

Multidisciplinary approach as the optimum for surgical treatment of retroperitoneal sarcomas in women

M. Brodak¹, J. Spacek², J. Pacovsky¹, E. Krepinska²

¹Department of Urology, Medical Faculty of the Charles University and Faculty Hospital, ²Department of Obstetrics and Gynecology, Medical Faculty of the Charles University and Faculty Hospital, Hradec Kralove (Czech Republic)

Summary

Introduction: The study aimed at evaluating surgical treatment results of retroperitoneal sarcomas (RPS) in female patients in terms of urological and oncological-gynecological collaboration. **Materials and Methods:** The authors performed a retrospective review of 17 women who underwent resection of a retroperitoneal tumor. The surgical results, complications, and both overall and disease-free survivals were evaluated. The assessment of a positive surgical margin and the size of the tumor were the second objective. The Kaplan-Meier survival analysis was used for statistical evaluation. **Results:** The median follow-up was 60 (26 - 128) months. The mean age was 55.4 (35 - 75) years. The mean size of tumors was 14.8 (6 - 45) cm. Local recurrences were recorded in three patients, while distal metastases were reported in one patient. Two patients died of distal metastases. The overall and cancer-specific survival was 87.5% and disease-free survival was 76.5%. **Conclusions:** Complete resection is the only effective treatment of retroperitoneal sarcomas. Presence of positive surgical margin is connected with a high risk of local recurrence regardless of an adjuvant chemo- and radiotherapy. The size of tumor had no impact on the survival or risk of local recurrence in the study group. The uro-gynecological collaboration was evaluated as well-suited in this part of oncological surgery.

Key words: Retroperitoneal sarcoma; Leiomyosarcoma; Liposarcoma; Malignant fibrous histiocytoma; Multidisciplinary collaboration.

Introduction

Retroperitoneal sarcomas (RPS) represent a heterogeneous group of uncommon malignant tumors and rank among soft tissue sarcomas (STS). STSs represent less than one percent of malignant diseases and 10% - 20% of them occur in the retroperitoneal space [1-6]. The most common histotypes are leiomyosarcomas, malignant histiocytomas, fibrosarcomas, and liposarcomas [2]. So far, more than 50 subtypes are known [7]. Most STS tumors occur within the fifth and the sixth decades of life [8]. The etiology and biologic behavior of these tumors is contingent. The most effective treatment method is complete surgical removal. Although effective, radiotherapy (RT) has restrictions due to the site of a tumor, close to an adjacent organ. Current chemotherapy (CHT) has limited efficacy. The size of RPSs is often very large at the time of diagnosis and their complete surgical removal is not always possible. Local recurrence is the main problem of management of these tumors. Main risk factors of recurrence include the positive surgical margin (PSM) and the histological type of the tumor [5]. Resection of a large RPS in female patients is a demanding and aggressive procedure. In such cases, it is advantageous to combine both oncologic and gynecologic needs of aggressive surgery with the urologist experience in retroperitoneal space surgery. The aim of this study was the evaluation of the results with multidisciplinary collaboration during surgical treatment.

Materials and Methods

A cohort of 17 women who underwent a surgical removal of RPS was subject in this evaluation in the period from 1998-2009. All these patients had abdominal and thoracic computed tomography (CT) before surgery. Magnetic resonance imaging (MRI) or colonoscopy was performed only in exceptional cases of suspected tumor infiltration into adjacent organs, especially into the bowels. Surgery was carried out in general anesthesia with antibiotic prophylaxis. Open surgery was performed in 16 patients while a laparoscopic approach was employed in one patient. Complete resection of the tumor was carried out in all patients. In patients with a tumor close to the ureters with dilatation of the upper urinary tract, a urethral catheter was introduced just before resection.

Complications were assessed as well as surgical results, with a focus on local recurrence, overall survival, and disease-specific survival. The data were statistically analyzed using Kaplan-Meier survival analysis. Sizes of tumors and presence of PSM were statistically analyzed for risk of recurrence or metastases. Wilcoxon rank-sum tests were used and *p* values less than 0.05 were considered statistically significant.

Results

The median follow-up time was 60 (26 - 128) months. The mean age of patients was 55.4 (35 - 75) years. The mean size of tumor was 14.8 (6 - 45) cm. A complete resection without PSM was performed in 14 (88%) cases. No infiltration into the gastrointestinal tract or main vessels was depicted. Table 1 shows histological types, presence of PSM, and next fate of the patients. Two nephrectomies and one splenectomy were performed during removal of RPS due to proximity of tumors. Bleeding was the most common complication. The median blood loss

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Table 1. — An overview of the female patients.

Patient	Histology of RPS	Size of tumor (cm)	Presence of PSM and use of adjuvant CHT + RT	Recurrence	Next fate of patients
1	liposarcoma	10 x 5	no	no	follow-up
2	liposarcoma	8 x 7	no	no	follow-up
3	gastrointestinal stromal tumor	7 x 7	no	no	follow-up
4	sinovial sarcoma	23 x 17	no	no	follow-up
5	liposarcoma	13 x 7	no	no	follow-up
6	malignant fibrous histiocytoma	24 x 20	no	no	follow-up
7	leiomyosarcoma	18 x 11	no	primary metastases	CHT and death 37 months after primary surgery
8	liposarcoma	33 x 20	no	no	follow-up
9	malignant schwannoma	6 x 6	no	no	follow-up
10	liposarcoma	18 x 10	no	no	follow-up
11	leiomyosarcoma	15 x 7	no	no	follow-up
12	lymphangioma	45 x 14	no	no	follow-up
13	hemangiopericytoma	45 x 25	no	no	follow-up
14	liposarcoma	10 x 7	no	no	follow-up
15	malignant fibrous histiocytoma	21 x 17	yes	local recurrence	second resection, combined CHT, third resection, and follow-up
16	malignant fibrous histiocytoma	48 x 26	yes	local recurrence	second resection, combined CHT, and follow-up
17	leiomyosarcoma	21 x 18	yes	local	overall 4 resections combined with CHT and died 38 months after the first surgery

during surgery amounted to 600 (150 - 2,500) ml. Nine patients received blood transfusion during surgery, and the median volume of transfused packed red cells was 900 ml. The median time of surgery was 196 (68 - 314) minutes. There was no perioperative mortality.

All the patients with PSM underwent CHT and RT after surgery. Disease-free survival was recorded in 13 patients (76%). Local recurrence was recorded in three patients with PSM (18%). Patients without PSM exhibited no local recurrence irrespective of the size of the tumor. There was only one exception in one patient (6%) without PSM who had primary pulmonary and hepatic metastases. The mean time from surgery to local recurrence was 26 (22 - 28) months. The treatment of local recurrence consisted in the surgical resection of a tumor combined with second-line CHT. In two patients, the second recurrence was treated by a third resection of the tumor and complemented by new-line CHT with trabectedin. One patient exhibited remission after the second resection and one patient after the fourth resection. The fourth resection was combined with amputation of the rectum and colostomy for infiltration of the rectal wall. Histologic results with local recurrence confirmed malignant fibrous histiocytomas in two patients and one leiomyosarcoma.

The overall and cancer-specific survival was 87.5%. Two patients died of metastatic disease. One patient died after the fourth resection with RT and CHT after the primary resection and second-line CHT after the second resection. Distant metastases followed at six months after the last resection and the patient died at 38 months after the first surgery. The second patient developed distal metastases without local recurrence at 28 months after the complete resection. Despite the CHT regimen, the patient died at 37 months after primary surgery. The histology of both suc-

cumbed patients was leiomyosarcoma as the primary tumors.

The Kaplan-Meier analysis of the overall survival and the disease-free survival are presented in Figures 1 and 2. The size of the removed RPS exerted no significant influence on the risk of local recurrence. The presence of PSM is the main risk factor for local recurrence.

Discussion

RPS is an uncommon but serious disease. The symptomatology is poor and unspecific and the most common symptoms are pain, weight lost, and a palpable tumor. Some tumors are discovered by chance on ultrasound or CT scans. This minimal symptomatology leads to late diagnosis and hence the RPSs are usually very large. The next reason for an extensive growth of a tumor is the absence of a natural barrier within the retroperitoneal cavity. Lahat *et al.* considered the size of a tumor was one of important prognostic factors for distant recurrence and disease-specific mortality in high-grade tumors. The higher risk was combined with a tumor size more than 15 cm [8]. The large tumors with their late presentation to surgery often result in an invasion of neighboring retroperitoneal organs, and thus their surgical resection is difficult or even impossible. Lewis *et al.* presented a cohort of 500 patients who underwent resection of RPS, with their complete resection rate amounting to 83%. The median survival in patients with complete vs incomplete resection was 103 and 18 months, respectively [9]. This short survival is similar to patients without surgical treatment and authors concluded that partial resection would be indicated only for patients with severe symptoms [9]. The most common site of RPS recurrence is localized.

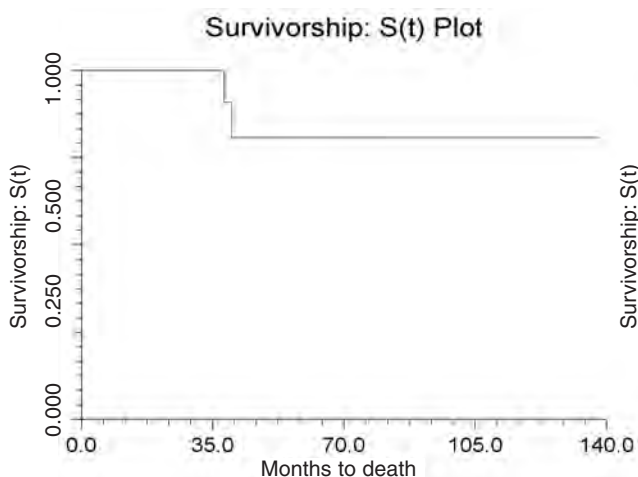


Figure 1. — Overall survival after RPS resection.

The rate of local recurrence ranges from 40% to 80% despite complete resection [4, 6, 9-12]. Distant metastases are rather rare. The therapy of local recurrence is surgical and often the third or more consequential surgical treatments are necessary. Lewis *et al.* reported the median survival after local recurrence amounting to 60 months in resected patients vs 20 months in unresected patients. Recurrent tumors were resected in 57% of patients with the first recurrence. This figure declines precipitously with further recurrences, dropping to 20% after the second recurrence, and down to 10% after the third recurrence [9]. The authors' experience was a little bit different: the size of the tumor had no influence on recurrence or survival. The presence of PSM was linked to local recurrence in all cases.

The most effective treatment of RPS consists in its surgical removal, but these tumors are usually very large at the time of diagnosis and complete resection is not possible in some cases. These giant RPSs also invade important organs in the retroperitoneal space and it is necessary to remove these organs, for instance a kidney, a part of the intestine, the uterus or great vessels [13-15]. Stoeckle *et al.* reported a cohort of 145 patients with RPS without distant metastases but only 94 patients (65%) underwent complete excision. The five-year overall survival rate was 49%. The authors recommended postoperative RT, which significantly increased a local control. On the contrary, grade 3 histology of tumors increased the probability of local recurrence [16]. Lewis *et al.* reported five-year local control rate in 59% of patients who underwent resection of tumor and five-year cause-specific survival rate was 54%. A significantly worse prognosis was recorded in high-grade tumor and liposarcomas [9]. The authors performed resection of adjacent organ during the removal of RPS in the study patients as well. In three cases, they performed resection of adjacent organ, two times nephrectomy, and one splenectomy. In the course of the removal of the local recurrence, they carried out resection of the rectum in one patient.

Gholami *et al.* reported about their own experience with regards to the surgical treatment of RPS. The authors emphasized complete resection and they removed the

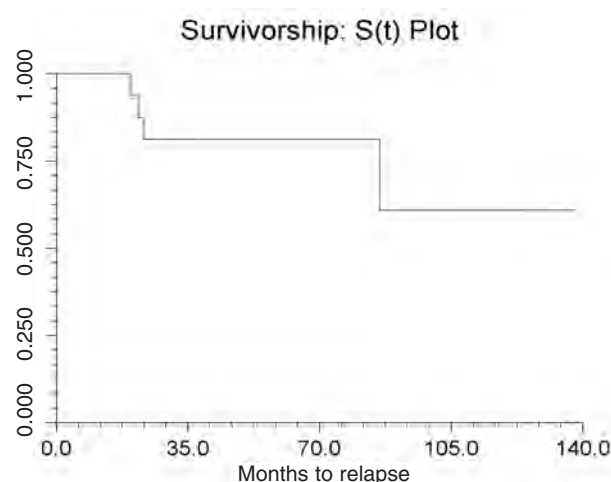


Figure 2. — Disease-free survival after RPS resection.

tumor with adjacent organs rather than peeling the tumor off. They reached 93% of complete resection without positive surgical margin. The five-year survival was 46% and local recurrence was the main problem even when complete resection had been achieved. The authors recommend close monitoring aimed at an early detection of the local recurrence. Even a small-sized recurrent tumor resulted in its successful removal. The authors concluded that RT and chemotherapy had no significant impact on the overall or recurrence-free survival [4].

This part of oncologic surgery is an evident example of possible multidisciplinary collaboration between urologists and gynecological oncologists. Historically the biggest experiences with radical surgery in retroperitoneal space belong to urologists. The presence of an oncological gynecologist is profitable, especially for improving aggressive surgical techniques in pelvis and retroperitoneal space.

Local recurrence is the main risk in management of RPSs. In an effort of reduction of local recurrence, RT was recommended. Some studies have demonstrated a certain impact on reduction of local recurrence but no impact on the overall or the tumor-specific survival [17]. Catton *et al.* reported that adjuvant RT after complete resection only delayed local recurrence [18]. According to other retrospective studies, adjuvant or intraoperative RT had no effect on local control and survival [4, 19, 20]. New techniques of RT such as intensity-modulated radiation therapy (IMRT) offer better results and reduction of adverse effects. The optimal role and timing of RT must be proven through further randomized studies.

CHT exhibits a very limited efficacy in the management of RPS. Older studies described some effects of doxorubicin and ifosfamide treatments [21]. CHT, however, possesses significant side-effects, especially in case of doxorubicin. In an effort to reduce toxicity, pegylated liposomal doxorubicin was administered. It is a modification of doxorubicin with similar antitumor activity and it was tested in the treatment of advanced STS [22, 23]. Trabectedin, originally tested for ovarian cancer, seems to be a promising drug in the treatment of metastatic STS. The given drug was tested in metastatic or non-resectable

STS with failure of standard doxorubicin and ifosfamide chemotherapy regimens [24, 25].

Some risk factors associated with worse prognosis have been described. The most common risk factor mentioned applies to an incomplete resection of the tumor [18-20, 26-28] and to a high-grade sarcoma [18, 20, 26]. Some authors reported worse survival in case of a large tumor, older patients, and/or male patients [17, 27]. According to the present data, completely removed large tumors had no worse prognosis. The removal of adjacent organs is necessary in individual cases of large tumors.

In conclusion, RPSs represent a rare but serious malignant disease with contingent prognosis. Surgery is the most effective treatment option and radical removal without residual tumor has the most important prognostic significance. Complete resection is the main goal of surgery, because PSM significantly increases the risk of recurrence. The size of tumor had no negative influence if the tumor was completely removed. The second surgical resection with second-line CHT was the method of treatment. The authors prefer multidisciplinary approach in the cases of the retroperitoneal tumors in this oncologic center. They want to emphasize that the presence of an onco-gynecologist and urologist is optimal, because retroperitoneal localization has specific characteristics. These rare surgeries have important educative meaning for both specialists.

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Address reprint requests to:

M. BRODAK, M.D., Ph.D.

Medical Faculty of the Charles University

and Faculty Hospital Hradec Kralove

Department of Urology, Sokolska 581

50005 Hradec Kralove (Czech Republic)

e-mail: brodak@fnhk.cz