P = .24$), sex (47.9% vs 41.7% male; $P = .17$), race (73.8% vs 72.7% Caucasian; $P = .88$), or functional status (97.7% vs 96.6% independent functional status; $P = 0.47$) in the recurrence vs no recurrence group, respectively (Table 1). Median follow-up was 4.3 years.

There was a statistically significant difference in the resection status between the two groups with more R0 resections in the no recurrence group, 64.8% vs 55.1%; $P = .05$. More patients

had high-grade tumors 68.8% vs 52.2%, $P = .01$ and necrosis noted 68.8% vs 55.3%, $P = .01$ in the recurrence group. There was no difference in the tumor size ($P = .06$), histologic subtype ($P = .12$), evidence of lymphovascular invasion ($P = .06$), organ invasion/adherence ($P = .13$), or lymph node positivity between the two groups ($P = .14$). In terms of neoadjuvant treatments, more patients in the recurrence group had chemotherapy, $P = .04$ whereas there was no difference in radiation therapy rate, $P = .59$ (Table 1).

3.2 | LR group

There were 126 patients who had 201 LR. Median age was 60 years; 64 (50.8%) were male; predominantly Caucasian, 95 (75.4%); and 116 (98.3%) had good functional status. Ninety-eight (77.8%) underwent surgical resection, 27 (21.4%) had chemotherapy, and 42 (33.3%) had radiation treatments for the recurrence (Table 2). Of those, 75 recurrences were noted in 49 (39.5%) patients who underwent R0 resections, 106 recurrences in 67 (54%) patients after R1 resections, 17 recurrences in eight (6.5%) patients after R2 resections, three recurrences in two (1.6%) patients where resection status was not available. The majority of LR were liposarcomas, 35 (27.8%) well-differentiated, 29 (23%) dedifferentiated, 10 (7.9%) pleomorphic, and 10 (7.9%) mixed cell/not otherwise specified.

On multivariate analysis of patients who had a complete resection (R0/R1), nodal disease (hazard ratio [HR] 3.89; $P = .0003$), and tumor rupture (HR 2.67; $P = .01$) were predictors of locoregional recurrence (Table 3). Of the remaining variables, even though histologic subtype was not statistically significant ($P = .18$), leiomyosarcomas had a lower rate of LR compared to dedifferentiated liposarcoma, pleomorphic liposarcoma, and undifferentiated pleomorphic sarcoma (HR 0.45, 0.47, and 0.36), respectively. Similarly, evidence of organ invasion, on pathologic analysis, showed a trend towards LR (HR 1.53; $P = .074$).

The 1-, 3-, and 5-year DSS estimates, from the time of initial diagnosis, for the LR group were 94.2%, 73.2%, and 59.8%, respectively. Median DSS was 6.8 years.

The 1-, 3-, and 5-year DSS from the time of LR was 80.3%, 46.5%, and 29.8%, with a median of 2.7 years.

3.3 | DR group

Eighty-two patients were included in the DR only group with 92 recurrences noted. The majority were leiomyosarcomas in 41 (50%) patients; median age was 64 years; 27 (32.9%) male; 54 (66.7%) Caucasian; and 77 (97%) were functionally independent. Surgical resection was performed in 56 (68.3%), while 37 (45.1%) had chemotherapy and 36 (43.9%) had radiation treatments (Table 2). Of those 58 occurred in 55 (67.9%) patients after R0 resection, 28 in 24 (29.6%) patients after R1 resection, five in two (5.6%) patients after an R2 resection and one recurrence in one patient (1.2%) whose resection status was not available.

After univariate and multivariate analysis for predictors of DR, histologic type ($P = .02$) was the only significant predictor (Table 3). Leiomyosarcomas have increased preponderance for DR compared to well-differentiated liposarcomas and mixed type liposarcomas; 15.26 (3.13, 74.48) and 3.6 (1.27, 10.22), respectively. Dedifferentiated liposarcomas, round cell/myxoid

liposarcomas, and pleomorphic liposarcomas also had statistically significant more DRs compared to well-differentiated liposarcomas; 8.91 (1.72, 46.06), 11.24 (1.86, 67.82) and 11.65 (2.07, 65.5). Tumor grade approached statistical significance with a $P = .08$.

The 1-, 3-, and 5-year DSS estimates, from the time of initial diagnosis, for the DR group were 89.7% (SE 3.5), 57.8% (6.2), and 50.7% (6.7), respectively. Median DSS was 5.8 years.

The 1-, 3-, and 5-year DSS from the time of DR was 75.0% (3.8), 41.9% (4.9), and 27.8% (4.9) with a median of 2.4 years.

For the largest histologic subgroups, median time to DR for undifferentiated pleomorphic sarcomas was 2.9 years, for leiomyosarcomas 3.6 years, and for liposarcomas more than 5 years (median not reached).

3.4 | CR group

Seventy-two patients had a combination of 140 LR and DRs. Forty-three (59.7%) were male; median age was 55.6 years; predominantly Caucasian, 57 (79.2%); with independent functional status 64 (97%). Resection was performed for 56 (77.8%), chemotherapy was administered in 32 (44.4%) and radiation was given for 26 (36.1%) of the recurrences (Table 2). Of the CRs, 77 occurred after R0 resection in 48 (66.7%) patients, 47 after R1 resection in 19 (26.4%) patients, 15 after R2 resection in four (5.6%) patients and one in one (1.4%) patient whose resection status was unknown. There was some variability in the histologic subtypes including 18 (25%) leiomyosarcomas, 14 (19.4%) dedifferentiated liposarcomas, and seven (9.7%) undifferentiated pleomorphic sarcomas.

We performed univariate and multivariate analyses to identify predictors for combined (local and distant) recurrence (Table 4). Tumor grade ($P = .006$) was the only predictor of CR with high-grade tumors having a higher rate of CR compared to low-grade; 2.29 (1.34, 3.92).

The 1-, 3-, and 5-year DSS estimates for the CR group, from the time of initial diagnosis, were 75.1% (SE 4.4), 53.9% (5.2), and 35% (5.2). Median DSS was 3.3 years.

The 1-, 3-, and 5-year DSS from the time of CR was 70.3% (5.7), 42.2% (6.5), and 27.2% (6.5) with a median of 2.4 years.

3.5 | Disease-specific survival

Univariate analysis was performed including age, sex, race, functional status, tumor size, histologic type, final margin status, tumor grade, node status, LR, DR, other organ involvement, tumor rupture, neoadjuvant and adjuvant radiation, and chemotherapy.

Patient age ($P = .0002$), tumor grade ($P = .02$), LR ($P = .0003$), and DR ($P < .0001$) were independent predictors of DSS (Table 4).

The 1-, 3-, and 5-year DSS, from the time of initial diagnosis, for patients who recurred vs not was 89.6% (SE 1.9) vs 93.5% (1.8), 66.0% (3.2) vs 88.4 (2.6), and 51.8% (3.6) vs 83.9

(3.3), $P < .0001$, respectively. Median DSS was 5.3 years for the recurrence vs 11.3+ years for the no recurrence group ($P < .0001$).

Median DSS after any type of recurrence, from the time of recurrence, was 2.5 years, with 1-, 3-, and 5-year survival being 77.6% (2.8), 46% (3.8), and 31.4% (4.0), respectively.

For our overall cohort, median locoregional RFS was 4.7 years, with 82.9% (SE 1.9), 60.2% (SE 2.7), and 48.2% (SE 3.1) recurrence-free at 1-, 3-, and 5 years, respectively. Median DR free survival was 9.5 years, with 81.0% (SE 1.9), 66.0% (2.5), and 57.8% (2.9) recurrence-free at 1-, 3-, and 5 years, respectively.

Median overall survival for the key histologic subtypes was 11.8 years for well-differentiated liposarcomas, 7.2 years for leiomyosarcomas, 4.2 years for dedifferentiated liposarcomas and 2.8 years for undifferentiated pleomorphic liposarcomas.

4 | DISCUSSION

The impact of recurrence to the oncologic outcomes after RPS resection is well documented in the literature, with significantly decreased survival in patients who suffer a recurrence.^{1,2,10} In this cohort, there was a statistically significant decrease in DSS for all types of recurrences with age, tumor grade, and presence of recurrence being significant predictors of survival. When the different subgroups were analyzed separately, certain histologic types, tumor invasion, nodal involvement, and tumor rupture were associated with LR for patients who underwent complete resection. Histologic type was the only predictor of DR whereas tumor grade was the only predictor of CR. Median survival was decreased by half for the recurrence group compared to the no recurrence group.

Both LR and DR were identified as independent predictors of survival on multivariate analysis, together with age and tumor grade. DSS from the time of diagnosis for the LR group was 6.8 years, which compares favorably with the median DSS for the DR and CR groups, 5.8 and 3.3 years. However, DSS, when measured from the time of recurrence, was similar for the LR, DR, and CR group were 2.7, 2.4, and 2.4 years, respectively; similar to what has been reported previously in the literature.^{1,10} Of the patients who underwent surgery for locoregional recurrence, the median re-recurrence interval was 2.2 years, with 12% of patients recurrence-free at 9 years. These results demonstrate that the better prognosis associated with LR does not persist with longer follow-up and cures are rare for any type of recurrence.^{1,10}

Histologic subtype was a predictor of both LR and DR as shown in previous studies.^{11–13} Both overall survival and RFS showed significant differences. When analyzed per histopathology, there are significant differences in overall survival and RFS, demonstrating a wide spectrum, with well-differentiated liposarcomas having median RFS of 4.3 years but overall survival of 11.8 years, while undifferentiated pleomorphic sarcomas had an RFS of 1 year with overall survival of 2.8 years. It is the biologic behavior as determined by the histologic subtype and tumor grade that appear to better determine the disease course. Next-generation sequencing and molecular targeting hold promise for targeted therapies tailored on the basis of specific biologic alterations.¹⁴

The optimal surgical approach to achieve surgical control of RPS is still debatable with some groups reporting improved outcomes with compartmental resections.^{5,15} In this cohort, tumor rupture and adjacent organ invasion were shown to be independent predictors of recurrence demonstrating the importance of an adequate oncologic resection at the initial operation without pursuing radical compartmental resections.¹⁶ Radiation therapy, either in the neoadjuvant or adjuvant setting has been studied in multiple retrospective reports with variable results.^{7,17,18} There has been an increase in the use of radiation therapy largely due to data published on extremity sarcomas. In our cohort, radiation therapy did not correlate with improved survival or decreased recurrence. Its role needs to be better delineated, especially in the absence of level I data. Toward this goal, the results of the first randomized clinical trial looking at the role of preoperative radiation therapy vs surgery alone in RPS (STRASS trial) are heavily anticipated.¹⁹

Limitations of this study include the retrospective nature of the review. Further, the variability of pathologic interpretation even amongst expert pathologists is inherent to any multi-institutional collaborative effort such as the present. Individual institutional practices pertaining to the multidisciplinary care of RPS also add to the complex decision process in the management of those cases. Our cohort of multiple academic institutions represents a more broad perspective into the management of those complex cases compared to a single center study. Furthermore, outcomes described in this study are likely not transferrable to low volume centers as was shown by recent studies investigating this question.^{20,21}

5 | CONCLUSIONS

This multi-institutional study represents one of the largest contemporary series looking at recurrences after resection of RPS. Tumor grade is a key determinant of overall prognosis and histologic type is a significant predictor of recurrence of any type. Chemotherapy and radiation in the adjuvant or neoadjuvant setting were not shown to be significant in predicting recurrences or significantly affecting survival. The significance of an adequate oncologic resection was underlined by the significance of negative margin and tumor rupture as predictors of LR.

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TABLE 1

Clinicopathologic characteristics

	Total	No recurrence	Recurrence	P values
Age, median (IQR)	60 (21.1)	60.2 (21.7)	59.8 (19.7)	.24
Sex, male	225 (45.2)	91 (41.7)	134 (47.9)	.17
Race				
White	363 (73.3)	157 (72.7)	206 (73.8)	.88
Black	53 (10.7)	26 (12)	27 (9.7)	
Latino	31 (6.3)	15 (6.9)	16 (5.7)	
Asian	20 (4)	7 (3.2)	13 (4.7)	
Other	6 (1.2)	2 (0.9)	4 (1.4)	
N/A	22 (4.4)	9 (4.2)	13 (4.7)	
Functional status				
Independent	457 (97.2)	200 (96.6)	257 (97.7)	.47
Dependent	13 (2.8)	7 (3.4)	6 (2.3)	
Tumor size, median (IQR)	13.8 (13)	12.5 (13)	14.6 (14)	.06
Histology				
Leiomyosarcoma	131 (26.3)	58 (26.6)	73 (26.1)	.12
Dedifferentiated liposarcoma	72 (14.5)	22 (10.1)	50 (17.9)	
Well-differentiated liposarcoma	82 (16.5)	42 (19.3)	40 (14.3)	
Pleomorphic liposarcoma	25 (5)	7 (3.2)	18 (6.4)	
Undifferentiated pleomorphic sarcoma	41 (8.2)	17 (7.8)	24 (8.6)	
Mixed type/NOS cell liposarcoma	30 (6)	15 (6.9)	15 (5.4)	
Sarcoma, other	96 (19.3)	48 (22)	48 (17.1)	
Sarcoma, NOS	21 (4.2)	9 (4.1)	12 (4.3)	
Final resection status				
R0	288 (59.3)	136 (64.8)	152 (55.1)	.05
R1	171 (35.2)	61 (29)	110 (39.9)	
R2	27 (5.6)	13 (6.2)	14 (5.1)	
Combined grade				
Unspecified	43 (9.1)	22 (10.6)	21 (7.9)	.01
Low-grade	139 (29.4)	77 (37.2)	62 (23.3)	

	Total	No recurrence	Recurrence	P values
High-grade	291 (61.5)	108 (52.2)	183 (68.8)	
Necrosis	231 (62.9)	88 (55.3)	143 (68.8)	.01
Lymphovascular invasion	30 (12.2)	8 (7.6)	22 (15.6)	.06
Other organ involvement				
None	250 (62.3)	119 (67.6)	131 (58.2)	.13
Adherent	72 (18)	29 (16.5)	43 (19.1)	
Invading	79 (19.7)	28 (15.9)	51 (22.7)	
Lymph node positive	18 (11.5)	4 (6.7)	14 (14.4)	.14
Neoadjuvant chemotherapy	31 (6.3)	8 (3.7)	23 (8.3)	.04
Neoadjuvant radiotherapy	62 (12.4)	25 (11.5)	37 (13.2)	.59

Abbreviations: IQR, interquartile range; NOS, not otherwise specified.

TABLE 2

Clinicopathologic characteristics for study groups

	LR (n = 126)	DR (n = 82)	CR (n = 72)	No recurrence (n = 218)
Histology				
Leiomyosarcoma	14 (11.1)	41 (50)	18 (25)	58 (26.6)
Dedifferentiated liposarcoma	29 (23)	7 (8.5)	14 (19.4)	22 (10.1)
Mixed type/NOS cell liposarcoma	10 (7.9)	1 (1.2)	4 (5.6)	15 (6.9)
Pleomorphic liposarcoma	10 (7.9)	2 (2.4)	6 (8.3)	7 (3.2)
Well-differentiated liposarcoma	35 (27.8)	2 (2.4)	3 (4.2)	42 (19.3)
Undifferentiated pleomorphic sarcoma	10 (7.9)	7 (8.5)	7 (9.7)	17 (7.8)
Sarcoma, NOS	4 (3.2)	5 (6.1)	3 (4.2)	9 (4.1)
Sarcoma, other	14 (11.1)	17 (20.7)	17 (23.6)	48 (22)
Male	64 (50.8)	27 (32.9)	43 (59.7)	91 (41.7)
Age, median (IQR)	60.0 (20.8)	64.3 (23.0)	55.6 (19.1)	60.2 (21.7)
Race				
Caucasian	95 (75.4)	54 (66.7)	57 (79.2)	157 (72.7)
African American	7 (5.6)	14 (17.3)	6 (8.3)	26 (12)
Latino	7 (5.6)	3 (3.7)	6 (8.3)	15 (6.9)
Asian	6 (4.8)	5 (6.2)	2 (2.8)	7 (3.2)
Other	2 (1.6)	2 (2.5)	0	2 (0.9)
N/A	9 (7.1)	3 (3.7)	1 (1.4)	9 (4.2)
Functional status				
Independent	116 (98.3)	77 (97.5)	64 (97)	200 (96.6)
Dependent	2 (1.7)	2 (2.5)	2 (3.0)	7 (3.4)
Tumor size, median (IQR)	17.5 (16)	11.8 (11)	12.3 (12)	12.5 (13)
Final resection status				
R0	49 (39.5)	55 (67.9)	48 (67.6)	136 (64.8)
R1	67 (54.0)	24 (29.6)	19 (26.8)	61 (29.0)
R2	8 (6.5)	2 (2.5)	4 (5.6)	13 (6.2)
Combined grade				
Unspecified	12 (9.8)	4 (5.1)	5 (7.8)	22 (10.6)

	LR (n = 126)	DR (n = 82)	CR (n = 72)	No recurrence (n = 218)
Low-grade	42 (34.1)	9 (11.4)	11 (17.2)	77 (37.2)
High-grade	69 (56.1)	66 (83.5)	48 (75)	108 (52.2)
Necrosis	46 (55.4)	52 (81.3)	45 (73.8)	88 (55.3)
Lymphovascular invasion	3 (5.1)	13 (29.5)	6 (15.8)	8 (7.6)
Other organ involvement				
None	57 (56.4)	41 (67.2)	33 (52.4)	119 (67.6)
Adherent	26 (25.7)	6 (9.8)	11 (17.5)	29 (16.5)
Invading	18 (17.8)	14 (23)	19 (30.2)	28 (15.9)
Lymph node positive	4 (11.1)	1 (4.5)	9 (23.1)	4 (6.7)
Multifocal	29 (23.0)	36 (43.9)	30 (41.7)	0
Surgery	98 (77.8)	56 (68.3)	56 (77.8)	218 (100)
Chemotherapy	27 (21.4)	37 (45.1)	32 (44.4)	28 (12.8)
Radiation therapy	42 (33.3)	36 (43.9)	26 (36.1)	55 (25.2)

Abbreviations: CR, combined recurrence; DR, distant recurrence; LR, local recurrence; N/A, not available; NOS, not otherwise specified.

TABLE 3

Multivariate analyses for local and distant recurrence

Local recurrence Multivariate analysis			Distant recurrence Multivariate analysis		
	P value	HR (if $P < .10$)	95% CI	P value	HR (if $P < .10$)
Histology	.18			.024	
LMS vs DDLPS		0.45	0.25–0.79		3.6
LMS vs PLPS		0.47	0.24–0.92		15.26
LMS vs UPS		0.36	0.17–0.79		8.91
Positive nodes	.0003	3.89	1.86–8.13		11.24
Other organ involvement	.074				0.3
Adherent vs none		1.44	0.94–2.20		11.65
Invading vs none		1.53	1.00–2.33		0.07
Invading vs adherent		1.06	0.64–1.75		0.07
Tumor rupture	.0099	2.67	1.27–5.62		0.1
				.08	
			Grade combined		
			Low-grade vs unspecified		1.93
			High-grade vs low-grade		1.49
			High-grade vs unspecified		2.89
					1.03–8.13

Note: Age, sex, race, functional status, tumor size, histology, final margin status, histologic grade, node positivity, local recurrence, distant recurrence, other organ involvement on pathology, tumor rupture, (neo)adjuvant chemotherapy, (neo)adjuvant radiotherapy were included in the univariate. Abbreviations: CI, confidence interval; DDLPS, dedifferentiated liposarcoma; HR, hazard ratio; LMS, leiomyosarcoma; MLPS, mixed type/NOS cell liposarcoma; NOS, not otherwise specified; PLPS, pleomorphic liposarcoma; RMLPS, round cell/myxoid liposarcoma; UPS, undifferentiated pleomorphic sarcoma; WDLPS, well-differentiated liposarcoma.

TABLE 4

Multivariate analyses for disease-specific survival and combined recurrence

Disease-specific survival Multivariate analysis				Combined recurrence Multivariate analysis			
	<i>P</i> value	HR (if <i>P</i> < .10)	95% CI		<i>P</i> value	HR (if <i>P</i> < .10)	95% CI
Age, per 5 y	.0002	1.16	1.07–1.25	Grade combined	.0059		
Grade combined	.023			Low-grade vs unspecified		0.71	0.32–1.62
Low-grade vs unspecified		1.26	0.35–4.57	High-grade vs low-grade		2.29	1.34–3.92
High-grade vs low-grade		3.05	1.02–9.09	High-grade vs unspecified		1.64	0.83–3.25
High-grade vs unspecified		2.42	1.07–5.49				
Distant recurrence	<.0001	2.94	1.90–4.57				
Local recurrence	.0003	2.24	1.44–3.48				

Note: Age, sex, race, functional status, tumor size, histology, final margin status, histologic grade, node positivity, local recurrence, distant recurrence, other organ involvement on pathology, tumor rupture, (neo)adjuvant chemotherapy, (neo)adjuvant radiotherapy were included in the univariate. Abbreviations: CI, confidence interval; HR, hazard ratio.