Popliteal Fossa Sarcomas

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Abstract

Background and Aim: Soft tissue sarcomas of the popliteal fossa are extremely rare tumors of mesenchymal origin accounting for 3%–5% of all extremity sarcomas. However, data regarding the tumor type, neurovascular involvement, and administration of radiation therapy before or after resection are limited. This study aimed to report on popliteal fossa sarcomas analyzing data from two institutions based on a relatively large patient sample.

Materials and Method: Twenty-four patients (80%; 9 men and 15 women) with a popliteal fossa soft tissue sarcoma were included in this study. The reviewed patient data included sex, age, duration of complaints, interval to diagnosis, radiology, pre- and postoperative biopsy, tumor histology, surgery type, complications, and pre- and postoperative oncologic and functional outcomes.

Results: The mean age of the patients was 48 ± 21.23 (range 3–72) years at the time of diagnosis. The most common histological diagnoses were synovial sarcoma (6 patients), hemangiopericytoma (2 patients), soft tissue osteosarcoma (2 patients), fusiform cell sarcoma (2 patients), and myxofibrosarcoma (2 patients). Local recurrence after limb salvage was observed in six patients (25%). At the latest follow-up, 2 patients died of the disease, 2 patients were still alive with progressive lung disease and soft tissue metastasis, and the remaining 20 patients were free from the disease.

Conclusions: Microscopically positive margins may not be an absolute indication for amputation. Also, negative margins do not provide a guarantee that local recurrence will not occur. Lymph node or distant metastasis may be predictive factors for local recurrence rather than positive margins.

Introduction

Soft tissue sarcomas of the popliteal fossa are extremely rare tumors of mesenchymal origin, accounting for 3–5% of all extremity sarcomas [1, 2]. The popliteal fossa region includes major structures such as popliteal vessels and posterior tibial and common peroneal nerves. Also, tumors are extracompartmental because of no barrier and may require extensive neurovascular reconstructions; therefore, they have a worse prognosis [3]. Soft tissue transfers may also be required in large tumors with skin invasion [4]. Advances in staging and limb-salvaging procedures and the use of radio-chemotherapy reduced amputation rates. Local micro-spread can be decreased by neoadjuvant radiation therapy, and unresectable lesions can become resectable in some cases with a neoadjuvant chemotherapy. Sciatic nerve sacrifice is no longer considered a contraindication for limb salvage [5]. Previous reports argued that survival is directly affected by tumor size and grade [4, 6]. However, data regarding the tumor type, neurovascular involvement, and the time of administration of radiation therapy are limited. Also, most of the studies on popliteal fossa sarcomas were based on small patient cohorts. In this study, the clinical aspects such as presentation and postoperative complications were evaluated. The local recurrence, metastasis, amputation and limb salvage rates were also investigated according to the tumor type, grade, size, neurovascular involvement, neoadjuvant therapies, and surgical techniques. This study aimed to

report on popliteal fossa sarcomas using data from two institutions based on a relatively large patient sample.

Materials And Method

The study was performed in accordance with the ethical standards of the Declaration of Helsinki. All patients provided informed consent before inclusion in the study, and a local ethics committee approved the study protocol. The present retrospective study consists of 24 surgically treated popliteal fossa tumor from January 2003 to December 2018. A manual search of the operating room records of senior surgeons was performed for the terms “soft tissue tumor,” “sarcoma,” and “popliteal fossa.” Of the 30 patients, 24 (80%; 9 men and 15 women) with soft tissue sarcoma were included in the present study. The reviewed patient data included gender, age, duration of complaints, interval to diagnosis, radiology, pre- and postoperative biopsy, tumor histology, surgery type, complications, and pre- and postoperative oncologic and functional outcomes. Eligibility criteria included patients having popliteal sarcomas, with a minimum follow-up of 2 years for survivors. For other patients, the duration of follow-up was defined by the last-documented clinical follow-up. Nonoperated patients and histologically unverified cases were excluded. All patients were staged according to the American Joint Committee on Cancer (AJCC). The functional scores were assessed using the Musculoskeletal Tumor Society Score (MSTS) and the Toronto Extremity Salvage Scores (TESS). All patients had neoadjuvant radiation therapy aiming to achieve negative surgical margins. Only patients with metastasis received postoperative chemotherapy. For other patients, the duration of follow-up was defined by the last-documented clinical follow-up. The presence of neurovascular invasion was accepted only if a pathological examination was confirmed. If the surgical margin was > 0.1 mm, it was considered intact. The popliteal fossa was defined as proximal-medial; the semimembranosus and semitendinosus muscles and as proximal-lateral the biceps femoris muscle. Two heads of the gastrocnemius muscle forms the distal border. The floor consisted of posterior distal femur, joint capsule, and popliteus muscle. Local recurrence and metastasis were investigated in scheduled follow-up controls.

Statistical analysis

Descriptive statistics were used to summarize the patient characteristics. The Fisher exact test was used to compare patients with respect to age, sex, primary disease site, and recurrence status. The Cox proportional-hazards regression models were used to evaluate the prognostic factors and survival rates. The Kaplan–Meier method was used to estimate the survival and recurrence according to neural and vascular involvement, metastasis, oncologic treatment, stage, and surgical margins. Statistical analysis was performed using the SPSS for Windows software package (version 13.0.0; SPSS).

Results

The mean age was 48 ± 21.23 (range 3–72) years. The mean follow-up was 41.79 ± 16.97 (range 24–120) months. The most common diagnoses were synovial sarcoma ($n = 6$), hemangiopericytoma ($n = 2$),

soft tissue osteosarcoma ($n = 2$), fusiform cell sarcoma ($n = 2$), and myxofibrosarcoma ($n = 2$). One low-grade fibromyxosarcoma, one clear-cell sarcoma, one extraskeletal chondrosarcoma and one low-grade myxoliposarcoma, one pleomorphic sarcoma, one Ewing sarcoma metastasis, one Ewing sarcoma, and one malign schwannoma were also identified. Two patients lesions could not be specified. All tumors except one were primary. The median tumor size was 7.73 ± 3.19 (range 1.5–32) cm. Lesions were low grade in 3 patients (grade I), intermediate grade (grade 2) in 3 patients, and high grade (grade 3) in 18 patients. At the time of diagnosis, pulmonary metastasis was identified in five patients (21%), liver metastasis in one patient (4%), lymph node metastasis in four patients (17%), and neural invasion in six patients (25%). The AJCC stages were as follows: three patients had stage Ib, three had stage II, six had stage IIIa, four had stage IIIb, and eight had stage IV disease. The patients are summarized in supplementum. Twenty-three patients encountered limb-salvaging surgery and one patient encountered a primary above-knee amputation. In one patient, 14 months after the initial, extraarticular knee-joint resection and prosthesis, a local recurrence was encountered with neurovascular invasion and an above-knee amputation was conducted. In another patient, 11 months after the initial surgery, extraarticular knee-joint resection and prosthesis were done, and a local recurrence was encountered. After two unsuccessful revision surgeries, a hip disarticulation was conducted. Surgical margins were negative in 20 patients and microscopically positive in 4 patients. All residual diseases were treated with revision surgeries. Chemotherapy was administered in eight patients (preoperatively in one, postoperatively in two, and both pre- and postoperatively in five patients). Neoadjuvant chemotherapy was intended to shrink the mass and provide a limb salvage in four patients. These patients had unresectable masses. Absent of response in one patient caused to amputation. Radiotherapy was administered in 14 patients, postoperatively in 6 patients (63 Gy) and preoperatively in 8 patients (50 Gy). All high-grade tumors except amputated patients underwent radiotherapy. Sciatic nerve branches in four patients, common peroneal nerve in two patients, deep peroneal nerve in one patient, and common peroneal and tibial nerve in one patient were resected. Local recurrence after limb salvage was recorded in six patients (25%). Preferences of patients with local recurrence are given in Table 2.

Table 2
Preferences of patients with local recurrences

Tumor type	Grade	At diagnosis	Margins	
Hemangiopericytoma	3	Neurovascular invasion	Positive	Post-op chemotherapy
Clear-cell sarcoma	3	Lymph node, liver metastasis	Negative	Pre-op radiotherapy
Synovial sarcoma	3	No metastasis	Negative	Pre-Post op radiotherapy
Chondrosarcoma	2	Lymph node metastasis	Negative	Pre-post op chemotherapy Post op radiotherapy
Ewing sarcoma metastasis	3	Lymph node lung metastasis	Negative	None
Osteosarcoma	3	Lymph node, liver metastasis	Negative	Pre-Post op chemotherapy

Lung metastasis developed in nine patients (38%) and liver metastasis in two (8%) after treatment. Details on lung metastasis and treatment are given in Table 3.

Table 3
Tumor type, metastasis site, metastasis time, and treatment

Tumor type	Metastasis Site	Metastasis Time (month)	Treatment
Hemangiopericytoma	Lung	6	Lobectomy + chemotherapy
Low differentiated. synovial sarcoma	Lung	9	Surgery + chemotherapy
Soft tissue osteosarcoma	Lung (bilateral)	0	Surgery + chemotherapy
Clear-cell sarcoma	Liver + lung	0/36	Pazopanib 800 mg tablet (once a day)
Synovial sarcoma	Liver	24	Died because of metastasis
Fusiform cell sarcoma	Lung	11	Lobectomy/Lymph node excision + chemotherapy
Synovial sarcoma	Lung	9	Lobectomy + chemotherapy

Postoperative complications included wound dehiscence in three patients. Postoperative radiotherapy regimen in one of them and preoperative radiotherapy regimens in two of them were used (Fig. 1). None required soft tissue reconstruction. No deep vein thrombosis was encountered in the present series. In a 3-

year-old patient, a femur fracture was encountered after 3 months from the initial surgery due to excessive periosteal stripping. Union was achieved with an elastic nail fixation. The MSTS score was evaluated in 22 patients, and the mean score was 81.2 (range 65.0–92.5). The TESS was evaluated in 22 patients, and the mean result was 77.4 (range 67.2–95). The worst result belonged to a patient who had an intralesional resection in another center. Postoperative radiotherapy at 66 Gy and wide re-resection were performed for this patient. No local recurrence was encountered in 2 years, but the patient died after the latter surgery because of multiple visceral metastasis (Fig. 2). The local recurrence rate was 6/24 (25%), and the mean recurrence time was 8.8 ± 2.3 months. The visceral metastasis rate was 9/24 (36%), and the mean time was 10.11 ± 3.2 months. Two patients needed amputation (above-knee and hip disarticulation) after limb salvage because of local recurrence. At the latest follow-up, two patients died of the disease, another two patients were still alive with progressive lung disease and soft tissue metastasis, and the remaining 20 patients were free from the disease.

Discussion

Soft tissue sarcomas of the popliteal fossa are extremely rare tumors of mesenchymal origin accounting for 3–5% of all extremity sarcomas. Turcotte et al. reported this rate as 2.7% in their series [1]. In the present sarcoma series, the incidence rate of popliteal fossa sarcomas was 1.3%. Recent studies showed that the use of radio-chemotherapy could produce limb-sparing rates of 65–95% [7, 8], which was 87.5% in the present cohort. Surgical margins are one of the most important factors affecting local recurrence [9]. In this study, the adventitia or the nerve sheath was routinely removed when the vessels or nerve was in close proximity. In a recent study authors reported that although the close proximity, vital tissues were surrounded by the tumor only in 11.5%. They concluded that carcinomas infiltrate, sarcomas displace the vessel and nerve [10]. Negative margins plus radiotherapy provide lower rates of local recurrence [11]. Radiation therapy has been reported as an adjuvant that improves the local recurrence rates [12]. However, radiotherapy is unable to control the positive margins. Local recurrences after popliteal soft tissue tumors are usually encountered within 2 years after the initial procedure [13]. Local recurrence after limb salvage was recorded in the present study in six patients (25%). Only in one patient, the surgical margins were positive. In four patients, lymph node metastasis was detected. In this regard, lymph node or distant metastasis might be predictive factors for a local recurrence. Turcotte et al. reported the recurrence rate of positive margin as 9% (1/11) in their series of 18 patients. In the present series, only one patient had positive margins, who had a local recurrence. The relationship between local recurrence and survival remains unclear. Two patients with local recurrence underwent amputation, and they had local recurrence. Also, lung metastases developed in one of them. Two deaths occurred due to synovial sarcoma and malignant peripheral nerve sheath tumor because of metastasis at diagnosis and early-term follow-up, respectively. The mean event-free survival was 13.8 months. Pritsch et al reported a series of 27 cases. They reported that 7% of patients had metastatic disease at diagnosis. The amputation rate was 14%. They also reported no difference between the amputees and the limb-salvage group according to survival [7]. The rate of local recurrence was 10% and the wound complication rate was 30%, in their series. In this study, the rate of metastatic disease at diagnosis was 25%. The amputation rate was 13%,

the local recurrence rate was 25%, the total complication rate was 29%, and the wound complication rate was 25%. Five-sixth of local recurrence cases and surgical margins were negative. This result was attributed to the fact that the surgical margins < 1 cm were accepted as intact. Neoadjuvant radiotherapy had a negative impact on wound tissue healing [14]. Also, radiation-induced fibrosis, lymphedema, and joint stiffness might alter the functional scores [15, 16]. In this study, no relationship was found between neoadjuvant radiotherapy and wound complications/lower functional scores. Wound complications might alter the functional scores. However, in this study, no complications were encountered in a patient in whom the medial hamstring and medial head of the biceps muscle with neoadjuvant radiotherapy were resected. In another patient, the gastrocnemius lateral head was resected, and no complications were encountered. In two other patients, the posteromedial corner reconstruction with allograft and rotational gastrocnemius flap was made with postoperative radiotherapy. No complications were encountered, and the mean TESS score was 85 in these two patients. Turcotte et al. reported the TESS and MSTS 1987 mean scores as 82.4% and 33/35, respectively. Bickels et al. reported 15 patients who underwent sciatic nerve resection. They reported good functional results [1]. The mean TESS and MTST 1993 scores were 77.4% and 81.2%, respectively, in this study. The sacrificed nerve branches of the sciatic nerve did not reduce the functional results. All below-average functional scores and local recurrences might belong to neurovascular stripping. Also, amputation, multiple metastases, and fracture might belong to lower scores. All preferences on the present series are given in Table 1. Data regarding detailed analysis of neurovascular involvement are limited. In two patients, the margins were positive. Four neural resections and three vascular by-passes were performed. Only in two patients who underwent neurovascular stripping (margins < 1 cm), local recurrence was detected. Hohenberger et al. reported 20 patients with soft tissue sarcoma invading neurovascular structures, but only four patients had popliteal fossa tumors [18]. No other study has evaluated neurovascular involvement so far. In the present study, five neural and eight vascular invasions were detected. Of the 20 patients with neurovascular stripping, only 5 (25%) had a local recurrence. Of the six patients with local recurrence, four patients had no pre-/postoperative radiotherapy.

The present study had several limitations. It was a retrospective study and was relatively small and heterogeneous. Second, the minimum follow-up was only 2 years. However, to our knowledge, this report is one of the largest series about popliteal soft tissue sarcomas in English literature. The rates of local recurrence and systemic disease increased only slightly during a longer follow-up because local recurrence and metastasis usually occur in first two years, and the median follow-up in this study was more than 70 months [10].

In conclusion, microscopically positive margins may not be an absolute indication for amputation. Also, negative margins do not provide a guarantee that local recurrence will not occur. Lymph node or distant metastases may be predictive factors for local recurrence rather than positive margins. Metastases at diagnosis or early term after surgery might increase the local recurrence despite negative margins. Therefore, in these patients, preoperative radiotherapy was suggested despite wound complication risk. Irradiation before re-resection in positive margins is not recommended; instead, the re-resection should be done first, followed by radiotherapy.

Declarations

Conflict of Interest: None.

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Consent for publication: Permissions were obtained from the patients.

Acknowledgements: Not applicable.

Ethics approval and consent to participate: This study was approved by the local ethical committee and informed consent has been taken from all participants.

Availability of data and materials: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Authors' contributions:

OE: Conception or design of the work, data collection and data analysis with interpretation.

AÇ: Data collection.

ET: Data analysis.

GA: Critical revision.

KÖ: final approval of the version to be published.

VG: Drafting the article critical revision of the article and final approval of the version to be published.

All authors read and approved the final manuscript.

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Tables

Due to technical limitations, table 1 is only available as a download in the Supplemental Files section.

Figures

Figure 1

(A) A polliteal "S" incision. (B) Neurovascular stripping from the tumor. (C) After the resection, some dead space was present. (D) A myxoid liposarcoma.

Figure 2

(A) Axial MRI of a popliteal tumor. (B) Skin incision that included the biopsy tract. (C) Neurovascular stripping from the tumor. (D) Tumor and neurovascular bundle proximity. (E) After the excision. (F) A myxofibrosarcoma. (G) Low-power histogram. (H) High-power histogram.

Supplementary Files

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