

Mid-term outcomes in the treatment of retroperitoneal sarcomas: a 12-year single-institution experience

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ABSTRACT

Aim To present the experience from collective data regarding patients with retroperitoneal sarcomas that have been operated in and followed up by the University General Hospital of Patras in Rion, Greece, between 2009 and 2020.

Methods A retrospective analysis of adult patients treated at our hospital with a diagnosis of primary retroperitoneal sarcoma who underwent tumour resection.

Results Data from 29 patients were analysed. The mean age at diagnosis was 56.1 years; 55.2% of patients were male (n=16). Liposarcomas (on histology) were identified in 19 (65.5%) patients, leiomyosarcoma six (20.7%), and other histologic subtypes in four (13.8%) patients. Tumours >5cm were presented in 27 (93.1%) patients. Negative margins were attained in 13 (44.8%) of all patients who underwent surgical resection. Five (17.2%) patients received neoadjuvant radiation, four (13.8%) postoperative radiation, and three (10.3%) patients received both chemotherapy and radiation prior to surgery with the rest of the patients being treated with surgical excision alone. A 3-year follow-up was successful in 21 (72.4%) patients; five (23.8%) patients died. In total, 16 (55.2%) patients were found to have a local recurrence, with no significant difference in patients' age, gender, tumour size, histology, negative surgical margin (R0) resection, neoadjuvant chemotherapy, or radiation therapy. There was a significant difference in the 3-year survival rate between patients having positive or negative surgical margins (p=0.027).

Conclusion The higher 3-year survival rate in patients with retroperitoneal sarcomas when achieving R0 resection warrant further investigation with a larger sample size across different institutions.

Key words: liposarcoma, negative surgical margins, radiotherapy, survival

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INTRODUCTION

Retroperitoneal sarcomas are a rare type of malignancy, accounting for about 15-20% of all soft tissue sarcomas (most commonly arising in the extremities), and overall, of about a 1-2% of all solid malignancies (1–7). The peak of their incidence is in the 5th decade of living, and it is estimated that on an annual basis they make approximately 0.5-1 out of 100 000 new cancer diagnosis (7). Previous radiation has been established as a risk factor for a future retroperitoneal sarcoma diagnosis (1,3,8). However, the diagnosis of a retroperitoneal sarcoma should prompt investigation whether it consist a manifestation of an inherited genetic disorder, such as nevoid basal cell carcinoma syndrome (Gorlin syndrome), familial adenomatous polyposis (Gardner syndrome), Li-Fraumeni syndrome, tuberous sclerosis (Bourneville disease), neurofibromatosis type 1 (von Recklinghausen's disease) (3,4,9,10).

Establishing the diagnosis of a retroperitoneal sarcoma is quite a challenging task for clinicians. To begin with, retroperitoneal tumours often present with non-specific symptoms, such as fatigue and weight loss, and at the time of the diagnosis tumours located in the retroperitoneal space have already grown at a point that poses a limitation to any surgical or other therapeutical interventions. Furthermore, the retroperitoneal space accommodates a large number of anatomical structures of diverse anatomical structure and functional role, from solid organs such as the ovaries, the pancreas and the kidneys, of major vascular formations such as the abdominal aorta and the inferior vena cava (6,7, 11-13). Therefore, a correlation with previous medical history is necessary for excluding other causes of retroperitoneal masses, such as metastatic malignancies in order to reach the diagnosis of a retroperitoneal neoplasia (7,8,10). CT scans are essential for further investigating a retroperitoneal mass, as they do not only demonstrate the relation of the mass to the other retroperitoneal organs and their connection, if existing, with local vasculature (if a CT angiography is performed), but could also provide evidence of the histological type of the underlying suspected sarcoma (Figure 1) (3,4, 14–16). For instance, the presence of regions rich in fat within the tumour might suggest, although its absence cannot rule out the diagnosis, the existence of a liposarcoma (17). Following radiological investigation, the

needle tumour biopsy is indicated in order to determine the exact histological type of the tumour, and it is of great importance for planning potential surgical interventions and stratifying the patient's overall survival rate (3,8,15,18). According to the existing literature, surgical excision of the tumour is the cornerstone of the treatment (18,19,21). It is of great importance that the margins of the excision are clear from cancerous cells, as a negative excision margin (R0). Excision increases the overall survival (3, 19-22). Adjuvant radiotherapy is further indicated after surgery in comparison to preoperative radiotherapy (23-26) because retroperitoneal sarcomas usually recur locally and do not usually metastasize (27-29).

The aim of this study was to present the experience from collective data regarding patients with retroperitoneal sarcoma that have been operated in and followed up by the University General Hospital of Patras in Rion, Greece, in the period 2009-2020.

MATERIALS AND METHODS

Materials and study design

Between January 2009 and December 2020, 45 patients underwent surgery for retroperitoneal tumour in tertiary General University Hospital in Patras/Greece (covering a population of approximately 1.5 million people). A total of 29 patients with histopathological diagnosis of soft tissue sarcoma were included in this retrospective study.

Methods

Data were collected from medical and operating theatre records, as well as from the Hospital-coded database including patient characteristics (age at operation, gender), length of hospital stay, operative time, and histological results.

Statistical analysis

Student's t-test for normally distributed variables, Mann-Whitney U test for skewed variables, and Fisher's exact tests were used to compare results between the groups. A $p < 0.05$ was considered statistically significant.

RESULTS

Data of a total of 29 patients were analysed (Table 1). The mean age at diagnosis was 56.1 years, and 16 (55.2%) patients were males. Liposarcomas (on

Table 1. Characteristics of 29 patients according to positive (Rx) and negative (Ro) surgical margins

Variable	Rx	Ro	p
No (%) of patients (n=29)	16 (55.2)	13 (44.8)	
Males/Females (16/13) (No)	9/7	7/6	>0.05
Mean±SD age (years)	55.9±7.9	56.2±11.3	>0.05
Hospitalization (±SD)(days)	11.8±12.4	9.3±7.4	<0.05
Mean±SD operative time) (minutes)	245±288.2	213±195.7	<0.05
Liposarcoma/other tumour types (19/10) (No)	10/6	9/4	>0.05
Tumour size >5cm (No)	16	11	>0.05
No of 3-year survival patients (n=21)	4 dead/ 4 alive	1 dead/ 12 alive	<0.05

histology) were identified in 19 (65.5%) patients, leiomyosarcoma six (20.7%), and other histologic subtypes in four (13.8%) patients. Tumours >5cm were presented in 27 (93.1%) patients.

Negative margins were attained in 13 (44.8%) of all patients who underwent surgical resection.

Five (17.2%) patients received neoadjuvant radiation, four (13.8%) postoperative radiation, as a radiation treatment. In total, neoadjuvant chemotherapy was received by five (17.2%) patients, while three (10.3%) patients received both neoadjuvant chemotherapy and radiation prior to surgery.

Among the patients with positive surgical margins, in six (37.5%) re-operation was warranted. The 3-year follow-up data were available for 21 (72.4%) patients, of which five (23.8%) died; a total of 16 patients (55.2%) from both groups had a local recurrence irrespective of their survival status. No significant differences in recurrence rates were observed. There was no significant difference in patients' age, sex, tumour size, histological classification, Ro resection status, receipt of neoadjuvant chemotherapy, or radiation therapy. A comparison of the 3-year survival rates between patients that achieved intra-operatively



Figure 1. Sixty-two-year-old man with recurrent retroperitoneal liposarcoma; CT scan shows a soft-tissue mass in retroperitoneum. The longest diameter is 12.5 cm (Mulita F, General University Hospital of Patras, 2021)

confirmed negative surgical margins with the patients that did not have them, revealed a statistically significant difference (p=0.027) (Table 1).

DISCUSSION

Retroperitoneal sarcomas are an uncommon type of solid malignancy with particularly poor prognosis, as the expected 5-year survival rate is about 36-58% (30), despite the fact that data from the 3-year follow up of our study suggest that survival can reach up to 72%. Similar results were recently published with regard to overall survival rates of 67.2% in a cohort of 89 patients (31). Analysing the predictive factors that contribute to patient survival, Giuliano et al. highlighted the importance of optimal surgical resection, with patients surviving up to 2.5 times longer when compared to a treatment strategy based on radiation therapy (32). Such findings are in line with our observation for patient survival, where we further note that Ro excision has distinct advantages over Rx excision. In accordance with existing literature regarding the incidence, the mean age of diagnosis of our patients of 56.1 years coincided with the statistically expected peak at the 6th decade of life (3,7,33). At the same time male patients slightly prevailed (55.2%) over females at rates similar to the current literature (males approximately at 60%) (3,7,33).

Surgical excision of the tumour remains the gold standard of treatment to date regardless of the histological type (1,3,7,17,21, 34–36), which on any occasion should be diagnosed through biopsy prior to the operation. Such operations can be quite a challenging task, not only because the tumour might be of a great size at the time of the diagnosis (1,4,12,17,37), for instance more than 5 cm in diameter in 93.1% of our patients (because they have plenty of anatomical space to expand) but also for the reason that retroperitoneal sarcomas might intersect with other major anatomical structures (35,38,39). Therefore, retroperitoneal sarcoma should be considered as an oncological and simultaneously surgical challenge, keeping in the mind that current data support negative margin excision as the best treatment option. An analysis of the National Cancer Database (NCDB) data for 2762 patients, revealed that those operated at larger, academic surgical centres (such as ours) achieved Ro resection in

approximately 55% of the cases, which is also in line with our results (40). Additionally, researchers emphasized the improved overall survival of patients treated at larger centres that was not solely attributed to proper surgical technique.

Regarding the epidemiology of the subtypes of primary retroperitoneal sarcoma the data from our study are similar to those of the existing literature: liposarcoma is the most frequent diagnosis (65.5%) (6,10,41), followed by leiomyosarcoma (20.7%) (1,35), while all other histological types (approximately about 70 different subtypes) make the remaining 13.8%.

It is of great importance that the tumour and potentially infiltrated organs are removed in block in one session, and that the excision is performed with clear from cancerous infiltration surgical margins. While in our hospital we achieved clear surgical margins in 44.8% of the patients, even greater percentages, up to 95% of complete resectability, have been reported (5). Reportedly, the greater the percentage of clear-margin resection leads to the greater rate of overall survival (3,4,19,30,42).

A recent study by Kwon et al. suggested that patient survival did not differ by receipt of adjuvant or neoadjuvant treatment or not, but was positively influenced when additional surgical resections were carried out in appropriate cases (43). This finding confirms that surgical treatment of retroperitoneal sarcomas remains the golden standard for survival, and adequate tumour debulking can be detrimental in the appropriate management of the disease. Surgical removal is also the most indicated treatment for metastases of primary retroperitoneal sarcoma (36,44) and/or local recurrence of primary tumour, which is the most common pattern (3,4,27,28). The decision whether a patient with primary retroperitoneal sarcoma should receive chemotherapy and/or adjuvant radiotherapy before and/or after the main surgical operation remains controversial. Current studies suggest that there is a moderately positive effect of adding preoperative radiation therapy to patients with non-metastatic, resectable retroperitoneal sarcomas (a reported hazard ratio for mortality was 0.88) (45). On the contrary,

authors of the same study reported an increase in patient mortality, when preoperative chemotherapy was added to the patient undergoing surgical resection of retroperitoneal sarcomas. It should be noted, that the apparent positive effect of radiation treatment prior to surgical resection could be attributed to tumour shrinking and devascularization, which facilitates the subsequent surgical excision, attributes that were not co-assessed at the particular study (27,29,35). Although histological type of the tumour might indicate a higher probability of susceptibility to chemotherapy such as in the case of dedifferentiated liposarcoma (46), preoperative chemotherapy is not considered a first-line treatment option (4,27,47,48). Preoperative radiotherapy, neither decreases the possibility of recurrence nor does it increase the overall survival according to the recent STRASS trial (3,25,49). On the same basis adjuvant radiotherapy does not seem to provide any benefit regarding overall survival (34), although it appears to contribute to an improved clinical outcome on many occasions (24,47,49,50).

In conclusion, retroperitoneal sarcomas constitute a rare type of intra-abdominal malignancy with complex anatomical implications. While chemotherapy regimens and radiation treatment remain viable adjuncts, surgical treatment with complete tumour excision (as stated by negative surgical margins), remains the golden standard for the treatment. Our audit indicates a significant difference in mid-term survival rates for patients with adequate tumour excision, when compared to excision with positive surgical margins, which further supports the surgical treatment as the most effective treatment option.

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