Int Surg 2022;**106:**112–120
DOI: 10.9738/INTSURG-D-19-00011.1

Retroperitoneal Liposarcoma: Treatment Outcome in Primary and Secondary Surgical Intervention

Ruth Ladurner[1], Jens Strohäker[1], Christian Birkert[1], Hans-Georg Kopp[2], Alfred Königsrainer[1], Robert Bachmann[1]

Departments of [1]General, Visceral and Transplantation Surgery and [2]Medical Oncology, University Hospital Tübingen, Tübingen, Germany

Background: Approximately 30% to 40% of all retroperitoneal soft tissue tumors are sarcomas, with liposarcoma prevailing in approximately 50% of these cases. Retroperitoneal liposarcomas typically show a high rate of local recurrence and late distant metastases. The aim of our retrospective analysis was to investigate the efficacy of treatment in our patients with liposarcoma.

Methods: Thirty-four consecutive patients underwent surgery in our clinic between October 2004 and November 2017. Liposarcomas arising from the mesenteric or abdominal adipose tissue or the pelvis were excluded.

Results: Of 34 patients, 23 (67.6%) presented with primary and 11 (32.4%) with recurrent disease. In 7 of the 34 patients (20.6%), a radical resection (R0) could be achieved, and in 27 patients (76.5%) resection was marginal (R1). Time to recurrence was not affected by neoadjuvant radiotherapy. Patients who underwent systemic chemotherapy followed by radiotherapy developed earlier recurrences ($P = 0.003$) than patients with neoadjuvant radiotherapy only. Overall survival was significantly better in the neoadjuvant group (P 0.045)

Conclusions: Combining surgical resection with neoadjuvant radiation treatment showed survival benefits in primary but not recurrent disease. Repeated surgery remains a valid approach in carefully selected patients, but all patients should be referred to a center of expertise in multimodal treatment approaches for retroperitoneal liposarcomas.

Key words: Retroperitoneal liposarcoma – Sarcoma surgery

Corresponding author: Robert Bachmann, MD, Department of General, Visceral and Transplant Surgery, University Hospital Tübingen, 72076 Tübingen, Germany.
Tel.: 00497071/2986611; E-mail: robert.bachmann@med.uni-tuebingen.de

The retroperitoneum is the anatomic space between the dorsal skeletal muscles and the ventral visceral organs. It reaches from the diaphragm cranially to the pelvis. The organs are localized inside this space, embedded in plenty of adipose tissue, which sustains and protects the organs. The inferior vena cava divides the retroperitoneum into a right and a left compartment and is an important structure in defining resectability and radical resection of tumors.

Benign lesions, at less than 5%, are rare in the retroperitoneum, whereas approximately 30% to 40 % of all diagnosed retroperitoneal soft tissue tumors are sarcomas. Sarcomas in the retroperitoneum are reported to have an annual incidence of 4 to 5 cases per 100,000 people in Europe.[1] Because of the local growth pattern, diagnosis of retroperitoneal sarcoma is often established late, frequently by chance, and often because of late symptoms caused by compression of adjacent structures or because of significant increase in abdominal girth, which often makes radical resection difficult. Nevertheless, curative surgery for these tumors is the preferred treatment option.

In order to initiate the correct treatment, histology should be obtained, even if images appear to be diagnostic. Retroperitoneal liposarcoma (RPLS) is the most common form, diagnosed in about 50% of all sarcomas, followed by leiomyosarcoma (21%) and other rare histologic subtypes.[2] These 2 most common histopathologic types have a different biologic behavior regarding local recurrence and the potential for distant metastases.

Whereas leiomyosarcomas are highly aggressive, having a 5-year survival rate between 0 and 20%[2] and carrying the risk of distant metastases developing in more than 50% of cases, liposarcoma are much more prone to local recurrence—rates approach nearly 100 %—and only rarely present with distant metastases, most commonly to the lungs. Therefore, the most important tumor burden in liposarcoma is locoregional, and surgery with curative intent is the mainstay of locoregional control.

Liposarcomas can be subdivided into 4 types: well-differentiated, dedifferentiated, myxoid, and pleomorphic, with most being well-differentiated and dedifferentiated. The last 2 types should probably be regarded as related entities because the latter often arises within the former.[3,4] Clinical distinctions between the various categories within the types of liposarcoma remain important because of their different modes of biologic behavior. However, a significant proportion (10%–20%) will dedifferentiate during the course of a mean period of 7 to 8 years, with the capacity to metastasize, irrespective of the extent of dedifferentiation.[5]

Based on the high local recurrence rate in patients with RPLS, a few recently published studies have demonstrated the efficacy of radiotherapy alone as well as the benefit of combining chemotherapy and radiotherapy to improve the sensitivity of liposarcomas to radiotherapy and to provide systemic coverage.[6,7] Furthermore, there have been limited data on the role of pseudoneoadjuvant treatment prior to resection of recurrent RPLS.

The purpose of our retrospective study was to investigate treatment in our patients with a diagnosis of primary or locally recurrent RPLS. We examine the incidence of recurrence, the therapy in the recurrence situation, and overall and recurrence-free survival.

Patients and Methods

Patients and data collection

During the study period between October 2004 and November 2017, we analyzed the data of all patients who underwent surgical resection for a primary or recurrent RPLS in our clinic. A total of 34 patients with abdominal liposarcoma met inclusion criteria. Patient clinical information and operative and histologic reports were reviewed retrospectively from the archives of the University Hospital Tübingen and from telephone inquiries to their primary physicians and treating oncologists. Wherever available we also used the information provided to us by the referring hospitals for the patients who experienced recurrence after external treatment. Ethics approval of the University of Tübingen was given (project number 550/2015B02). Because of the retrospective nature of the study there is no possibility for written consent (Table 1).

Definitions

Primary disease was defined as presentation to our hospital at the time of initial diagnosis (including 1 patient who underwent R2 resection at an outside hospital and who was referred for urgent completion). Recurrent disease was defined as presentation to our hospital with locally recurrent disease after initial (R0/R1) resection.

Beginning in 2011, we introduced standard preoperative biopsy in all patients on first presentation to confirm the histologic diagnosis and to

define the need for neoadjuvant therapy using a core needle biopsy with a 12- to 16-gauge diameter. In cases of G2/G3 liposarcoma and patients with recurrent events, (pseudo)neoadjuvant radiotherapy or chemotherapy, or both, was requested before aggressive radical surgery. Patients were only withheld neoadjuvant treatment if they experienced severe comorbidities and/or were older than 70 years.

The overall goal of surgical resection in primary RPLS was gross resection of the tumor with en bloc removal of infiltrated organs and/or retroperitoneal musculature to achieve negative margins on pathology, which were defined as tumor cells within 1 mm of the stained tumor's surface.

The line between a left- or right-sided RPLS was by definition the inferior vena cava to differentiate between a left and a right retroperitoneal compartment. Bilaterally extending sarcomas or sarcomas exceeding the inferior vena cava line at presentation were defined as not radically resectable.

Tumor size was determined as the maximum tumor diameter by our pathologists and radiographic investigation. Adequate surgical resection was evaluated based on a pathology and surgical report. Microscopically clear margins were defined if the tumor was not within 1 mm or more of the edge of the inked surgical margin. According to the World Health Organization classification primary histology was classified into 4 distinct subtypes: well-differentiated, dedifferentiated, myxoid/round cell, and pleomorphic. The grading was documented according to the French Federation of Cancer Centers Sarcoma Group grading systems in grade 1, 2, 3, or 4.[2]

Data analysis

Patient follow-up was done at our sarcoma center or at specialist outpatient clinics and physician practices at 6-month intervals. Disease status (alive, dead of disease, or dead of other causes without evidence of recurrence) was documented. Local recurrence was defined as any clinical and radiologic evidence of tumor regrowth at the primary site in the retroperitoneal space. Distant metastases were diagnosed by radiologic confirmation of sarcoma at distant sites.

Disease-free survival and overall survival were also recorded. Recurrence-free survival was defined from date of primary complete resection to date of any recurrence, local or distant. Overall survival was defined from the date of primary resection to date of death.

Statistics

All statistics were performed with IBM SPSS Statistics for Windows, version 26.0 (IBM Corp, Armonk, New York). Comparison between groups was carried out by χ^2 test or Fisher exact test for nominal variables and Mann-Whitney U test or Kruskal-Wallis test for continuous variables, as appropriate. A probability of less than 0.05 was considered to be statistically significant. All P values reported are results of 2-sided testing. Where needed, Bonferroni correction was applied.

Results

During the study period, 34 patients with RPLS matched the inclusion criteria. Median age at presentation was 59 years (range, 35–81 years). The sex distribution was almost equal (16 female, 18 male). A total of 23 patients (67.6%) presented to the University Hospital Tübingen with recently diagnosed liposarcoma. One of these 23 patients had an incomplete resection at an outside hospital and was admitted for completion of resection. The other 11 patients (32.4%) presented to our hospital with locally recurrent disease after initial resection at another hospital. Of the total of 11 patients with recurrent sarcoma, 7 patients were admitted for the first episode of recurrence, 3 for the second, and 1 for the third recurrence. Overall mean size of the LPS during primary resection was 21 cm (range, 5–44 cm). The mean size of all primary lesions presented to our hospital was 25 cm (range, 10–44 cm).

The clinical goal in primary RPLS was complete radical resection of the tumor in the right or left compartment with en bloc removal of closely associated organs. In recurrent disease, our desired surgical treatment was radical resection, as organ sparing as possible. Within the patient total (n = 34), a radical resection (R0) could be achieved in 7 patients (20.6%). Table 2 presents the therapeutic procedures of the study population. All 34 patients had surgical intervention as part of the therapy.

A total of 10 of the 34 patients underwent neoadjuvant treatment. They had all presented to our center with untreated primary disease. Five of those patients had percutaneous radiation (± ifosfamide sensitizing), and 5 had percutaneous radiochemotherapy following a median of 4 (range, 3–5) cycles of doxorubicin/ifosfamide. Median radiation dose for these patients combined was 50.4 Gy (range, 42.2–50.4 Gy).

Table 1 Patient characteristics

	Total
Median age (range) on primary resection, y	59.5 (35–81)
Sex, male, n (%)	18 (52.9)
Site, right, n (%)	20 (58.8)
Neoadjuvant treatment, n (%)	10 (34.3)
CTX	0
RCTX	5 (17.2)
RTX	5 (17.2)
Primary resection at UKT, n (%)	23 (67.6)
Histologic subtype, n (%)	
Well-differentiated	7 (20.6)
Dedifferentiated	20 (58.8)
Myxoid/round cell	2 (5.9)
Pleomorphic	1 (2.9)
Unspecified	4 (11.8)
Median tumor size, cm (range)	21 (5–44)
Grading, n (%)	
G1	7 (20.6)
G2	17 (50)
G3	10 (29.4)
Resection margins, n (%)	
R0	7 (20.6)
R1	27 (79.4)
R2	0
Recurrence rate, n (%)	28 (80)
Nephrectomy during primary procedure, n (%)	16 (47.1)
Nephrectomy overall, n (%)	24 (70.6)

CTX, chemotherapy; RCTX, radiochemotherapy; RTX, radiotherapy.

Table 2 Total amount of organs resected during each surgery[a]

Extent of resection (multiple organs possible)	No.	Percentage
Neoadjuvant treatment		
Chemotherapy followed by radiation	5	15%
Radiotherapy	5	15%
First procedure (n = 34)		
Tumor only	12	35%
Tumor +		
Nephrectomy	16	47%
Adrenalectomy	6	18%
Colectomy, partial	10	29%
Pancreatectomy, partial	1	3%
Splenectomy	1	3%
Liver resection	0	
Orchiectomy	2	6%
Bowel resection	1	3%
Diaphragmatic resection	1	3%
Pseudoneoadjuvant treatment		
Chemotherapy followed by radiation	2	11%
Radiotherapy	1	5%
Second procedure (n = 19)		
Tumor only	9	47%
Tumor +-		
Nephrectomy	6	32%
Adrenalectomy	0	
Colectomy, partial	4	21%
Pancreatectomy, partial	4	21%
Splenectomy	2	11%
Liver resection	1	5%
Orchiectomy	0	
Bowel resection	1	5%
Diaphragmatic resection	1	5%
Pseudoneoadjuvant treatment		
Chemotherapy followed by radiation	1	14%
Third procedure (n = 7)		
Tumor only	5	71%
Tumor +-		
Nephrectomy	1	14%
Adrenalectomy	0	
Colectomy, partial	0	
Pancreatectomy, partial	0	
Splenectomy	0	
Liver resection	0	
Orchiectomy	0	
Bowel resection	1	14%
Diaphragmatic resection	0	

[a]The first column shows the number of patients that only underwent organ-sparing tumor resections followed by the amount of organs that had to be resected.

Three other patients received 5 cycles of doxorubicin/ifosfamide of adjuvant chemotherapy after primary resection according to the Interdisciplinary German Sarcoma group (IAWS) protocols.

Of the patients who developed recurrence but had not undergone radiation therapy, 4 received pseudoneoadjuvant radiation therapy; in 3 patients it was combined with pseudoneoadjuvant doxorubicin/ifosfamide chemotherapy. For 3 patients it was the first recurrence, and for 1 it was the second. All 4 underwent repeat laparotomy afterwards. Three were marginally resectable (R1) and 1 was not.

When irresectable disease was found, most patients underwent palliative chemotherapy. Most of them were treated with varying cycles of doxorubicin and ifosfamide, 1 patient received gemcitabine, and a few had second-line treatment with pazopanib, olaratumab, and/or ecteinascidin.

Histologic workup

Regarding histologic workup, the sarcomas in patients with primary disease (n = 23) were well differentiated (G1) in 3 (13%), moderately differentiated (G2) in 12 (52.2%), and poorly differentiated (G3) in 8 (34.8%) cases. In the referred patients with recurrent disease (n = 11), there were 4 well differentiated (G1; 36.3%), 5 moderately differentiated (G2; 45.4%), and 2 poorly differentiated (G3; 18.1%). Except for 1 patient with sarcoma recurrence, all patients were staged T2b. According to the World Health Organization classification, primary histology was classified as well differentiated in 7 of the 34 patients (20.6%; primary sarcoma n = 3,

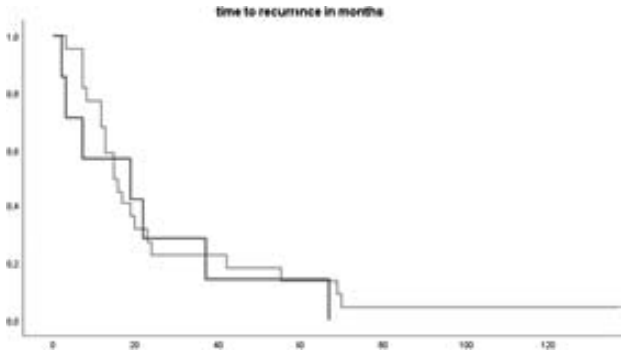

Fig. 1 Probability of recurrence comparing pretreated patients (red) with patients who underwent primary resection (blue). Log rank: 0.636.

recurrent sarcoma n = 4), dedifferentiated in 20 (58.8%; primary sarcoma n = 15, recurrent sarcoma n = 5), and myxoid/round cell in 2 patients (5.9%). One of the patients exhibited a pleomorphic subtype. In 4 patients the pathology report was inconclusive of which subtype was present and slides/tissue was no longer available.

Surgical and survival outcome

Of the 34 patients studied in this analysis 7 patients had complete (R0) resections; 27 were considered R1 by the pathologist; and 29 patients developed recurrent disease, whereas 5 did not. Local recurrence was the same between the patients that had complete resection and R1 resections (85% each; Fisher exact test 1.000).

Time to recurrence, which was defined as the time between the initial resection and the first date new LPS lesions were diagnosed on imaging or by histology (if imaging was inconclusive) was a mean of 27 months (StD ±27 months; range, 7–156 months). There was no statistical difference between the time to recurrence in the neoadjuvant and the surgery only group (Mann-Whitney *U* test 0.664; Fig. 1).

We also performed subanalyses comparing only the patients who had been pretreated with chemotherapy followed by radiotherapy to those who only underwent radiotherapy. Primary inoperable patients who underwent chemotherapy followed by radiotherapy had significantly earlier tumor recurrence (Fig. 2).

Tumor recurrence was found in 29 of 34 patients (85%). The mean time to recurrence was 27 months (StD ± 32 months; range, 2–156 months). There was no difference in the rate of recurrence with regard to the resection margins (R0, 6/7 [85%] versus R1, 4/27 [85%]; *P* 1.000). The time to recurrence appeared to be longer for R0 resections; however, the difference was not statistically significant (40 ± 58 versus 23 ± 22 months, *P* 0.893).

The rate of recurrence was 7 of 10 patients (70%) who underwent neoadjuvant treatment prior to resection and 22 of 24 patients (92%) primarily treated surgically (*P* 0.138). The time to recurrence was 22 months in the neoadjuvant group (StD ± 23 months; range, 2–67 months) compared with 28 months in the other group (StD ± 34 months; range, 3–156 months; *P* 0.628).

Of the 29 patients who developed recurrence 22 underwent a second laparotomy. Of these patients, 19 were resectable: 7 complete (R0) and 12 marginal (R1).

The mean follow-up for all patients was 68 months (StD ± 54 months; range, 7–236 months) since their primary resection. The neoadjuvant group had a median follow-up of 67 months (StD

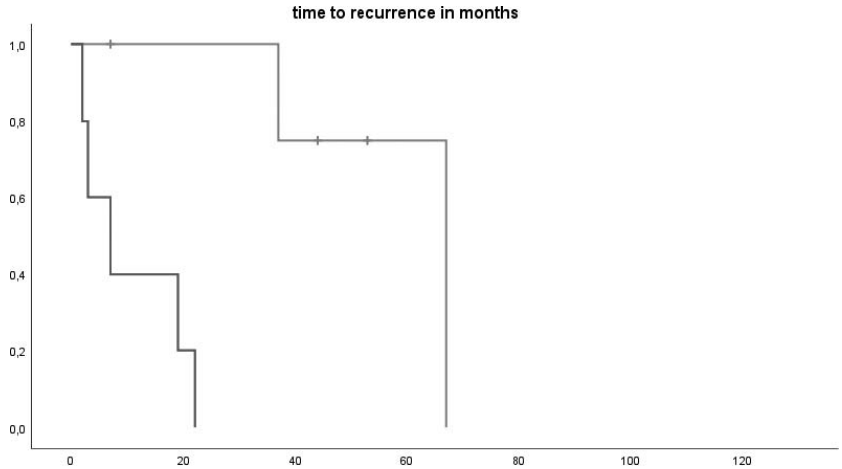

Fig. 2 Time to recurrence comparing 5 patients each who underwent either neoadjuvant chemotherapy followed by radiotherapy (red) or neoadjuvant radiotherapy only (blue). Log rank test *P* = 0.003.

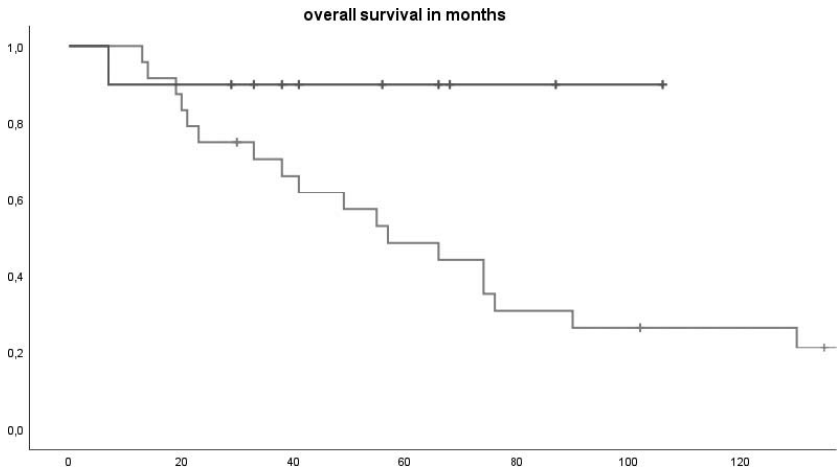

Fig. 3 Overall survival comparing pretreated patients (red) to patients who underwent primary resection (blue). Log rank: 0.045.

± 55 months; range, 7–106 months), whereas the surgery group had a median follow-up of 74 months (StD ± 62 months; range, 13–236 months). During this study period 15 patients have died of their disease, 2 patients died of other diseases (stroke and metastatic rectal cancer), 14 are alive to date, and 3 are lost to follow-up. However, in all 3 cases their primary care physicians considered them dead, since they had not seen those patients in years, and the patients had experienced extensive tumor burden and/or been under palliative care when they had last seen them.

Figure 3 shows overall survival comparing pretreated patients to patients who underwent primary resection (with or without adjuvant chemotherapy), with a significant survival benefit for the patients who underwent neoadjuvant radiation (log rank *P* 0.045).We also compared all patients who had tumor resections, including nephrectomy, during their first surgical procedure (excluding open biopsy). This was true for 16 patients. The other 18 patients had marginal kidney-sparing sarcoma excisions removing the tumor as well as infiltrated mesentery/bowels. There was no difference in tumor recurrence (not shown) and no difference in survival among these 2 groups. There was also no difference in median tumor size, grading, or histologic subtype between these groups. Figure 4 shows overall survival of patients with marginal resections compared with radical resection.

Discussion

Because of the large extent of the retroperitoneum, retroperitoneal sarcomas typically develop undetected, silently growing, often without any clinical symptoms for a long time. The median size of our retroperitoneal soft tissue masses was 21 cm (range, 5–44 cm) for all our patients on their first presentation.

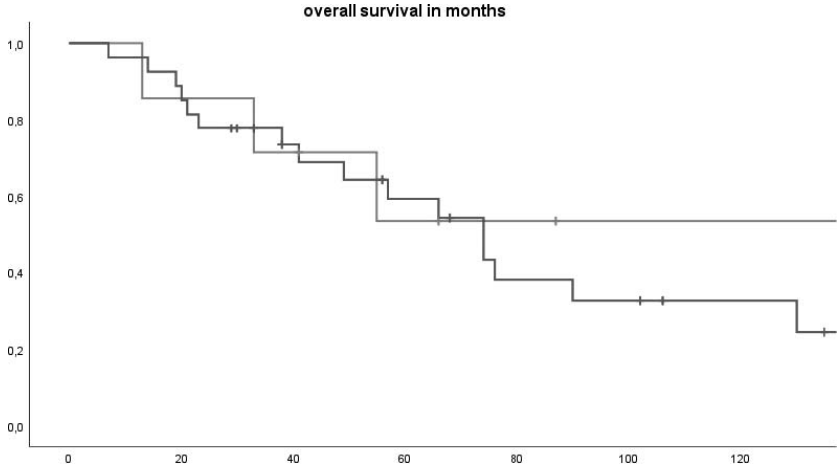

Fig. 4 Overall survival of patients with marginal resections (red) compared with radical resection (blue). Log rank: 0.646.

RPLSs are malignant tumors that rarely metastasize, and if they do, they do so only late in the course of the disease; however, nearly all of our patients have developed local recurrence. This is similar to the rates described in the literature. Local control is the most important determinant of survival because most patients with this type of sarcoma die in the absence of metastases.[8] Surgery therefore remains the most effective treatment in achieving tumor-free and overall patient survival. Many authors have found a prolonged postoperative survival time in patients with tumor-negative margins.[4–6] Nevertheless, incomplete surgical resection is frequent,[9,10] and even complete surgical excision is associated with disappointing rates of local recurrence.[11,12] In our collective we report 78% of R1 resections in patients primarily operated on in the sarcoma center, as well as 82% in those referred to us for recurrent disease. Furthermore, all patients in this study had an overall recurrence rate of 79.5%. Excluding the patients who had been referred for recurrent disease we still have to report 18 of 23 patients with tumor recurrence (78%), which is slightly higher than the roughly 60% described by Pawlik and Heslin.[11] Neoadjuvant treatment did not really improve these numbers: 70% of the pretreated patients developed tumor recurrence. What is notable is the earlier recurrence in the patients who had received neoadjuvant chemotherapy prior to radiation. To our knowledge this has not been described elsewhere. Of course, larger numbers are highly necessary to get more insights into this observation.

The extent of surgery depends on whether the tumor is in the right or the left compartment. Patients experiencing right-sided RPLS undergo tumor resection with en bloc resection of the right hemicolon by an anterior approach and en bloc resection of the right kidney posteriorly. Complete access to the vena cava inferior is provided by this procedure. The duodenum and the head of the pancreas must then be removed by the Kocher maneuver, and the right liver lobe must be rotated as well after incision of the falciform and coronary ligament and the right triangular ligament. Frequently only a marginal resection between the sarcoma and the liver or the head of the pancreas and the duodenum is possible. Concerning morbidity, liver resection or pancreaticoduodenectomy, or both, are generally not recommended because of increased morbidity.[13] Patients with RPLS in the left compartment undergo en bloc left hemicolectomy with the sarcoma and left kidney, as well as distal pancreatectomy and splenectomy. Resection and replacement of the abdominal aorta, inferior to the superior mesenteric artery, in patients with sarcoma on the left side was never necessary in our patients. Resection and replacement of the infrarenal inferior vena cava has been performed once in our institution. Over the years we have also developed from a more aggressive to a more conservative (*i.e.*, organ-preserving) strategy. Nonetheless, there is an ongoing debate among surgical oncologists specializing in the field regarding what constitutes optimal surgery for retroperitoneal sarcoma, weighing the oncologic benefits of radical multivisceral resection with a possible increase in early and late morbidity and keeping in mind that radical surgery might not influence the inherent natural biology of the disease.[14–16] Pollock *et al*[17] support a possibly less aggressive surgical approach incorporating organ preservation, especially for patients with dedifferentiated sarcomas, which have a higher probability of developing distant metastases than well-differentiated sarcomas do. Tseng *et al*[18] support the suggestions made by Neuhaus *et al*,[19] who have pointed out that in some patients the entirety of retroperitoneal fat may be at risk of disease. Further investigation into the biology of this disease is needed.

Considering the number of patients in our study, the distribution in primary and recurrent sarcomas, and the varying treatment strategies, we can neither promote nor refuse the conclusions of Pollock *et al*.[17] However, what we saw is that only 1 patient who underwent nephrectomy during the primary procedure showed actual infiltration of the kidney. Tumor recurrence and overall survival seemed uninfluenced, which is why we try to avoid abdominal compartment resections.

Nevertheless, the strategy in our center has been to achieve a complete resection with a wide microscopic margin along the maximum surfaces by removing additional and easily disposable organs while performing a marginal excision along critical structures. In 2012 E-Surge, a master class in sarcoma surgery, and the EORTC soft tissue and bone sarcoma group provided technical guidelines with a standardized approach to these tumors.[20]

In the case of recurrence, and regarding greater morbidity and the missing impact of extended resection on long-term survival, surgical resection is marginal and is more or less limited to the recurrent tumor. Hamilton *et al*[21] provided data on patients they had treated neoadjvuantly in the recurrence setting. They provide data on 30 (26

RPLS) patients with recurrent or residual disease whom they treated with radiotherapy prior to subsequent resection. They reported a 5-year OAS of about 56% from the second resection.[21] Of the patients who underwent pseudoneadjuvant radio-(chemo)therapy at our center, nearly half were inoperable after completing the pretreatment, and the others certainly did not meet 60% 5-year OAS, and thus it is hard to deduct recommendations from our cases. However, the 5-year OAS after secondary resection was 50%. This was also the main criticism posed in a recent review by Bagaria *et al*.[22]

In sarcomas of the extremities, radiotherapy has shown marked improvements in local control.[23] Previous analyses regarding morbidity[24,25] have demonstrated a moderate rate of perioperative morbidity. Because RPLSs have the highest rate of local recurrence of all different histologic types of sarcoma, locally directed radiotherapy before surgery can improve the outcome of radical compartmental surgery.

Because neoadjuvant treatment was introduced at our center in 2011, the largest patient group in our retrospective study (21 out of 34 patients) underwent surgery without any additional treatment. Three patients prior to 2011 were given adjuvant chemotherapy (doxorubicin/ifosfamide), with mixed results. To date 9 of 10 patients who underwent neoadjuvant radio(chemo)therapy are alive. At a mean follow-up of 53 months only 1 death has been reported, whereas in the surgical group less than 60% of patients were alive after 50 months.

Few studies have assessed the long-term outcomes of modern radiotherapy for RPLS administered before surgery compared with surgery alone, and large trials are warranted. A larger cohort from Pennsylvania matched 174 patients who underwent neoadjuvant radiotherapy with a group of patients who underwent surgery only. They showed a small benefit for the patients who underwent neoadjuvant treatment,[26] whereas Stucky *et al*[7] showed better local control but no oncologic benefit for neoadjuvant radiation therapy in retroperitoneal soft tissue sarcomas (of which 68% were RPLS). Some also report a survival benefit only for well-differentiated RPLS.[27] The results of the STRASS(EORTC) trial failed to demonstrate a benefit for preoperative radiotherapy for RPS. In the exploratory analysis, preoperative radiotherapy may benefit the LPS subgroup.[28] Following the STRASS, another randomized study is in progress. STRASS 2 is going to address the role of neoadjuvant chemotherapy [Surgery With Our Without Neoadjuvant Chemotherapy in High Risk RetroPeritoneal Sarcoma (STRASS2)]. In a phase 2 study the effect of trabectedin in advanced RPLS and well-differentiated/dedifferentiated liposarcoma is under evaluation (EudraCT Number: 2012-005428-14).

Conclusions

The results summarized in this paper are based on a retrospective analysis of patients with RPLS at a sarcoma center. Prospective randomized studies concerning the management of these tumors are difficult to perform. The therapy of these sarcomas often is not evidence based and is performed according to retrospective data and personal experience. Even though 70% of our patients developed recurrent disease, neoadjuvant radiotherapy appears to have positive benefit on the outcome.

Acknowledgments

The data sets used and/or analyzed during the current study are available from the corresponding author on reasonable request. The authors declare no conflict of interest. Ruth Ladurner and Robert Bachmann did the literature research and wrote the manuscript. Jens Strohäker and Christian Birkert collected data and did statistical evaluation. Alfred Königsrainer and Hans-Georg Kopp helped with literature research and wrote parts of the manuscript. The authors take full responsibility for the work.

References

1. ESMO/European Sarcoma Network Working Group. Soft tissue and visceral sarcomas: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2012; **23**(suppl 7):vii92–99
2. Ardoino I, Miceli R, Berselli M, Mariani L, Biganzoli E, Fiore M *et al*. Histology-specific nomogram for primary retroperitoneal soft tissue sarcoma. *Cancer* 2010;**116**(10):2429–2436
3. Dalal KM, Kattan MW, Antonescu CR, Brennan MF, Singer S. Subtype specific prognostic nomogram for patients with primary liposarcoma of the retroperitoneum, extremity, or trunk. *Ann Surg* 2006;**244**(3):381–391
4. Singer S, Antonescu CR, Riedel E, Brennan MF. Histologic subtype and margin of resection predict pattern of recurrence and survival for retroperitoneal liposarcoma. *Ann Surg* 2003; **238**(3):358–370
5. 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):1–9

6. Zhao X, Li P, Huang X, Chen L, Liu N, She Y. Prognostic factors predicting the postoperative survival period following treatment for primary retroperitoneal liposarcoma. *Chin Med J (Engl)* 2015;**128**(1):85–90
7. Stucky CC, Wasif N, Ashman JB, Pockaj BA, Gunderson LL, Gray LJ. Excellent local control with preoperative radiation therapy, surgical resection, and intra-operative electron radiation therapy for retroperitoneal sarcoma. *J Surg Oncol* 2014;**109**(8):798–803
8. 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**(3):355–363
9. Hassan I, Park SZ, Donohue JH, Nagorney DM, Kay PA, Nasciemento AG *et al*. Operative management of primary retroperitoneal sarcomas–a reappraisal of an institutional experience. *Ann Surg* 2004;**239**(2):244–250
10. Stoeckle E, Coindre JM, Bonvalot S, Kantor G, Terrier P, Bonichon F *et al*. 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**(2):359–368
11. Pawlik TM, Pisters PWT, Mikula L, Feig BW, Hunt KK, Cormier JN *et al*. Long-term results of two prospective trials of preoperative external beam radiotherapy for localized intermediate- or high-grade retroperitoneal soft tissue sarcoma. *Ann Surg Oncol* 2006. **13**(4): p. 508–517.
12. Heslin MJ, Lewis JJ, Nadler E, Newman E, Woodruff JM, Casper ES *et al*. Prognostic factors associated with long-term survival for retroperitoneal sarcoma: Implications for management. *J Clin Oncol* 1997;**15**(8):2832–2839
13. Tseng WW, Tsao-Wei DD, Callegaro D, Grignani G, D'Ambrosio L, Bonvalot S *et al*. Pancreaticoduodenectomy in the surgical management of primary retroperitoneal sarcoma. *Eur J Surg Oncol* 2018;**44**(6):810–815
14. Gronchi A, Pollock RE. Quality of local treatment or biology of the tumor: which are the trump cards for loco-regional control of retroperitoneal sarcoma? *Ann Surg Oncol* 2013;**20**(7):2111–2113
15. Raut CP, Swallow CJ. Are radical compartmental resections for retroperitoneal sarcomas justified? *Ann Surg Oncol* 2010;**17**(6): 1481–1484
16. Strauss DC. Patterns of recurrence in retroperitoneal liposarcomas: reflecting surgical approach or tumor biology? *Ann Surg Oncol* 2014;**21**(7):2113–2116
17. Gronchi A, Pollock R. Surgery in retroperitoneal soft tissue sarcoma: a call for a consensus between Europe and North America. *Ann Surg Oncol* 2011;**18**, 2107–2110.
18. Tseng WW, Madewell JE, Wei W, Somaiah N, Lazar AJ, Ghadimi MP *et al*. Locoregional disease patterns in well-differentiated and dedifferentiated retroperitoneal liposarcoma: implications for the extent of resection? *Ann Surg Oncol* 2014;**21**(7):2136–2143
19. Neuhaus SJ, Barry P, Clark MA, Hayes AJ, Fisher C, Thomas JM. Surgical management of primary and recurrent retroperitoneal liposarcoma. *Br J Surg* 2005;**92**(2):246–252
20. Bonvalot S, Raut CP, Pollock RE, Rutkowski P, Strauss DC, Hayes AJ *et al*. Technical considerations in surgery for retroperitoneal sarcomas: position paper from E-Surge, a master class in sarcoma surgery, and EORTC-STBSG. *Ann Surg Oncol* 2012;**19**(9):2981–2991
21. Hamilton TD, Cannell AJ, Kim M, Catton CN, Blackstein ME, Dickson BC *et al*. Results of resection for recurrent or residual retroperitoneal sarcoma after failed primary treatment. *Ann Surg Oncol* 2017;**24**(1):211–218
22. Bagaria SP, Gabriel E, Mann GN. Multiply recurrent retroperitoneal liposarcoma. *J Surg Oncol* 2018;**117**(1):62–68
23. Yang JC, Chang AE, Baker AR, Sindelar WF, Danforth DN, Topalian SL *et al*. Randomized prospective study of the benefit of adjuvant radiation therapy in the treatment of soft tissue sarcomas of the extremity. *J Clin Oncol* 1998;**16**(1):197–203
24. Kelly KJ, Yoon SS, Kuk D, Qin L-X, Dukleska K, Chang KK *et al*. comparison of perioperative radiation therapy and surgery versus surgery alone in 204 patients with primary retroperitoneal sarcoma: a retrospective 2-institution study. *Ann Surg* 2015;**262**(1):156–162
25. Bartlett EK, Roses RE, Meise C, Fraker DL, Kelz RR, Karakousis GC. Preoperative radiation for retroperitoneal sarcoma is not associated with increased early postoperative morbidity. *J Surg Oncol* 2014;**109**(6):606–611
26. Ecker BL, Peters GM, McMillan MT, Sinnamon AJ, Zhang PJ, Fraker DL *et al*. Preoperative radiotherapy in the management of retroperitoneal liposarcoma. *Br J Surg* 2016;**103**(13):1839–1846
27. De Wever I, Laenen A, Van Limbergen E, Pre-operative irradiation for retroperitoneal liposarcoma: results of a pilot study. *Acta Chir Belg* 2013;**113**(5):315–321
28. Bonvalot S, Gronchi A, Le Pechoux C, Swallow CJ, Strauss DC, Meeus P *et al*. STRASS (EORTC 62092): a phase III randomized study of preoperative radiotherapy plus surgery versus surgery alone for patients with retroperitoneal sarcoma. *J Clin Oncol* 2019;37(suppl 15):11001–11001.