Management of Primary and Recurrent Soft-tissue Sarcoma of the Retroperitoneum

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From 1982 to 1987, 114 patients underwent operation at Memorial Sloan-Kettering Cancer Center for soft-tissue sarcoma of the retroperitoneum. A retrospective analysis of these patients defines the biologic behavior, surgical management of primary and recurrent disease, predictive factors for outcome, and impact of multimodality therapy. Complete resection was possible in 65% of primary retroperitoneal sarcomas and strongly predicts outcome ($p < 0.001$). The rate of complete resection was not altered by histologic type, size, or grade of tumor. These patients had a median survival of 60 months compared to 24 months for those undergoing partial resection and 12 months for those with unresectable tumors. Forty-nine per cent of completely resected patients have had local recurrence. This is the site of first recurrence in 75% of patients. These patients undergo reoperation when feasible. Complete resection of recurrent disease was performed in 39 of 88 (44%) operations, with a 41-month median survival time after reoperation. Tumor grade was a significant predictor of outcome ($p < 0.001$). High-grade tumors ($n = 65$) were associated with a 20-month median survival time compared to 80 months for low-grade tumors ($n = 49$). Gender, histologic type, size, previous biopsy, and partial resection *versus* unresectable tumors did not predict outcome by univariate analysis. Adjuvant radiation therapy and chemotherapy could not be shown to have significant impact on survival. Concerted attempt at complete resection of both primary and recurrent retroperitoneal soft-tissue sarcoma is indicated.

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In 1954 PACK AND Tabah[1] first reported the Memorial Sloan-Kettering Cancer Center (MSKCC) experience with retroperitoneal sarcoma from 1926 to 1951. They defined the clinicopathologic features and emphasized aggressive surgical management. These principles are unchanged. Current chemotherapy for retroperitoneal sarcomas is ineffective and toxicity of radiotherapy limits the use of adequate, potentially therapeutic doses. The anatomic location and invasiveness of retroperitoneal sarcomas often prevents resection with adequate margins. When the principles of sarcoma management learned from the treatment of extremity soft-tissue sarcoma cannot be applied, outcome is adversely affected.

A recent series of patients with retroperitoneal sarcoma is reviewed to focus on issues of biologic behavior, surgical management of primary and recurrent neoplasms, factors predictive of outcome, and impact of multimodality therapy.

Materials and Methods

Adult patients (more than 16 years old) admitted to MSKCC from July 1982 to July 1987 with the diagnosis of retroperitoneal sarcoma were identified in the Department of Surgery Prospective Sarcoma Database. Patients who underwent an operation at MSKCC for primary or recurrent retroperitoneal sarcoma are the basis for this study.

All pathologic slides were reviewed by one pathologist (SIH) to confirm histologic diagnosis and grade. Survival was calculated according to the method of Kaplan and Meier.[2] The log-rank test was used to compare differences in survival distributions observed in subsets of patients.[3] All survival curves include operative deaths. All survival endpoints are based on death from disease, although only one patient died of other causes. Survival duration was measured from time of initial operation at MSKCC, which accounts for the prolonged survival seen in some patients admitted for a second or subsequent operation during the period 1982 to 1987.

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Results

From July 1982 to July 1987, 995 adult patients were admitted to MSKCC with the diagnosis of soft-tissue sarcoma. Of these, 146 patients (15%) had a retroperitoneal neoplasm. One hundred fourteen patients underwent an operation at MSKCC for the primary or recurrent tumor and form the basis of this review.

There were 67 male and 47 female patients. The median age at diagnosis was 57 years (range, 17 to 82 years). Sixty-three (55%) patients were treated for primary disease at MSKCC. Thirty-three patients presented to MSKCC with a first recurrence, 12 with a second recurrence, and six with a third recurrence (Table 1).

Liposarcoma (50%) and leiomyosarcoma (29%) comprised the majority of the histologic types (Table 2). Sarcomas are graded as either low or high at MSKCC.[4] The histologic grade of sarcoma was low in 43% and high in 57% (Table 2). Size of diameter of the primary tumor was 5 to 10 cm in seven patients, 10 to 20 cm in 46, and more than 20 cm in 61 patients. No tumor was less than 5 cm in diameter at presentation. By the AJCC staging system,[5] there were 49 G1T2N0M0 (stage I), 61 G3T2N0M0 (stage III), 1 G3T2N1M0 (stage III), and 3 G3T2N0M1 (stage IV). By the MSKCC staging system, all retroperitoneal sarcomas in this series had at least two of the three unfavorable signs as all were deep and measured more than 5 cm.

Patients generally presented with an abdominal mass (78%) and pain (50%). Neurologic symptoms, primarily sensory, were described in 27% of patients. Weight loss of more than 5 kg was noted in 7% of patients.

One hundred fourteen patients underwent 151 operations at MSKCC. Major morbidity (*e.g.*, pulmonary embolus, myocardial infarction, sepsis) occurred after 14% of the operations and minor morbidity (*e.g.*, wound infection, atelectasis) occurred in 9%. The 30-day operative mortality rate was 4% (6 of 151 operations); all but one postoperative death occurred after operation for unresectable recurrent disease. Cause of death included sepsis, myocardial infarction, and multiple-organ failure and no deaths were due to progression of disease.

Complete resection was defined as resection of all gross disease. Positive microscopic pathologic margins were noted in 12 of 41 complete resections for primary neoplasms. This did not predict early recurrence or death from disease. Complete resection at first MSKCC operation was performed in 59% of cases and ranged from 65% for primary neoplasms to 44% for recurrent disease (Table 1). The rate of complete resection was not altered by histologic type, size, or grade of tumor (low, 61% complete resection; high, 57% complete resection). Resection of adjacent organs was required in 83% of patients undergoing complete resection. Fifty-three per cent had one organ resected and 30% had more than one organ resected. Resected adjacent organs included kidney (46%), colon (24%), and pancreas (15%) (Table 3). Pathologic involvement of the kidney was noted in 2 of 30 nephrectomies. Major vascular resection, vena cava, common iliac artery or vein, was performed in 7 of 67 completely resected patients. Eighteen of thirty-three (54%) initially unresectable patients referred to MSKCC had complete resection of their tumors.

Partial resection designated operations in which more than 80% of the tumor was resected but gross residual disease was present. Twenty-five patients had partial resection at MSKCC for primary or recurrent tumor. The histologic types were liposarcoma (14), leiomyosarcoma (6), and other sarcomas (5). There were 17 low-grade sarcomas and 8 high-grade sarcomas. Low-grade liposarcoma accounted for 11 of 25 partial resections. Six patients have had more than one partial resection. Adjacent organs were rarely resected in this group.

Patients found to have unresectable disease generally had a biopsy only, although some had resection of bulky tumor to relieve bowel obstruction. Forty-six patients were

TABLE 2. *Distribution of Adult Retroperitoneal Sarcomas by Histologic Type and Grade*

Histology	Low Grade	High Grade	Total (%)
Liposarcoma	34	23	57 (50%)
Leiomyosarcoma	6	27	33 (29%)
Hemangiosarcoma	3	4	7 (6%)
Fibrosarcoma	4	2	6 (5%)
Malignant fibrous histiocytoma	0	5	5 (4%)
Malig. peripheral nerve tumor	1	3	4 (4%)
Alveolar soft part sarcoma	1	0	1 (1%)
Embryonal rhabdomyosarcoma	0	1	1 (1%)

TABLE 1. *Retroperitoneal Soft-tissue Sarcoma Resectability at First MSKCC Operation*

	Complete Resection		Partial Resection		Unresectable	
Status at First Presentation	n	%	n	%	n	%
Primary sarcoma, n = 63	41	65%	9	14%	13	21%
First recurrene, n = 33	18	55%	5	15%	10	30%
≥ second recurrence, n = 18	8	44%	3	17%	7	39%
All patients, n = 114	67	59%	17	15%	30	26%

TABLE 3. *Retroperitoneal Soft-tissue Sarcoma: Resection of Adjacent Organs at Primary Operation*

Organ Resected	% of Patients
Kidney	46
Colon	24
Pancreas	15
Major vascular	10
Spleen	10

TABLE 4. *Retroperitoneal Sarcomas: Basis for Unresectability (n = 46)*

Basis	% of Patients
Vascular involvement	43
Peritoneal implants	28
Distant metastasis	19
Extensive disease	17
Root of mesentery involvement	8
Spinal cord involvement	6

TABLE 5. *Retroperitoneal Soft-tissue Sarcoma: Distribution of Distant Metastases by Histologic Type*

Histology	No. of Patients	No. of Pulmonary Mets.	No. of Hepatic Mets.
Liposarcoma	57	4	0
Leiomyosarcoma	33	3	7
Other sarcoma	24	0	3
Total	114	7 (6%)	10 (9%)

Mets., metastases.

unresectable at time of primary (13 of 63 [21%] patients) or recurrent (33 of 88 [38%] patients) operation at MSKCC. Forty-three per cent had extensive vascular involvement of the aorta or other vessels, *e.g.*, vena cava or iliac vessels, as the indication for unresectability. Peritoneal implants indicated unresectability in 28% and distant metastases in 19% (Table 4). Sixty-three per cent of these patients had high-grade tumors and 37% were low grade. Forty per cent of these sarcomas measured 10 to 20 cm and 60% measured more than 20 cm in diameter.

Univariate analysis of prognostic factors determining survival are shown in Table 5. Grade (Fig. 1) and resectability (Fig. 2) significantly affected survival ($p < 0.001$). Median survival time for the 49 patients with low-grade sarcomas was 80 months compared to 20 months for 65 patients with high-grade sarcomas. Complete resection was associated with 64-month median survival compared to 24 and 12 months for partially resected and unresected patients, respectively. Age less than 53 years was a significant factor positively affecting survival time ($p < 0.05$). Gender, histologic type, size, previous biopsy, adjuvant radiotherapy, adjuvant chemotherapy, and partial *versus* unresectable operation were not shown to be statistically significant prognostic factors for survival time.

At 31 months median follow-up, 33 of 67 (49%) patients who underwent complete resection at MSKCC for primary or recurrent disease have recurred. Twenty of thirty-seven (54%) completely resected high-grade sarcomas have recurred compared to 13 of 30 (44%) low-grade sarcomas. The median time to recurrence, for those who recurred, was 15 months for high-grade sarcomas and 42 months for low-grade sarcomas (range, 2 to 144 months; Fig. 3).

Local recurrence was the predominant site of first recurrence (Table 6). Local recurrence was the only site of

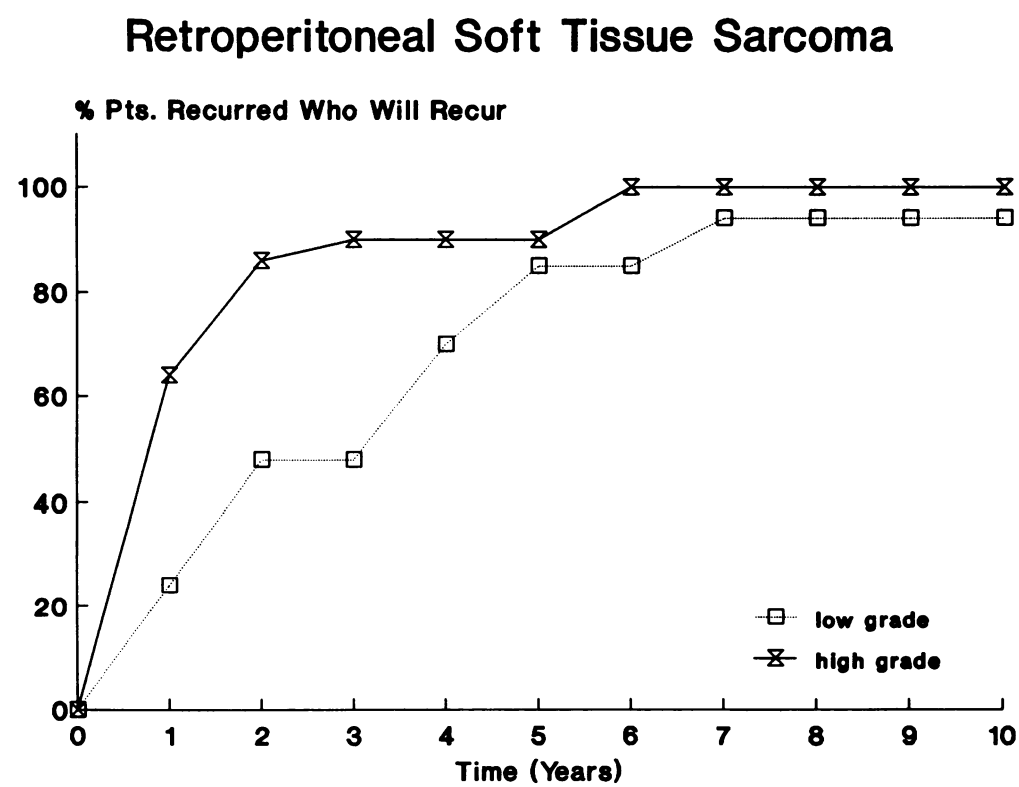

FIG. 1. Proportion of alive patients is plotted against time from first MSKCC operation according to the method of Kaplan and Meier for patients with high-grade or low- grade soft-tissue sarcoma of the retroperitoneum.

SURVIVAL OF 114 PATIENTS WITH RETROPERITONEAL SARCOMA BY RESECTABILITY

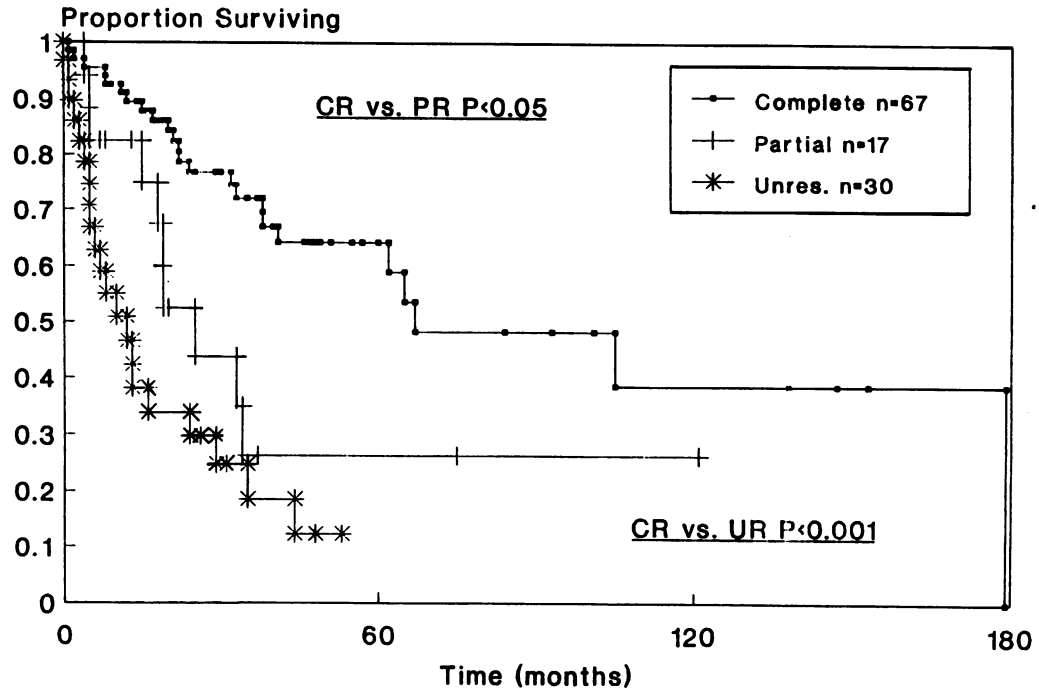

FIG. 2. Proportion of alive patients is plotted against time from first MSKCC operation according to the method of Kaplan and Meier for patients undergoing complete resection, partial resection, or unresectable operations for soft-tissue sarcoma of the retroperitoneum.

SURVIVAL OF 114 PATIENTS WITH RETROPERITONEAL SARCOMA BY GRADE

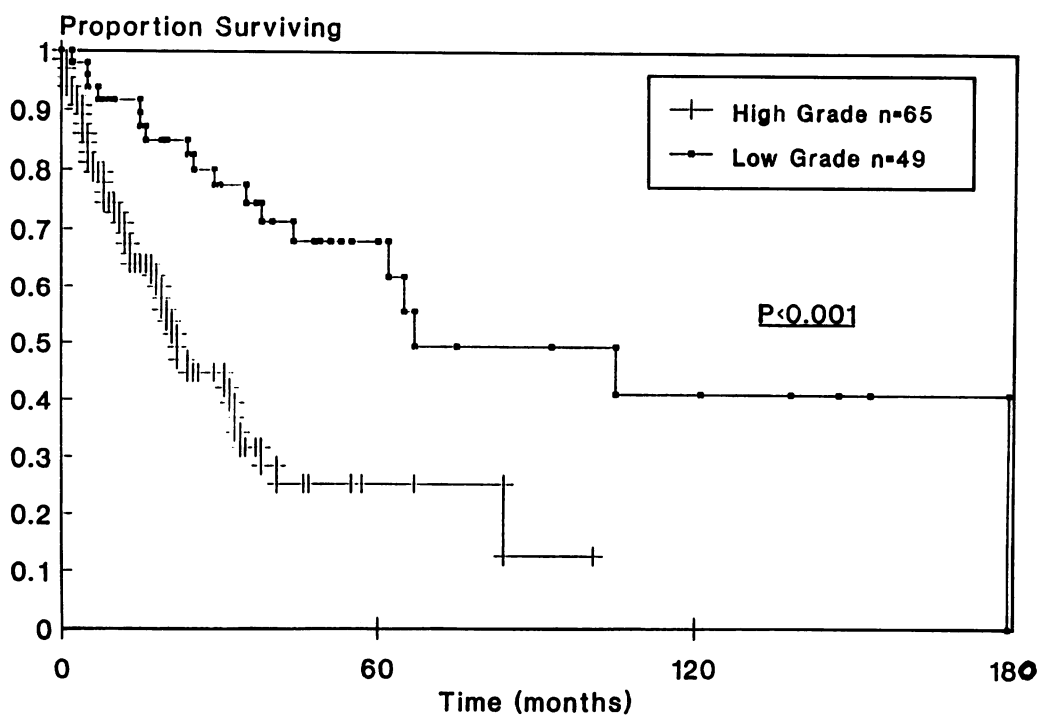

FIG. 3. Cumulative recurrence is plotted against time for patients who recurred after complete resection of high-grade or low-grade soft-tissue sarcoma of the retroperitoneum.

TABLE 6. *Retroperitoneal Soft-tissue Sarcoma: Site of First Recurrence After Complete Resection*

Site of Recurrence	Primary Disease (n = 41)	Recurrent Disease (n = 39)
Local only	12	22
Local and liver	3	1
Liver only	1	0
Lung only	2	1
Total	18 (44%)	24 (62%)

first recurrence in 75% of patients treated for primary retroperitoneal sarcoma. After complete resection of recurrent disease, 90% of recurrences were again local. Median survival from time of local recurrence was 24 months (range, 9 to 167 months). Median survival after recurrence was 15 months for high-grade sarcomas and 30 months for low-grade sarcomas.

Synchronous metastases were observed in three patients, two with hepatic metastases and one with lung metastases. Only 1 of 114 (0.8%) patients developed regional nodal metastases. Metachronous distant metastases developed in an additional 14 patients. The lung was a site of metastases in 7 of 114 (6%) patients and liver in 10 of 114 (9%) patients (Table 7). Eight of thirty-three leiomyosarcomas and 0 of 57 liposarcomas metastasized to the liver. Fourteen of seventeen patients with distant metastasis had high-grade sarcomas. Two patients with pulmonary metastases were resected, with one having no evidence of disease (NED) at 2 months follow-up and one dead of disease (DOD) 11 months after thoracotomy. One patient has had two hepatic wedge resections for metastatic leiomyosarcoma and shows no evidence of disease at 18 months follow-up. Median survival from time of distant metastases was 14 months (range, 4 to 48 months).

In the absence of clear signs of unresectability, patients with local or distant recurrence were surgically explored.

TABLE 7. *Retroperitoneal Sarcomas: Prognostic Factors for Survival by Univariate Analysis*

Factor	p value
Grade (high *vs.* low)	<0.001
Resectability	
Complete resection *vs.* unresectable	<0.001
Complete resection *vs.* partial resection	<0.05
Partial resection *vs.* unresectable	NS
Age (<53 years *vs.* >53 years)	<0.05
Sex (male *vs.* female)	NS
Histology	
Liposarcoma *vs.* leiomyosarcoma	NS
Liposarcoma *vs.* all others	NS
Leiomyosarcoma *vs.* all others	NS
Size (>20 cm *vs.* 10–20 cm)	NS
Previous biopsy	NS
Adjuvant radiation therapy	NS
Adjuvant chemotherapy	NS

Sixteen of 63 patients primarily treated at MSKCC have recurred. Fourteen (88%) were considered operable and five (31%) had complete resection for recurrent disease. Fifty-one patients referred to MSKCC with recurrent retroperitoneal sarcoma underwent reoperation and 26 (51%) had complete resection. Histologic distribution was liposarcoma (35; 54%), leiomyosarcoma (16; 25%), and other sarcomas (14; 21%). Thirty-seven (57%) patients had high-grade sarcomas and 28 (43%) had low-grade tumors. This distribution is identical to that seen in patients with primary disease. The median time to recurrent operation was 19 months from diagnosis (range, 1 to 180 months).

There were 88 operations for recurrent disease. Sixteen per cent major morbidity and 8% minor morbidity was observed. There were five 30-day operative deaths (6%). Each of these patients had unresectable disease and in three of five patients the operation was for palliative intent.

Recurrent sarcomas of the retroperitoneum were completely resected in 39 of 88 (44%) operations (Table 8). Complete resection was possible in 49%, 42%, and 33% of first, second, and third recurrences, respectively. Resection of an adjacent organ was required in 20 of 39 (51%) completely resected recurrences. The most commonly resected organs were the colon (10) and small intestine (7). Completely resected patients had a 48-month median survival time compared to 21 and 15 months for partial and unresectable patients, respectively (Fig. 4). Fourteen of sixty-five patients with operable recurrences (22%) showed no evidence of disease at median follow-up of 38 months (range, 9 to 167 months). Nine of these patients had low-grade tumors.

Adjuvant therapy was given to 18 of 41 (44%) patients after complete resection of primary sarcomas. Ten received an adriamycin-containing chemotherapy regimen and 11 received radiation therapy (~4500 rad). No differences in survival could be detected in these nonrandomized groups.

Unresectable and metastatic disease were treated with adriamycin as a single agent or in combination, or by phase I drugs. Few partial responses and no complete responses were observed. Radiation therapy was used in 22% of patients with persistent disease, with no significant responses documented. Brachytherapy was used in 7 of

TABLE 8. *Retroperitoneal Soft-tissue Sarcoma Operations for Recurrent Sarcoma*

	Complete Resections		Partial Resections		Unresectable	
No. of Recurrences	n	%	n	%	n	%
Recurrence 1 (n = 47)	23	49	7	15	17	36
Recurrence 2 (n = 26)	11	42	6	23	9	35
Recurrence 3 (n = 15)	5	33	3	20	7	47
Total (n = 88)	39	44	16	18	33	38

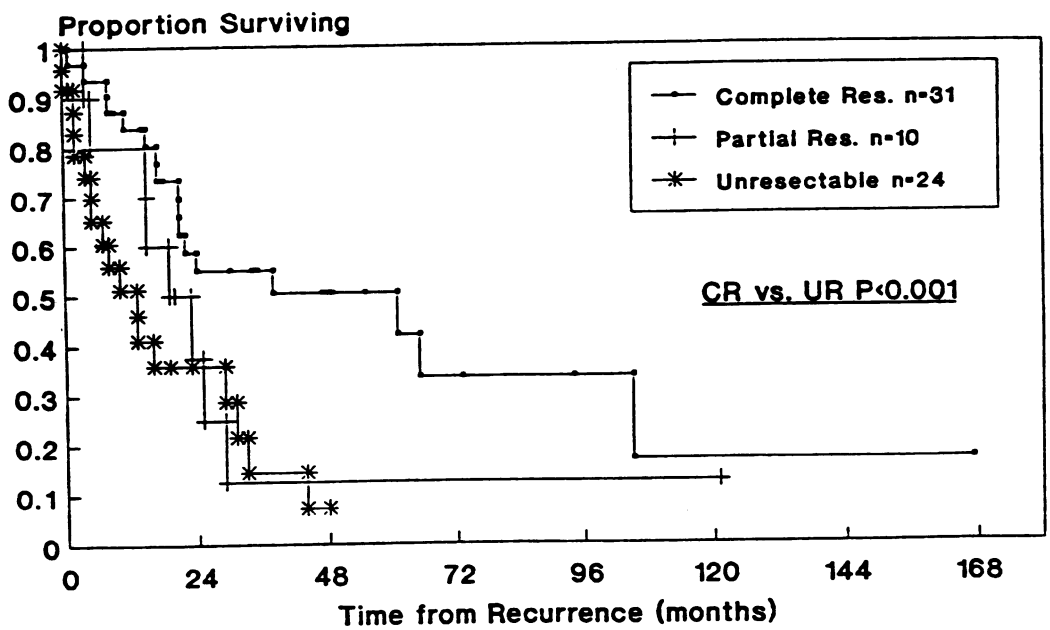

FIG. 4. Proportion of alive patients is plotted against time from first recurrence operation at MSKCC according to the method of Kaplan and Meier for patients undergoing complete resection, partial resection, or unresectable operations for recurrent soft-tissue sarcoma of the retroperitoneum.

25 partial resections. One patient has no evidence of disease at 141 months. The others had local progression of disease and death from 12 to 22 months later.

Discussion

The retroperitoneum is the site of 146 of 995 (15%) soft-tissue sarcomas treated at MSKCC from 1982 to 1987. Pooled data from several series[1,6-9] shows that 85% of the tumors arising from the retroperitoneum are malignant and 35% are sarcomas. Histologic type is predominantly liposarcoma (50%) and leiomyosarcoma (29%). Previous reviews have described specific behavior of retroperitoneal liposarcoma,[10,11] leiomyosarcoma,[12,13] malignant fibrous histiocytoma,[14] and synovial cell sarcoma.[15] Histologic type alone does not predict outcome, although patterns of metastasis vary by histology. The pathologic grade of the tumor is high in 57% of patients with retroperitoneal sarcoma and low in 43%. This is the strongest predictor of survival and is the dominant basis for the AJC staging system. Lymph node metastases are rare (0.8%) and do not play a role in the surgical management of these patients.

Because surgical resection is essential, careful preoperative evaluation is necessary, but a liberal exploration policy is used. Preoperative evaluation should include computed tomography (CT)[16] or magnetic resonance imaging (MRI).[17] Angiography is uncommonly used[18] and MRI often obviates the need for venography. Bilateral renal function must be ascertained because nephrectomy is often performed (37%). Bowel preparation is indicated because 33% undergo bowel resection. Synchronous metastases were seen in 7% of patients, with the lung (41%) and liver (59%) the most common ultimate site of metastases. Thus metastatic survey includes chest x-ray and CT/MRI of the liver.

Preoperative needle biopsy is not practiced.[4] Intraoperative open biopsy is reserved for unresectable tumors or tumors that must be distinguished from lymphoma. A transperitoneal approach is always used. A wide *en bloc* resection of the tumor with a margin of normal tissues is indicated. This is only possible with the frequent resection of adjacent organs (83%). Resection of kidney, colon, pancreas, spleen, and major vascular structures should be anticipated and is not an indication of unresectability.

With this approach 65% of patients with primary retroperitoneal sarcoma were completely resected. This compares to rates of 38% to 70% in previous surgical series[9,19-23] (Table 9). The median survival time after complete resection was 60 months.

Partial resection was performed in 16% of the operations for primary or recurrent retroperitoneal sarcoma. This was designed for palliation to relieve obstruction or reduce the size of an intra-abdominal mass. Nephrectomy is not performed when only incomplete removal of the

TABLE 9. *Retroperitoneal Soft-tissue Sarcoma: Survival After Complete Resection of Primary Sarcoma*

Series	Years Studied	No. of Patients	5-year Survival (%)
Cody[19] (MSKCC)	1951–1974	47	40
Glenn[22] (N.C.I.)	1975–1981	37	23
Kinsella[23] (N.C.I.)	1980–1985	35	40
Braasch[9] (Lahey)	1930–1960	15	40
Wist[25] (Norway)	1978–1982	13	50
Karakousis[20] (Roswell Park)	1957–1980	27	64
McGrath[21] (M.C.V.)	1964–1982	18	70
Current series (MSKCC)	1982–1987	41	74
Total		233	50

tumor is possible. No improvement in survival could be statistically shown for this therapy *versus* biopsy only. Extensive retroperitoneal involvement characterizes many low-grade liposarcomas prohibiting complete resection. Some of these patients have had prolonged palliation and survival (range, 2 to 160 months) with partial resection.

Forty per cent of patients were unresectable at primary or recurrent operation at MSKCC. Vascular invasion most frequently limits resectability. Unsuspected hepatic metastases, extensive disease, involvement of the root of the mesentery, or peritoneal implants were also factors limiting resection.

The overall 5-year survival rate for patients with retroperitoneal sarcoma is 15% to 35%.[24–26] This compares unfavorably with soft-tissue sarcoma of the extremity, which has a 5-year survival rate of 75% to 85%. Univariate analysis shows low-grade ($p < 0.001$), complete resection ($p < 0.001$), and age less than 53 years ($p < 0.05$) to be significant predictors of survival. Sex, size of primary, previous biopsy, histologic type, adjuvant therapy, and partial *versus* unresectable operation did not affect survival time.

Several staging systems have been proposed for soft-tissue sarcoma.[27] Each places appropriate emphasis on the grade of tumor. In this series patients with a high-grade sarcoma have a 25% 5-year survival rate compared to 65% for low-grade tumors. Similar results are reported in other series.[19,24]

Complete resection of primary retroperitoneal sarcoma in this series led to an actuarial 5-year survival rate of 74%. Pooled data[9,19–23,25] from 233 patients with completely resected primary soft tissue of the retroperitoneum shows ~50% 5-year survival. This is compared with 5-year survivals in this series after partial resection of 35% and unresectable disease of 15%. Other surgical series[19–21] support the poor 5-year survival rate associated with partial resection (8% to 33%) and unresectable patients (3% to 10%).

All series of retroperitoneal sarcoma report high local recurrence rates ranging from 40% to 82%.[19,21–24,28] With median time to recurrence of 15 months and 44 months for high- and low-grade tumors, a period of intense follow-up is defined. Patients are evaluated with physical examination every 2 to 3 months. Abdominal mass, pain, or other abdominal symptoms indicate the need for CT/MRI study. For the first 2 to 3 years, asymptomatic patients should have a CT or MRI scan at 6-month intervals to detect local recurrence. The recorded survival rates after complete resection of recurrent disease argue for surgical intervention at the time of diagnosis. Most of these patients were also symptomatic, affording an opportunity for palliation as well. The size of this series does not allow accurate assessment of the influence of lead time bias and its independent role in improved survival, or of whether in asymptomatic disease aggressive resection of CT identified disease necessarily improves survival.

With median follow-up of 31 months, 49% of patients in this series have experienced recurrence. Local recurrence is the predominant site of first recurrence (75%). These rates are compared to the reported 10% to 15% local recurrence rate associated with multimodality treatment of extremity soft-tissue sarcoma.[28–31] There is potential survival benefit for improved local control of retroperitoneal sarcomas.[32]

In the absence of distant metastases, patients with recurrent intra-abdominal disease are assessed for resectability and are surgically explored. Morbidity (24%) is comparable to operations for primary disease. A 6% operative mortality rate was observed, accounting for five of the six 30-day operative deaths in this series. Recurrent retroperitoneal sarcomas were resected completely in 44% of these operations. Grade, size, and histologic type do not predict resectability of recurrent disease and should not determine operability. Resection of adjacent organs should be anticipated. Median survival time after complete resection of recurrent disease is 48 months compared to 15 months for unresectable patients. Despite this, recurrent disease predicts further recurrences and ultimate death from disease. Fourteen to sixty-five (22%) patients who had operable recurrences are NED. The median survival from time of recurrence is 24 months.

High local recurrence rates for retroperitoneal sarcomas define a need for more effective local therapy. Experience with soft tissue sarcomas of the extremity argues for adjuvant radiotherapy for high-grade lesions.[29,30] There is no prospective trial assessing efficacy of adjuvant radiation therapy for retroperitoneal sarcomas. Despite the use of 5400 rad postoperative adjuvant radiation therapy, the abdomen was the first site of recurrence in 69% of patients.[23] This is comparable to other surgery-only series.[19–21] Major toxicity to retroperitoneal structures and severe radiation enteritis (15% to 22%) is reported.[23,25]

TABLE 10. *Retroperitoneal Soft-tissue Sarcoma: Local Recurrence After Adjuvant Radiation Therapy*

Series	No. of Patients	Radiation Dose (rad)	% Local Recurrence
Cody[19] (MSKCC)	15	Unreported	66
Lindberg[31] (M. D. Anderson)	21	6000–7000	38
Glenn[22] (N.C.I.)	37	5400	30
Kinsella[23] (N.C.I.)	35	2000 IORT + 3500 ERT or 5000–5500 ERT	51
Wist[25] (Norway)	10	5000	50
Current series (MSKCC)	11	4500	45

Adjuvant radiation therapy was used in this series in 11 of 41 patients with completely resected primary disease. There has been no statistically significant overall or disease-free survival in the treatment group. These results are compared to other series reporting the use of adjuvant radiation therapy[19,22,23,31,33] (Table 10). Timing of radiotherapy (pre- *versus* postoperative) and optimal dose have not been conclusively determined for retroperitoneal sarcomas.[33,34]

Intraoperative radiation therapy (IORT) is feasible,[35,36] although dose limitations are evident experimentally[37] and in clinical application.[23] A recent trial comparing IORT (2000 rad) and external radiation therapy (ERT) (3500 to 4000 rad) to ERT only (5000 to 5500 rad) showed no statistical difference in overall survival, disease-free survival, local control, or in-field control.[23] While the incidence of radiation enteritis was reduced, peripheral neuropathy was more frequent in the IORT group. The impracticality of the method of IORT makes this an unreasonable choice.

Adjunctive brachytherapy has been associated with a decrease in local recurrence after complete resection of high-grade extremity soft-tissue sarcoma.[29] Adjuvant brachytherapy was used in this series in four patients with retroperitoneal sarcoma with no unique toxicity. No improvement in survival or in local control could be ascertained from this limited experience. Large area of risk and proximity to major vascular structures may limit the application of adjuvant brachytherapy for retroperitoneal sarcoma. Other adjuvant modalities, including intraoperative photodynamic therapy[38] and hyperthermia,[39] have not yet been shown to be efficacious.

Radiation therapy for unresectable retroperitoneal sarcoma is associated with local progression of disease and death in all but the unusual case.[25,33,40] It is reserved for selected palliative indications.

There is no evidence to support the use of adjuvant chemotherapy for retroperitoneal sarcoma.[41] In one series a cohort of 37 patients with complete resection of high-grade retroperitoneal sarcoma received postoperative radiation therapy. Twenty-one of these patients were treated with adjuvant chemotherapy (adriamycin, cytoxan, methotrexate) and 16 received no additional therapy.[22] There was no improvement in disease-free survival or overall survival rate observed in the chemotherapy group. Major toxicity due to the chemotherapy was encountered in this protocol. Similar therapy did show improved survival time for extremity high-grade soft-tissue sarcoma.[42] Other series have shown no improved survival with adjuvant chemotherapy for soft-tissue sarcoma.[43,44] Neither series was large enough to comment on efficacy based on primary site. There was no apparent benefit accrued to 10 of 41 patients receiving adjuvant chemotherapy in this series. A phase I study evaluating toxicity of preoperative chemotherapy followed by resection of high-grade retroperitoneal sarcoma is now being investigated.

Adriamycin-based multidrug chemotherapy regimens are used in the treatment of unresectable or metastatic soft-tissue sarcoma. Considering all primary sites, complete response has been reported in 15% to 35% of patients.[44–46] In this series, 29 patients received adriamycin-containing chemotherapy regimens and no complete responses were recorded.

In contrast to extremity soft-tissue sarcoma, sarcomas of the retroperitoneum are characterized by high local recurrence rates, more frequent hepatic metastases, and poor responsiveness to tolerable radiation doses and chemotherapy. The confines of the retroperitoneum limit the ability of the surgeon to perform a complete resection of the tumor without the frequent resection of adjacent organs or vascular structures. Both primary and recurrent soft-tissue sarcoma of the retroperitoneum can be completely resected in most patients, thus affording improved survival rates. The histologic grade of the tumor and the resectability are the significant predictors of outcome.

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