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Assessment of Surgical Treatment and Long-Term Follow-up Results of Extremity Liposarcomas: A Single Center Experience

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Abstract

Background: The aim of this study was to determine the clinical and histological features, management strategy, treatment outcomes, and mortality rates of patients who underwent surgery due to extremity liposarcoma (LPS) in our center.

Methods: The study included patients whom underwent surgery due to extremity LPS in a tertiary oncology center, between January 2002 and December 2014. The data were obtained from the hospital records. Age, gender, lesion localization, tumor size, histopathological analyses, surgical techniques, adjuvant treatments, local recurrence rates, and mortality were noted.

Results: A total of 103 patients (54 males, 49 females) with a mean age of 52.4 years (min-max 19-80 years) were included. The mean follow up period was 57.7 months. Swelling was the most common symptom (97%). The thigh and gluteal region were the most commonly involved localizations. Mxyoid/round cell and well-differentiated LPSs were the two most commonly seen subtypes (57.2% and 17.6%, respectively). Extremity salvage surgery was performed in 96 (93.2%) cases. Adjuvant treatment was applied to 99 (96.1%) patients. Infection, drop foot, or hematoma was seen in 17 patients. Recurrence was seen in 18 patients (17.4), and mean recurrence time was 17 months. The recurrence rate was higher in myxoid/round shaped LPSs. The 5 and 10-year survival rates were 94.1% and 87.3%, respectively.

Conclusion: When planning the management, factors such as surgical margin, tumor grade, age of the patient, size of the tumor, histopathological type, and localization should be considered. It should be noted once again that bone and soft tissue tumors should be treated in specialized institutions with experienced and adequate staff and equipment

Keywords: Liposarcomas; Retroperitoneum; Sarcomas; Histopathologic

Introduction

Liposarcoma (LPS), the primary malignant tumor of fat tissue, is the most common type of soft tissue sarcoma, and accounting for up 15%-25% of all sarcomas [1]. LPS is classified into five histological subtypes according to the World Health Organization as follows; well-differentiated/atypical lipomatous tumor, myxoid/round

cell, dedifferentitated, pleomorphic, and otherwise specified [1]. While atypical and well-differentiated LPSs are low-grade tumors with a good prognosis, de differentitated, pleomorphic, and round cell LPSs have a poor prognosis with high metastatic rates [2].

In general, LPSs are seen in adults after 50 years of age. However, occasionally they are also reported in young adults and children. Although LPS may be seen anywhere in the body, the most common localisations are the retroperitoneum and extremities, especially in the thighs. It should also be kept in mind that there may be differences in the localities of the lipomas according to the histopathological type [1,3]. Surgery is the primary treatment option for extremity LPS, but the type of surgery depends on tumor localization, histology, and stage [4-6]. Limb-sparing surgery is often preferred [7]. In addition, adjuvant chemotherapy and radiotherapy (RT) are very important for reducing morbidity and mortality, and preventing recurrence [8]. Clinical characteristics, histopathological features, or imaging properties of extremity LPSs have been reported in literature [1,4-7], although there are limited data about outcomes and mortality rates, and published studies have included small sample sizes. Therefore, the aim of this study was to determine the clinical and histological features, management strategy, treatment outcomes, and mortality rates of patients who underwent surgery due to extremity LPS in our center.

Materials and Methods

Study Design and Participants

The study included a total of 103 patients who underwent surgery due to extremity LPS, in Dr. Abdurrahman Yurtarslan Ankara Oncology Training and Research Hospital, Department of Orthopedcis and Traumatology, between January 2002 and December 2014. Patients who refused the treatment, were lost in follow-up or did not attend regular follow-up examinations, had a follow-up period of < 3 months, did not complete the treatment protocol, or were transferred to other centers were excluded. This study protocol was approved by the Local Ethics Committee, and informed consent was obtained from the patients.

Data Collection

The data were obtained from the archives of the Orthopedics and Traumatology Department and the hospital data processing system. Patient records were analyzed retrospectively by scanning existing files and film archives. Patients starting treatment were evaluated when they came to the outpatient clinics. Age, gender, lesion localization, tumor size, histopathological analyses, surgical techniques, adjuvant treatments, local recurrence rates, and mortality were noted. All RT and chemotherapy sessions were applied in our hospital.

Statistical Analysis

Statistical Package for Social Sciences (SPSS Inc., Chicago, IL) 13.0 for Windows program was used for statistical analysis. Descriptive statistics were stated as mean, standard deviation, minimum-maximum or frequency (%). The Chi-square test was used to compare categorical data. The Student's t test was used for the comparison of continuous variables between groups. A value of $p<0.05$ was accepted as statistically significant.

Results

Evaluation was made of a total of 103 patients (54 males, 49 females) with a mean age of 52.4 years (min-max 19-80 years). Clinical and demographic data such as age, gender, main symptom, tumour localization, and histopathological diagnosis are summarized in Table 1.

Variables	Data
Age (year) (mean, min-max)	52.4 (19 – 80)
Gender n, (%)	
Male	54 (52.4)
Female	49 (37.6)
Follow-Up Period (months)	57.7 (6-128)
Primary n, (%)	81 (78.6)
Recurrence n, (%)	22 (21.4)
Main Symptom	
Swelling	97 (94.1)
Pain	6 (5.9)
Time of Recurrence (month)	
(median, min-max)	17 (6-24)
Localization n, (%)	
Thigh	62 (60.2)
Gluteal	13 (12.6)
Knee, popliteal, cruris	16 (15.6)
Elbow, forearm	4 (3.8)
Shoulder, arm	8 (7.8)
Histopathologic Diagnosis	
Myxoid, round cell	59 (57.2)
Well differentiated	18 (17.6)
Pleomorphic	12 (11.7)
Dedifferentiated	9 (8.7)
Mixed	5 (4.8)

Table 1: Clinical and Demographical Characteristics of the Patients.

Variables	Data
Surgery Techniques n, (%)	
Wide resection	85 (82.5)
Marginal Resection	5 (4.8)
Hip disarticulation	3 (2.9)
Over knee amputation	4 (3.8)
Wide resection + Proximal femur resection prosthesis	3 (2.9)
Wide resection + Distal femur resection prosthesis	3 (2.9)
Extremity Salvage Surgery n, (%)	96 (93.2)
Tumor Size mean (min-max) cm	12.6 (1-34)
Adjuvant Treatment n, (%)	99 (96.1)
Radiotherapy	72 (69.9)
Chemotherapy	0
Radiotherapy + Chemotherapy	27 (26.3)
None	4 (3.8)
Surgical margin negative	83 (80.5
Surgical margin positive	20 (19.5))
Postoperative Complications n, (%)	
Infection	12 (77.5)
Drop foot	3 (17.6)
Hematoma	2 (11.9)

Table 2: Management Characteristics.

The treatment modalities, tumor size, and post-treatment complications are summarized in Table 2. Marginal resection was applied to 5 (4.8%) patients; 3 patients with anterior forearm and 2 patients with popliteal region involvement, as the localization was close to major vessels or nerves. Extensive bone resection and tumor resection prosthesis was applied to 6 (5.8%) patients due to adjacent bone or bone invasion to achieve a negative surgical margin. Local recurrence was seen in 12 of the patients with surgical margin positive, but no local recurrence was seen in 8 patients. Bed resection was applied to 8 patients and 12 patients with surgical margine positive received adjuvant treatment without any surgical intervention. Of these 12 patients with local recurrence, 3 were patients who had previously undergone bed resection. Hematomas and infections were treated just after the diagnosis. Drop foot improved during the follow-up without any sequelae. In the histopathological subgroups of 4 patients who did not receive adjuvant therapy, 3 were well-differentiated LPS, and 1 was myxoid liposarcoma.

The recurrence and metastatic rates according to the postoperative histopathological types are given in Table 3. The rate of recurrence was higher in marginally resected patients compared to patients who underwent extensive resection ($p < 0.05$). The recurrence rate of the patients with a previous history of recurrence was higher than that of primary cases (60%vs 6.2%) ($p<0.05$). The mortality rates and survival analyses are shown in Table 4. The 5 and 10-year survival rates were 94.1% and 87.3%, respectively.

Variables	Data
Local Recurrence	
Yes	18 (17.4)
No	85 (82.6)
Recurrence	
Total	18/103 (17.4%)
Primary cases	5/81 (6.2%)
Recurrence cases	13/22 (60%)
Recurrence time after operation (month)	17 (6-24)
Histopathology of the recurrent cases	
Myxoid/round shape	13 (72.2)
Pleomorphic	3 (16.6)
Dedifferentiated	2 (11.2)
Metastasis	
Yes	21 (20.4)
No	82 (29.6)
Metastasis Organ	
Lung	13 (61.9)
Lung + Bone	5 (23.8)
Bone	1 (4.8)
Lung + Intra-abdominal organ	2 (9.5)
Histopathology of the metastatic cases	
Myxoid/round shape	9 (42.8)
Pleomorphic	6 (23.8)
Dedifferentiated	5 (23.8)
Mixed	1 (4.9)

Table 3: Characteristics of the Recurrence.

Variables	Mortality
Mortality Rate n, (%)	19/103 (18.4)
0-5 year	6 (31.5)
5-10 year	13 (68.5)
Mortality Time (month)	72.2 (6-111)
Survival %	
5 year	94.1
10 year	87.3
Histopathological analyses	
Mortality n/total, Survival (%)	
Well differentiated	0/18 (100)
Myxoid/round shape	9/59 (84.7)
Pleomorphic	4/12 (66.6)
Dedifferentiated	2/9 (77.7)
Mixed	4/5 (20)
Total	19/103 (81.6)

Table 4: Mortality and Survival Rates.

Discussion

In respect of the clinical features and symptoms of LPS, the most common presentation has been reported to be swelling [9]. In the current study, the main complaint was swelling in 94.1% of cases, followed by pain. The clinical behavior of liposarcomas also varies according to histopathological subtypes. Well-differentiated and low-grade LPSs are not prone to metastasis. However, high-grade LPSs and poorly differentiated histopathological subtypes tend to be more aggressive and metastatic [9,10]. According to the results of this study, myxoid/round shape and pleomorphic LPS were the most recurrent and metastatic LPS subtype.

Well-differentiated LPSs are the most common subtypes of soft tissue tumors classified by the World Health Organization. Myxoid LPS is the second most frequent manifestation [2]. However, in a study by Dervişoğlu 29 of the LPS case were myxoid, 11 well-differentiated, two dedifferentiated, and two pleomorphic LPS [11]. In another study comprising 94 cases performed by Kim, et al. [12] 50 (53.2%) cases showed well-differentiated LPS as the most common subtype and myxoid liposarcoma was observed in 22 (23.4%) cases. In a study published by Nemanqani, et al. [13], myxoid liposarcoma was the most common subtype in 41 patients (56.2%) from a total of 73. In the current study, 59 (57.2%) patients had myxoid/round cell, 12 (11.7%) pleomorphic, 9 (8.7%) dedifferentiated, 5 (4.8%) mixed, and 18 well-differentiated LPS. The most common type was myxoid LPS in this study, which was consistent with the results of the studies by Nemanqani, et al. and Üstündağ and Dervişoğlu. Fiore, et al. [14] reported that pure myxoid LPS ranked 2nd and constituted 30% of all LPSs. The current study included only extremity LPS, and the myxoid LPS rate was found to be 57%.

LPS is generally seen in the 40-60 years age range [1]. However, rare cases have been reported in children between 10 and 15 years of age. Shmookler and Enzinger [15] studied 17 children diagnosed with LPS, the youngest of whom was a male patient diagnosed with myxoid LPS in the right axillary at the age of 11 years. The youngest patient in the current study was a 19-yearold male patient with a myxoid LPS localized in the proximal and medial thigh.

Studies of LPSs in terms of gender distribution have shown that they are seen more frequently in males. In a study conducted by Kim, et al. [12] 53 cases were male (56.4%), 41 were female (43.6%), and the average age of the patients was 56 years (range, 20-80 years). Pilotti, et al. [16] reported that 58% of the cases were male and 40 were female, and the mean age was 56 years (range, 15-76 years). In the current study, the 103 patients comprised 54 (52.4%) males and 49 (47.6%) females with a mean age of 52.4 years (range, 19-80 years).

Some studies have shown that extremity localization has a better prognosis compared to retroperitoneal placement in well-differentiated LPS [17,18]. The recurrence rate has been reported as 43% in well-differentiated LPS and 91% in retroperitoneal patients. In the current study, no local recurrences were observed in well-differentiated LPSs.

In a study of 99 cases by Reitan, et al. [19] local recurrence was found to be lower because of the better resection of small-sized LPSs and higher rates of negative surgical outcomes. Similarly, in a study conducted by Orson, et al. [20] local recurrence was reported at a lower rate and prognosis was likely to be better if the tumors were smaller than 15 cm in size. In the current study, the local recurrence rate was lower in patients with negative surgical margins compared with those with positive surgical margins. Tutar and Gedikoglu reported local recurrence in 11 (22%) of 50 patients, 3 of which had multiple recurrences [21]. In the current study, the incidence of local recurrence within the postoperative follow-up period of 103 patients who underwent surgery was 17.4% (18 patients). The average recurrence time

was 17 months (6-24 months). In the same study above-mentioned by Tutar and Gedikoğlu, the recurrence rate was seen to be decreased when a negative surgical margin was obtained and this negative surgical margin, as the most important indicator of surgical quality, was said to be the most important factor determining the duration of local recurrence-free survival [21].

When metastatis is taken into consideration, LPS is known to frequently metastasis in the lungs and bones. In a study by Evans of 16 patients with metastatic myxoid LPS, 7 metastases were determined in the lungs, 8 in the bones, and 12 in other soft tissue areas. In the current study, only 13 patients (61.9%) had lung metastasis, 5 (23.8%) were determined with lung+bone metastasis, 1 (4.9%) with only bone metastasis, and 2 (9.4%) with pulmonary+intraabdominal organ metastasis. Although these findings differ from those of the Evans study, they are consistent with other results in literature [22,23].

Fiore, et al. [14] reported the local recurrence rates in pleomorphic LPSs as 19.4% in primary tumors, and 20.6% in distant metastases. In the current study, 6 of 12 pleomorphic LPS cases (28.5%) were distant metastases and 3 (16.6%) were local recurrences.

Another study by Henricks, et al. [24] investigated 155 cases of diffusing LPS. Local recurrence was determined as 41%, and distant metastasis as 17%. Of these patients, 28% died due to dedifferentitated LPS. In the current study, there were9 cases of dedifferentiated LPS, and only 2 (11.2%) of these patients had local recurrence during the follow-up period and 5 (23.8%) had distant organ metastasis.

In a study of 99 patients with liposarcoma by Kim, et al. [12] the average follow-up was 48 months. In the study, the mean follow-up period was 57.7 months (range, 6 to 128 months). Therefore, these results can be considered of value due to the longer time period.

Suit and Spiro stated that 60-65 GyRT after surgery in patients who had undergone organ preservation surgery instead of amputation, and who had a closer than 2 cm or positive surgical margin had local control equal to radical amputative surgery techniques alone [25]. Wilson, et al. [26] reported the5-year local control rate of 'preoperative and postoperative RT and conservative surgery as95%. Of 9 patients with microscopically positive surgical margins, only 1 developed local recurrence after RT, which indicates the efficacy of RT in soft tissue sarcomas. In the current study, 99 of 103 patients were given adjuvant RT after surgery. Of the 4 patients who did not receive RT, 3 were well-differentiated LPS and the surgical margins were negative. Local recurrence and distant metastasis were not detected during the follow-up of these 3 patients. The other patient who was not given RT treatment was a 19-year old male patient with myxoid LPS. The postoperative surgical margin of this patient was reported as negative and the tumor site was proximal to the thigh. RT was not applied as the localization was in the proximal medial region of the thigh and there was a potential risk of infertility as a side effect of RT. There was no distant metastasis or local recurrence by 24 months and the patient is still in follow-up.

Conclusion

In conclusion, extremity LPS are usually seen in adulthood, with the thigh and gluteal region as the most involved localizations. Myxoid/round cell LPS is the most common histopathologic subtype, followed by the well-differentiated LPS. Extremity preserving surgery with wide resection seems to be very effective. Adjuvant therapy is required, taking into consideration the location, subtype, and grade of the tumour. Achieving a negative tumour margin is vital for the reduction of mortality and recurrence rates. Patients with a history of recurrence are at higher risk of recurrence. The recurrence rate was higher in cases of myxoid/round shape LPS. The 5 and 10-year survival rates were 94.1% and 87.3%, respectively. When planning the management, factors such as surgical margin, tumor grade, age of the patient, size of the tumor, histopathological type, and localization should be considered. Extremity preservation surgery should be planned if an adequate and healthy margin can be achieved after resection, as the recurrence rate is low and a better function will be obtained than amputation. Adjuvant therapies should be considered to reduce recurrence and mortality. However, it should be kept in mind that RT has a positive effect on local recurrence incases of negative surgery margin. Therefore, the surgical method is the most important factor for survival, and thus it must be emphasised once again that bone and soft tissue tumors should be treated in specialized institutions with experienced and adequate staff and equipment.

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