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Prognostic Factors of Retroperitoneal Soft-Tissue Sarcomas

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Key Words
Sarcoma · Soft-tissue · Surgery · Prognosis

Summary
Background: Retroperitoneal soft-tissue sarcomas are rare malignant tumors and make up 1% of all adult malignancies. We aimed to evaluate the morbidity, the mortality, and the prognostic factors that affect survival of the patients with retroperitoneal soft-tissue sarcoma in this study. **Patients and Methods:** 27 adult patients with retroperitoneal soft-tissue sarcoma underwent surgery between 1992 and 2005 in our clinic. Long-term survival and the independent prognostic factors that affect survival, e.g. age, gender, type of resection (complete resection, partial resection, or only laparotomy and biopsy), site of the tumor, invasion to adjacent organs, tumor size, type of tumor histology, histologic grading, stage of the tumor, and adjuvant radiochemotherapy application, were evaluated. **Results:** Overall survival rate was 58.1% at 1 year, 58.1% at 3 years, and 32.3% at 5 years. Resection type (p = 0.002), grade (p = 0.011), and stage (p = 0.005) were the prognostic features identified by univariate analysis. Among the significant prognostic factors in the univariate analysis, only two factors, surgical resection (p = 0.011, hazard ratio = 15.570) and tumor grade (p = 0.002, hazard ratio = 12.491), proved to be independently significant in the multivariate analysis. **Conclusion:** The completeness of resection and tumor grade significantly influence overall survival in this tumor entity.

Schlüsselwörter
Sarkome · Weichgewebe · Chirurgie · Prognose

Zusammenfassung
Hintergrund: Retroperitoneale Weichgewebssarkome sind seltene bösartige Tumoren und machen etwa 1% aller malignen Erkrankungen bei Erwachsenen aus. Unser Ziel war es, in dieser Studie die Morbidität und die Letalität auszuwerten und die prognostische Faktoren zu bestimmen, die das Überleben der Patienten mit Weichgewebssarkomen beeinflussen. **Patienten und Methoden:** 27 erwachsene Patienten mit Weichgewebssarkomen wurden zwischen 1992 und 2005 in unserer Klinik operiert. Die Langzeitüberlebensraten und die unabhängigen prognostischen Faktoren, die das Überleben beeinflussen wie Alter, Geschlecht, Art der Resektion (komplette Resektion, partielle Resektion oder nur Laparotomie und Biopsie), Lokalisation des Tumors, Invasion zu den angrenzenden Organen, Tumorgröße, Art von Tumorhistologie, histologische Grading, Stadium des Tumors, adjuvante Radiochemotherapie wurden ausgewertet. **Ergebnisse**: Die Gesamt-Überlebensrate betrug 58,1% nach 1 Jahr, 58,1% nach 3 Jahren und 32,3% nach 5 Jahren. Resektionsart (p = 0,002), Tumorgrad (p = 0,011) und Tumorstadium (p = 0,005) wurden in der univariaten Analyse als signifikante prognostische Faktoren ermittelt. Von den in den univariaten Analysen signifikanten prognostischen Faktoren waren nur zwei Faktoren, nämlich die komplette chirurgische Resektion (p = 0,011, «hazard ratio» = 15,570) und die niedriggradige Tumoren (p = 0,002, «hazard ratio» = 12,491), auch in der multivariaten Analyse unabhängig signifikant. **Schlussfolgerungen:** Die Vollständigkeit der Resektion und der Tumorgrad beeinflussen erheblich die Gesamt-Überlebensrate bei dieser Tumorentität.

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Introduction

Retroperitoneal soft-tissue sarcomas (RSTS) are rare malignant tumors and make up 1% of all adult malignancies. These tumors may arise at any site in the body where soft tissues are located. Only 10–15% of them are located in the retroperitoneum. RSTS tend to be relatively large compared to tumors elsewhere in the body [1–3]. The various types of retroperitoneal sarcomas are derived from mesenchymal cells that present as different histologic types depending on their cell origin. These include liposarcomas, leiomyosarcomas, malignant fibrous histiocytomas, fibrosarcomas and malignant peripheral nerve sheath tumors [1, 2, 4]. Patients with RSTS tend to have a poor prognosis with a high local recurrence rate and a low 5-year survival rate [1, 2, 5]. Surgery is the principal mode of therapy and offers the most favorable prognosis after complete resection [1–3, 6].

In this study, we aimed to evaluate the morbidity, the mortality, and the prognostic factors that affect survival of the patients with RSTS.

Patients and Methods

In our clinic, 27 adult patients with RSTS underwent surgery between 1992 and 2005. Patients with metastatic RSTS, visceral sarcomas with gastrointestinal origin, lymphomas, carcinoid tumors, desmoids, genitourinary tract tumors, and aggressive fibromatosis were excluded. Hospital records of the patients were reviewed for clinicopathological findings, treatment modalities, morbidity, mortality, course of the disease and survival. The patients were followed up by outpatient visits and telephone interviews.

Tumors were graded as either high or low according to differentiation, cellularity and amount of stromal necrosis, pleomorphism, and frequency of mitotic figures. Histologic subtypes were classified as well-differentiated, dedifferentiated, myxoid/round cell, or pleomorphic. The tumors were classified according to the staging system of the International Union Against Cancer (UICC) [7].

Ultrasound scan (US), CT, MRI, and intravenous pyelography (IVP) were the diagnostic imaging methods used. Renal function of both kidneys was tested preoperatively. The patients underwent surgery after colonic lavage and double-J urinary tract catheter placement. A laparotomy through a wide median incision was performed in each case. The aim of surgery was en bloc resection of the tumor, including invaded adjacent organs and tissues if there are any. Margins of the resected material were evaluated both macroscopically and microscopically in six dimensions (superior, inferior, medial, lateral, anterior, and posterior). A clear margin indicated that microscopically there was no tumor at least 1 mm or more from the edge of the specimen. The margin was considered positive if there was extension of tumor to within <1 mm of the edge of the specimen microscopically. Resection was regarded as complete if the margins of the resected material were clear. If only laparotomy and biopsy were performed or microscopically positive margins were reported, the procedure was considered to be palliative. Adjuvant treatment was given to the patients who had microscopically proven residual tumor and who had a high-grade disease.

Early postoperative morbidity and mortality were noted. Perioperative mortality was defined as death occurring within 30 days after surgical treatment. Survival was calculated in months from the time of surgery to the last follow-up or death.

Table 1. Patients' characteristics, tumor histopathology, and type of surgery

Patients and tumor characteristics	Number of patients
Age, years	
Mean (range)	57.62 ± 14.89 (21–75)
≤65	18
>65	9
Gender	
Male	11
Female	16
Grade	
Low	14
High	13
Size, cm	
Mean (range)	17.58 ± 7.08 (7–39)
≤20	7
>20	20
Pathological types	
Liposarcoma	11
Leiomyosarcoma	7
Malignant fibrous histiocytoma	5
Rhabdomyosarcoma	2
Fibrosarcoma	1
Neurofibrosarcoma	1
Site	
Lateral	17
Midabdomen	8
Pelvic	2
Lympf node involvement	
pN0	23
pN1	4
Stages	
I	14
III	9
IV	4
Surgical resection	
Complete resection	18
Partial resection	7
Laparotomy and biopsy	2
Visceral resection	
With complete resection	15
With partial resection	4

Survival analyses were made by the Kaplan-Meier method, and the differences were evaluated by the log-rank test. The patients who died in the early postoperative period were excluded from the survival analysis. Long-term survival and the independent prognostic factors that affect survival, e.g. age, gender, type of resection (complete resection, partial resection, or only laparotomy and biopsy), site of the tumor, invasion to adjacent organs, tumor size (cm), type of tumor histology, histologic grading, stage of the tumor, adjuvant radiochemotherapy application, were evaluated by using univariate analysis methods. Significance was determined by chi-square analysis. Simultaneous association of multiple variables was performed using the Cox proportional hazards regression model to estimate the simultaneous effect on overall survival. Independent variables that showed statistical significance in the univariate analysis were then entered into multivariate analysis. The prognostic factors were compared by hazard ratio and the 95% confidence interval. Stepwise selection was used to find the most significant factors. A p value of < 0.05 was considered statistically significant for all patients. Median survival time was

Table 2. Survival analysis and univariate analysis of prognostic factors in patients with RSTS

Patients' characteristics	Median survival time, months	95% confidence interval	p*	Survival rate, %			p†
				1-year	3-year	5-year	
Age							
≤65 years	60.0 ± 22.83	15.25–104.75	0.6418	55.10	55.10	27.55	0.646
>65 years	50.25 ± 11.31	28.07–72.43		63.73	63.73	63.73	
Gender							
Female	71.0 ± 42.86	0–155.01	0.1201	75.21	75.21	45.13	0.137
Male	14.0 ± 2.60	8.91–19.09		41.67	41.67	20.83	
Surgical resection							
Curative surgery	71.0	–	0.0001	86.81	86.81	48.23	0.002
Palliative surgery	11.0 ± 1.49	8.08–13.92		6.35	–	–	
Site							
Mid abdomen	11.0 ± 3.87	3.42–18.58		31.11	31.11	0	
Lateral	71.0 ± 41.63	0–152.59	0.0114	65.32	65.32	43.55	0.066
Pelvic	still alive	stil alive		100.00	100.00	100.00	
Visceral resection							
No	47.25 ± 8.41	30.77–63.73	0.8945	66.67	66.67	40.00	0.896
Yes	15.0 ± 32.91	0–79.50		50.77	50.77	25.38	
Size,cm							
≤10	54.50 ± 11.84	31.29–77.71		63.64	63.64	63.64	
11–20	60.00 ± 35.40	0.00–129.39	0.5408	53.85	53.85	17.95	0.563
>20	42.20 ± 11.95	18.78–65.62		66.67	66.67	66.67	
Pathological type							
Liposarcoma	42.70 ± 10.32	22.47–62.92		51.02	51.02	51.02	
Leiomyosarcoma	71.0 ± 0	71.0–71.0	0.3974	100.00	100.00	33.33	0.443
Others	15.0 ± 2.78	0–55.73		46.67	46.67	15.56	
Grade							
High	12.0 ± 1.80	8.48–15.52	0.0009	30.67	30.77	0	0.011
Low	67.88 ± 5.61	56.89–78.87		91.67	91.67	65.48	
Stage							
I	71.0	–		100.0	100.0	33.33	
III	15.0 ± 3.93	7.30–22.70	0.0002	42.86	42.86	0	0.005
IV	8.0 ± 3.29	1.56–14.44		–	–	–	
Adjuvant chemotherapy							
No	71.0 ± 10.18	51.04–90.96	0.0615	68.57	68.57	38.10	0.079
Yes	12.0 ± 1.10	9.85–14.15		20.00	20.00	-	
Adjuvant radiotherapy							
No	71.0 ± 10.17	51.07–90.93	0.0967	73.86	73.86	41.04	0.115
Yes	14.0 ± 2.98	8.16–19.84		33.33	33.33	–	
All patients	71.00 ± 35.02	2.36 – 139.64		58.12	58.12	32.29	

*Log-rank test.
†Chi-square test.

given with standard error (SE). Statistical Package for Social Sciences (SPSS 10.0, Chicago, IL, USA) for Windows was used for the statistical analyses.

Results

Of the patients 16 were female and 11 were male. The mean age was 57.62 ± 14.89 years ranging between 21 and 75 years. The most common symptoms were abdominal pain (23 cases) and abdominal mass (21 cases). Other symptoms were weight loss (19 cases), dyspepsia (18 cases), fever (12 cases), constipation (7 cases), and nausea and vomiting (5 cases). All patients were symptomatic at the time of diagnosis.

Abdominal US was performed for location, local invasion and distant metastases of the tumor in each case. Thoraco-abdominal CT, MRI, and IVP were performed in 25, 9 and 7 patients, respectively. Mean tumor size was 17.58 ± 7.08 cm ranging between 7 and 39 cm. Considering histologic type, liposarcoma was the most common type (11 cases, 40.7%), followed by leiomyosarcoma (7 cases, 25.9%). The remaining were malignant fibrous histiocytoma, rhabdomyosarcoma, fibrosarcoma, and neurofibrosarcoma. Fourteen cases (51.9%) had low-grade and 13 (48.1%) high-grade tumors. Regional lymph

Table 3. Multivariate analysis of independent prognostic factors

Variable	Hazard ratio	95% confidence interval	p
Surgery (curative vs. palliative)	15.570	1.899–127.77	0.011
Grade (high vs. low)	12.491	2.603–59.928	0.002
Stage (III vs. I)	0.000	0.00–9.29	0.948

node metastases were encountered in only 4 (14.8%) patients. Fourteen patients had stage I, 9 stage III, and 4 stage IV disease. Tumors were located in the lateral quadrants of the abdomen in 17 cases, in the mid abdomen in 8 cases, and in the pelvis in 2 cases. Two cases (7.4%), one with abdominal sarcomatosis and the other with direct invasion of the aorta, had nonresectable disease at the time of surgery, and only biopsy was performed. The tumors were removed completely in 25 cases, and the resected material included invaded adjacent organs and tissues in 19 of them. Although the margins of the surgical specimens of all 25 cases were macroscopically tumor free, histopathological examination revealed microscopically positive margins in 7 cases, 4 of which had received visceral resections (table 1). The most frequently involved organs were the kidneys (8 cases) followed by the colon (7 cases). Other resected organs were the stomach (2 cases), the ileum (2 cases), the ovaries (1 case), the spleen (1 case), and the urine bladder (1 case).

Median hospital stay was 11 days (1–25 days). One patient (3.7%) died of acute myocardial infarction. A total of 7 major morbidities developed in 5 patients. Left diaphragm injury (2 cases), pleural effusion (2 cases), evantration (1 case), subphrenic abcess (1 case), acute myocardial infarction (1 case).

Six of the patients did not receive any adjuvant treatment. Ten had radiotherapy, 6 had chemotherapy alone, and 4 had both radiotherapy and chemotherapy postoperatively.

Median follow-up was 34 months, ranging between 1 and 125 months. Twelve patients died of malignant disease during the follow-up period. 14 patients are still alive, and 11 of these patients have no evidence of disease. Local recurrence developed within 8–30 months (mean 15 months) in 6 patients, one of which also developed hepatic metastases. Two other patients had pulmonary metastases without any local recurrence in the 6th or 55th month. These two patients died on the 8th or 60th postoperative month. All cases that underwent only partial resection or incisional biopsy and 4 patients in the radical surgery group died during the follow-up period. Four patients underwent re-resections after local recurrence but two did not undergo re-operations, one because of associated systemic diseases and the other because of the patient's own refusal.

The overall survival rate was 58.1% at 1 year, 58.1% at 3 years, and 32.3% at 5 years. The median survival time was 71 months for the patients who underwent radical resection and 11 months for those who underwent palliative resection ($p = 0.0001$). One-year, 3-year and 5-year survival rates for patients who underwent radical surgery were 86.8, 86.8 and 48.2%, respectively. In the palliative surgery group, 1-year survival rate was 6.3%, but 3-year survival could not be reached. Univariate analysis was performed to evaluate the relationship between clinicopathological features and survival of the patients. Of the 11 clinical and pathological variables entered in the analysis, three variables were found to have significant influence, i.e. resection type ($p = 0.002$), tumor grade ($p = 0.011$), and tumor stage ($p = 0.005$). Evaluation of the prognostic factors and the results of univariate analysis are shown in table 2. Among the multiple significant prognostic factors in the univariate analysis, only two factors, surgical resection ($p = 0.011$, hazard ratio = 15.570), and tumor grade ($p = 0.002$, hazard ratio = 12.491), proved to be independently significant in the multivariate analysis (table 3).

The survival curves according to histological grade and type of resection are shown in figures 1 and 2.

Discussion

Retroperitoneal sarcomas are asymptomatic at the early stages. Thus, most of the patients present with a huge tumor mass. When symptoms are present, they relate to the mass effect of the tumor or to local invasion. Their large size and the complexity of the retroperitoneal anatomy bring about difficulties in the management of retroperitoneal sarcomas. RSTS grow to larger sizes before they become clinically apparent and involve important vital structures that preclude surgical resection [1, 2, 8]. The majority of the patients present with abdominal mass and pain [1]. The most common symptoms in our study were abdominal pain and mass, too.

Reports on the influence of tumor size on survival are conflicting. Bautista et al. [4] have reported that patients with tumors of large size had lower overall survival rates. However, large size was not an independent prognostic factor in some other reports [5, 6, 9, 10]. In our series, 74% of the patients had a tumor greater than 20 cm in diameter, and statistical analysis did not show any reverse effect on overall survival ($p = 0.563$).

Retroperitoneal sarcomas are malignant tumors with an aggressive course and high local recurrence rate [11]. The biological behavior of RSTS is controlled by the histologic grade rather than the histologic type. Histologic grade is one of the most important prognostic factors with regard to local control and survival [2, 5, 9, 12]. Low tumor grade was identified as an

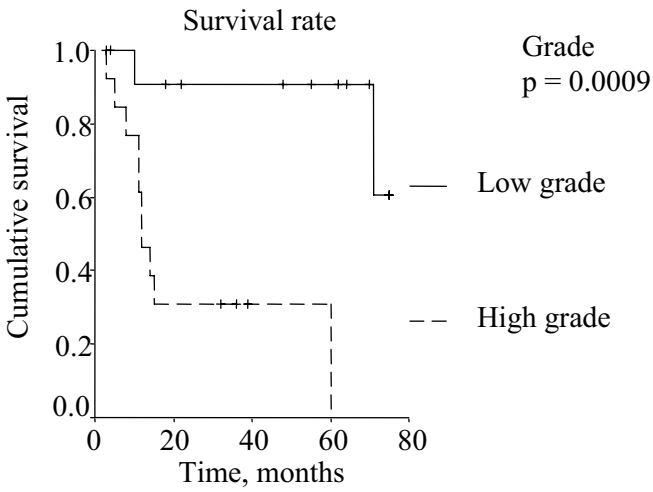

Fig. 1. Survival according to histological grade. The survival rates for patients with high-grade tumors were lower than those of the patients with low-grade tumors (p = 0.0009, log-rank test).

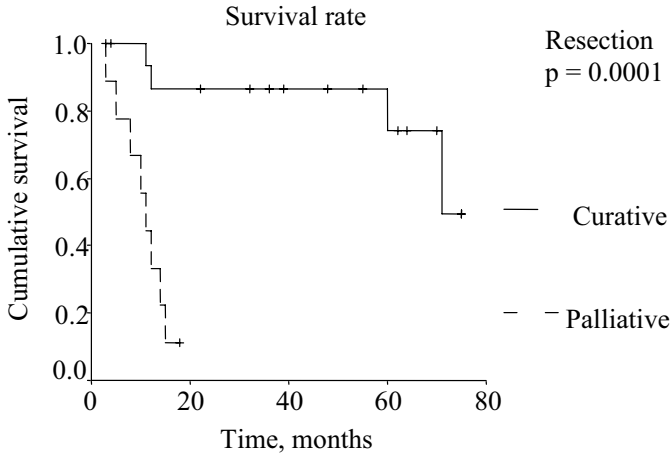

Fig. 2. Survival according to the type of surgery. The survival rates for patients with palliative surgery were lower than those of the others (p = 0.0001, log-rank test).

important prognostic factor in studies on sarcomas being associated with significantly longer median survival times [2, 13, 14]. Median survival time for low-grade sarcomas was 67 months, whereas it was only 12 months for high-grade tumors in our study (p = 0.0009). In our study, low tumor grade was one of the independent predictive factors for overall survival in multivariate analysis.

Complete resection of the tumor is of crucial importance for long-term survival. The goal of surgery in RSTS is en bloc resection of the tumor, including invaded tissues and organs. The importance of complete resection as a major determinant of prognosis has been demonstrated in many studies [5, 8, 13–15]. The ability to completely resect a RSTS remains the most important predictor of local recurrence and overall survival and perhaps the most important factor in survival outcome [10, 13, 14]. It is difficult to distinguish RSTS from normal retroperitoneal fat because of the high degree of adipocyte differentiation. Thus, it is often difficult to obtain a margin of normal tissue around the tumor [13]. Complete resection varies from 38 to 74% in most reports [3, 9, 15]. The rate of complete resection in this study was 66.7%. Completeness of the resection was evaluated by histopathological examination in each case. We did not perform intraoperative frozen section analysis in any of the cases because in general frozen section analysis of fatty tissue is not particularly useful. It is very hard to freeze fat without significant artifact and obtain an accurate histological diagnosis. Univariate analysis demonstrated that after curative surgery the 5-year survival rate was 48.2%, whereas after palliative surgery the 1-year survival rate amounts to only 6.3%. Complete resection was found to be the most important, statistically significant predictive factor that effects survival in multivariate analysis.

Soft tissue sarcomas frequently invade adjacent tissues aggressively [3, 14–18]. A pseudocapsule forms between the tumor and normal tissues. This pseudocapsule consists of both compressed normal cells and malignant cells. This can be an explanation for frequent local recurrence. Thus, the possible existence of micrometastases requires excision of the tumor with 2 to 3 cm clear margins [2]. On the other hand, it is not always possible to obtain tumor-free margins because of adjacent critical organs, vessels, and bony structures [8]. Multivisceral resections are required in the majority of cases (63–86%), most frequently involving the kidney, colon, small bowel, and pancreas [1]. In this study, adjacent organ resections were performed if necessary. 19 patients (70.4%) underwent multivisceral resections, and the most frequently removed organs were the kidneys and the colon. A complete resection could be achieved in 14 of 19 multivisceral resection patients (73.7%). Visceral resection had a negative effect on survival; however, the difference was not statistically significant for survival rates (p = 0.8945).

The prognosis of patients with RSTS is poor but 5-year survival rates vary greatly, ranging between 15 and 50% [14, 19]. The 5-year overall survival rate was found to be 46% in a large series of 165 patients from the French Federation of Cancer Centers Sarcoma Group database in Bordeaux being treated between 1980 and 1994 [5]. In the present study, the overall 5-year survival rate of 32.3% was similar to that of previously published series of RSTS.

Since recurrent RSTS may be resected, the patients should be followed meticulously for early detection of local recurrences [8]. Repeated US and CT after initial surgery can demonstrate recurrences which usually develop during the first two postoperative years [2]. Mäkelä et al. [8] reported that local recurrences occurred in a median of 27 months. Aggressive surgical resection of recurrent tumors continues to form the basis of treatment of recurrence, since no survival advantage associated with radiotherapy or chemotherapy in cases of totally re-

sected, nonresectable, residual, or recurrent disease has ever been demonstrated [1, 6, 13]. In their review on soft-tissue sarcomas, Hoss et al. [2] reported local recurrence rates after complete resection between 30 and 50%. Local recurrence developed in 6 of 18 cases (33.3%) with complete resection, and recurrences were detected after a median period of 15 months in our series. Four patients underwent re-resection after local recurrence, 2 of them had a complete resection while the other 2 had a partial resection.

The efficacy of radiation treatment is not so clear in RSTS. In most studies, radiotherapy had no impact on local control [6, 13, 14, 20]. However, Mendanhall et al. [21] reported that postoperative radiotherapy decreased the likelihood of local recurrence although no impact on survival could be demonstrated. To date, no randomized trial has evaluated the role of adjuvant radiation for RSTS [1, 8]. The role of adjuvant chemotherapy has remained also controversial, with no significant benefit in overall survival so far [1, 3, 21–23]. Moreover, there has been a series of patients who received a heterogeneous mixture of chemotherapy and radiotherapy, with no beneficial effect on survival [13]. The effect of adjuvant therapy urgently needs to be tested in large randomized multicenter trials [8, 16]. In our study, the use of adjuvant radiotherapy and chemotherapy did not affect survival. However, the number of patients treated is too small to reach any conclusion concerning the efficacy of these modalities.

In summary, RSTS tend to be large bulky tumors. The completeness of resection and tumor grade significantly influence overall survival. Tumor stage did not retain its predictive significance in multivariate analysis.

Literatur

1 Windham TC, Pisters PWT: Retroperitoneal sarcomas. Cancer Control 2005;12:36–43.
2 Hoos A, Lewis JJ, Brennan MF. Weichgewebssarkome – prognostische Faktoren und multimodale Therapie. Chirurg 2000;71:787–794.
3 Malerba M, Doglietto GB, Pacelli F, Carriero C, Caprino P, Piccioni E, Crucitti P, Crucitti F: Primary retroperitoneal soft tissue sarcomas: results of aggressive surgical treatment. World J Surg 1999;23: 670–675.
4 Bautista N, Su W, O'Connell TX: Retroperitoneal soft-tissue sarcomas: prognosis and treatment of primary and recurrent disease. Am Surg 2000;66: 832–836.
5 Stoeckle E, Coindre JM, Bonvalot S, Kantor G, Terrier P, Bonichon F, Nguyen Bui B, for the French Federation of Cancer Centers Sarcoma Group. Prognostic factors in retroperitoneal sarcoma: a multivariate analysis of a series of 165 patients of the French Cancer Center Federation Sarcoma Group. Cancer 2001;92:359–368.
6 Bevilacqua RG, Rogatko A, Hajdu SI, Brennan MF: Prognostic factors in primary retroperitoneal soft-tissue sarcomas. Arch Surg 1991;126:328–334.
7 Wittekind C, Greene FL, Hutter RVP, Klimpfinger M, Sobin LH: TNM Atlas, 5. Aufl. Heidelberg, Springer, 2004, pp 177–182.
8 Mäkelä J, Kiviniemi H, Laitinen S: Prognostic factors predicting survival in the treatment of retroperitoneal sarcoma. Eur J Surg Oncol 2000;26: 552–555.
9 Jaques DP, Coit DG, Hajdu SI, Brennan MF: Management of primary and recurrent soft-tissue sarcoma of the retroperitoneum. Ann Surg 1990;212: 51–59.
10 Storm FK, Mahvi DM: Diagnosis and management of retroperitoneal soft-tissue sarcoma. Ann Surg 1991;214:2–10.
11 Erzen D, Sencar M, Novak J: Retroperitoneal sarcoma: 25 years of experience with aggressive surgical treatment at the Institute of Oncology, Ljubljana. J Surg Oncol 2005;91:1–9.
12 Ferrario T, Karakousis CP: Retroperitoneal sarcomas: grade and survival. Arch Surg 2003;138: 248–251.
13 Singer S, Corson JM, Demetri GD, Healey EA, Marcus K, Eberlein TJ: Prognostic factors predictive of survival for truncal and retroperitoneal soft-tissue sarcoma. Ann Surg 1995;221:185–195.
14 Kilkenny JW 3rd, Bland KI, Copeland EM 3rd: Retroperitoneal sarcoma: the University of Florida experience. J Am Coll Surg 1996;182:329–339.
15 Dalton RR, Donohue JH, Mucha P Jr, van Heerden JA, Reiman HM, Chen SP: Management of retroperitoneal sarcomas. Surgery 1989;106, 725–733.
16 Lewis JJ, Leung D, Woodruff JM, Brennan MF: Retroperitoneal soft-tissue sarcoma: Analysis of 500 patients treated and followed at a single institution. Ann Surg 1998;228:355–365.
17 Alvarenga JC, Ball ABS, Fisher C, Fryatt I, Jones L, Thomas JM: Limitations of surgery in the treatment of retroperitoneal sarcoma. Br J Surg 1991; 78:912–916.
18 Catton CN, O'Sullivan B, Kotwall C, Cummings B, Hao Y, Fornasier V: Outcome and prognosis in retroperitoneal soft tissue sarcoma. Int J Radiat Oncol Biol Phys 1994;29:1005–1010.
19 Zornig C, Weh HJ, Krull A, Schwarz R, Dieckmann J, Rehpenning W, Schroder S: Retroperitoneal sarcoma in a series of 51 adults. Eur J Surg Oncol 1992;18:475–480.
20 Shiloni E, Szold A, White DE, Freund HR: High-grade retroperitoneal sarcomas: role of an aggressive palliative approach. J Surg Oncol 1993;53: 197–203.
21 Mendenhall WM, Zlotecki RA, Hochwald SN, Hemming AW, Grobmyer SR, Cance WG: Retroperitoneal soft tissue sarcoma. Cancer 2005; 104:669–675.
22 Mazanet R, Antman KH: Adjuvant therapy for sarcomas. Semin Oncol 1991;18:603–612.
23 Orlow I, Drobnjak M, Zhang ZF, Lewis J, Woodruff JM, Brennan MF, Cordon-Cardo C: Alterations of INK4A and INK4B genes in adult soft tissue sarcomas: effect on survival. J Natl Cancer Inst 1999;91:73–79.