

# Statistically based survival rate estimation in patients with soft tissue tumors

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## Abstract

Although most soft tissue tumors are benign, with a high healing rate after surgical excision, there is a variety of malignant tumors with differences in progression and prognosis. The study aimed to assess the survival rate in patients diagnosed with this pathology, based on the patient's characteristics (age, gender, race), as well as the tumor's histological type, differentiation degree, location and size.

The retrospective study included a group of 103 patients diagnosed during 2010 and 2017 in our department. Considering the high healing rate of benign tumors, only the group of neoplastic patients (45 cases) was involved in the survival rate estimation, assessing tumor characteristics and individual comorbidities. Within this lot, we emphasized a predominance of neoplasm in patients aged over 50 years (32 cases), men (29 cases), and localization of the neoplasm in the thigh (23 cases). The predominant histopathological type, liposarcoma, was diagnosed in 67% of the cases, with dimensions over 6 cm and with local extension.

There have been significant variations in mortality between the different histological subtypes (liposarcoma vs. synovial sarcoma). Local recurrences were showed in 18 cases of liposarcoma in the first 2 years after the surgical excision, with an increased aggressiveness of this neoplasm in men over 50 years. 12 cases developed distant metastasis, and until the end of the study, 7 deaths were reported in 3 cases involving associated comorbidities.

The five-year survival is inversely proportional to the extent of the tumor and the local invasion, as well as to the age of the patient. An overall survival rate is difficult to appreciate in the context of a heterogeneous group of tumors so it must be evaluated for every histological subtype taking into account the patient's particularities.

Keywords: survival rate, sarcomas, mortality, prognostic factors

## Introduction

Tumorigenesis represents a complex process by which healthy tissue progressively transforms from a normal phenotype into an abnormal colony of proliferating cells. Soft tissue tumors represent a highly

heterogeneous group of tumors that arise from mesodermal tissue, most commonly from the connective, muscle, adipose, neural, vascular, and lymphatic tissues. Benign tumors, which more closely resemble normal tissue, have a limited capacity for autonomous growth, with a high healing rate after surgical excision and a

low rate of local recurrence. Malignant tumors are relatively uncommon accounting for approximately 1% of all adult cancers [1], with a distinct age distribution, site of presentation, natural biological behavior, and prognosis. Long-term survival depends on patient age and tumor type, accurate initial staging, surgical excision and early detection of disease recurrence [2].

The true incidence of this group of tumors has generally been under-reported. In 2010, around 3300 people were diagnosed with soft tissue sarcoma in the UK [3], and approximately 9000 new cases are diagnosed in the USA annually [4].

As with other malignant neoplasm, the etiology is unknown, although there are certain genetic associations like mutations in the NF1 gene [5], inherited mutations in the RB gene [6] or in the TP53 tumor suppressor gene [7]. Among other recognized causes, what should be mentioned are various physical and chemical factors, exposure to ionizing radiation or acquired immunological defects.

The aim of this study was to assess the survival rate in patients diagnosed with this pathology, based on the patient's characteristics (age, gender, race), as well as the tumor's histological type, differentiation degree, location and size based on an outcome calculator [8] (still underdevelopment).

## Materials and methods

The retrospective study was performed on a group of 103 patients with soft tissue tumors of the locomotor system diagnosed from 2010 through 2017 in our department. We excluded 58 patients from this lot, whose diagnostic after surgical excision and histopathological examination revealed a benign soft tissue tumor, so only the group of neoplastic patients (45 cases) was involved in the survival rate estimation.

Following the clinical examination, most patients reported a painless mass, although

pain was reported in 7 cases. We evaluated the consistency of the mass, tenderness on palpation, relationship to adjoining structures and range of motion, as well as signs of inflammation. Non-specific symptoms included painless lump or swelling, numbness, weight loss and fatigue.

The paraclinical evaluation of a suspected soft tissue tumor began with conventional X-ray examination, which is an excellent method for the assessment of osseous involvement, or the evaluation of the presence of mineralization that may be suggestive of a certain diagnosis.

Following the confirmation of a soft tissue mass, in small and superficial lesions, ultrasonography was particularly useful in the assessment of the nature of the "lump" – solid or cystic – size, shape, location, vascularity, and anatomical relationships to adjoining structure.

Magnetic Resonance Imaging (MRI) was performed for local staging, definition of fascial planes, evaluation of bony involvement, compartment boundaries, and neurovascular bundles.

Computed Tomography (CT) is the most effective modality for detailed evaluation of osseous architecture by being able to assess osseous remodeling, periosteal reaction, or subtle areas of mineralization. Given the ability of soft tissue sarcomas to metastasize hematogenous, especially to the lung, each patient was evaluated for pulmonary metastasis with a CT scan of the chest. Scintigraphy was used for the assessment of osseous metastases and to differentiate active lesions from inactive lesions (chondroid tumors). In selected cases, a preoperative embolization was conducted.

Laboratory tests were performed for each patient diagnosed with soft tissue tumor. Complete blood cell count, ESR, CRP ruled out infection and leukemia, serum protein electrophoresis for multiple myeloma, alkaline phosphatase to evaluate if there is a metabolic bone disease, metastatic disease, osteosarcoma, Ewing sarcoma, lymphoma, or Paget disease.

The histopathological diagnosis was based on current 2013 World Health Organization (WHO) [9] classification, which divided these tumors into 12 groups according to their histogenesis. The reference pieces were processed by the classical paraffin inclusion method and stained with Hematoxylin-Eosin and, for the determination of immunophenotypic characters, the paraffin blocks were sectioned and analyzed using different immunohistochemical markers.

There are many grading systems. They are generally based on evaluation of histomorphological features, including cellularity, cellular pleomorphism, mitotic activity, and necrosis [10]. In this study, we used the Enneking staging system [11] and AJCC staging system [12].

## Results

Soft tissue sarcomas may occur at any age, most often in the middle aged and older adults. The retrospective study conducted included a group of 45 patients aged 20-95 years old, with an average age of 53 years old.

We emphasized a predominance of neoplasm in patients aged over 50 (32 cases) and the sex distribution revealed a high incidence of neoplasm in men (29 cases).

The most common localization of the lesion was in the thigh (23 cases) followed by arm, elbow and other localizations and the most frequent histological type encountered was liposarcoma diagnosed in 30 cases due to high rate of local recurrence (Fig. 1).

Fig. 2 shows a well-differentiated liposarcoma. There is a proliferation of relatively mature adipocytes, which, unlike those in lipoma (benign), show a significant variation in shape and size, with hyperchromatic nuclei, located eccentrically. Focal, monocyte or multifocal lipoblasts with nuclei are indented by cytoplasmic vacuoles. Based on patient's and tumor's characteristics combined with

the "soft tissue sarcoma outcome calculator", the survival rate estimated for this subtype was 95%, unlike dedifferentiated liposarcoma, whose 5-year survival rate was calculated by applying the same criteria and adjusted to individual characteristics was only 53%. The behavior of this subtype was that of a high-grade sarcoma with deep localization, increased dimensions, and a high rate of local recurrence – first 2 years (Fig. 3,4).

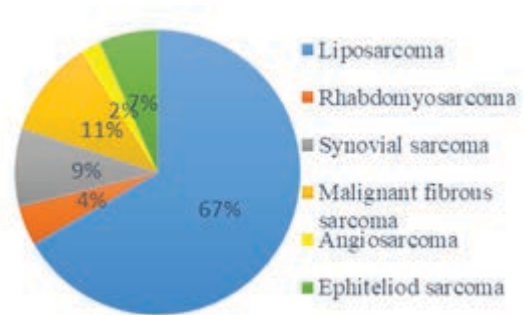


Fig. 1 Histological type distribution

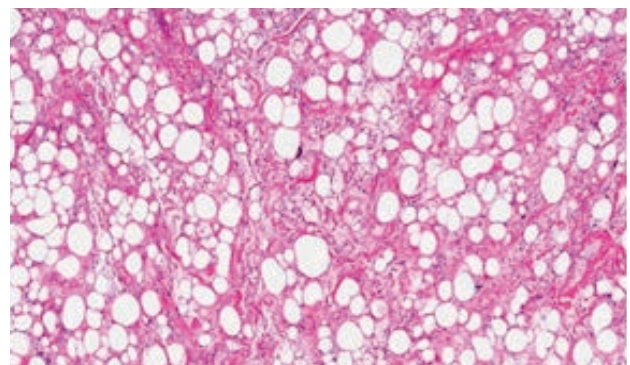


Fig. 2 HP aspect – liposarcoma

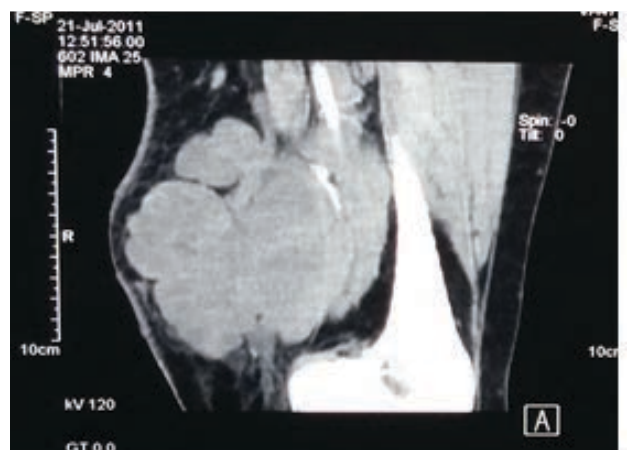


Fig. 3 Liposarcoma – distal thigh – first presentation

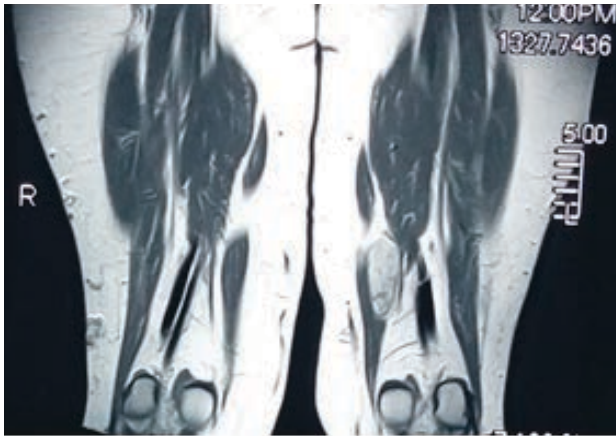


Fig. 4 Liposarcoma – recurrence - first 2 years

We retrospectively assessed the relationship between tumor dimension and histologic grade.

28 cases were diagnosed as high grade of which 18 cases were large sized (>10 cm) and 7 cases had pulmonary metastases at the time of diagnosis (Fig. 5).

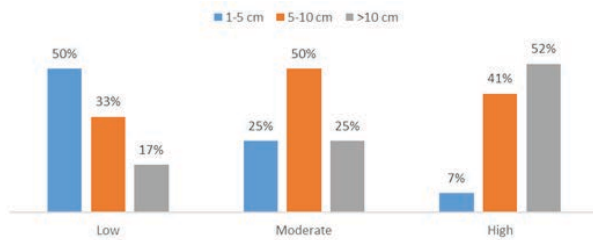


Fig. 5 Correlation between tumor size and HP grade

Calculation of the mean survival rate is difficult to assess in the context of a heterogeneous tumor group, taking into account the need to evaluate each histopathological subtype in correlation with patient characteristics.

Fig. 6,7 show the gross aspect of different subtypes of soft tissue tumors, each of them with a different grade of differentiation. Therefore, it can be concluded that high-grade epithelioid sarcoma is associated with areas of necrosis and hemorrhage, while the low-grade fibrosarcoma may appear well circumscribed but non-encapsulated, with a fleshy aspect. An increased mortality rate has

been reported especially in elderly patients who were diagnosed with large size sarcomas, with high histological grade and associated comorbidities.

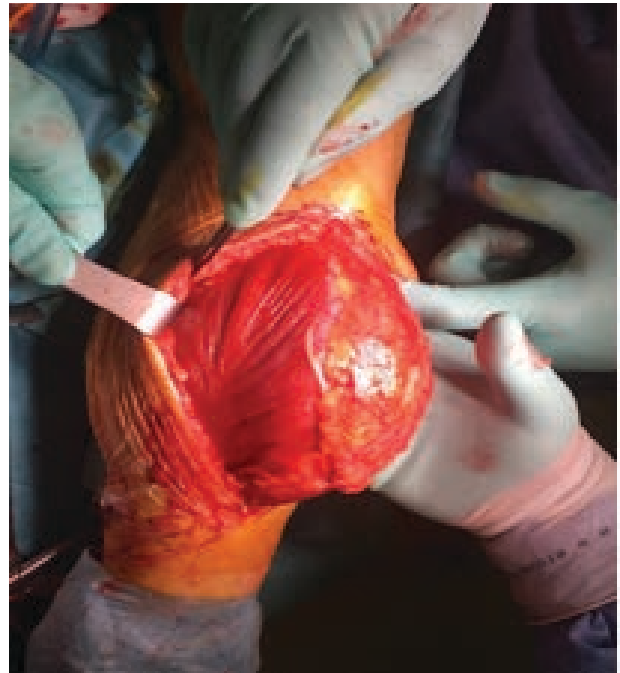


Fig. 6 Gross aspect of a low-grade fibrosarcoma

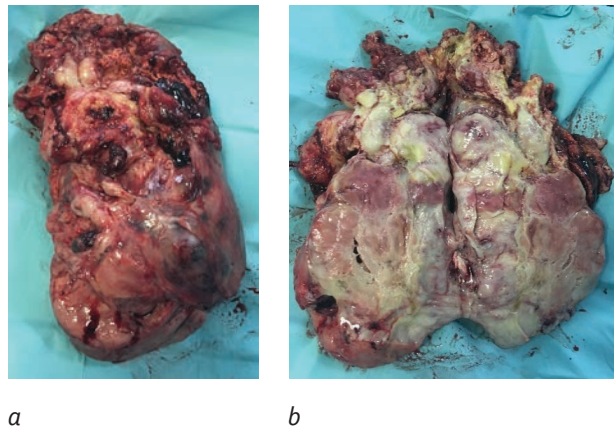


Fig. 7 Gross aspect of a high-grade epithelioid sarcoma  
A. Note the irregular shape of a 14 cm tumor, with hemorrhagic areas  
B. Longitudinal section - note the areas of necrosis and central hyalinization

The mortality rates of different subtypes of soft tissue sarcomas shown below (Fig. 8) were calculated at the time of diagnosis based on patient's characteristics and tumors' characteristics. We concluded that high-grade

sarcomas had a high mortality rate especially in the elderly patients with other comorbidities, unlike young patients who had a better prognosis, which led to a better survival rate.

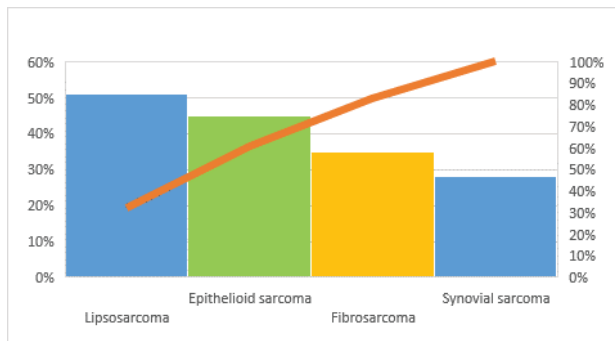


Fig. 8 5-year mortality rate

## Discussions

Soft tissue tumors are characterized by their diversity in the histologic appearance and in their biologic behavior, as well as in anatomical origin. Imaging of soft tissue tumors requires a multimodality approach, with no single imaging modality being ideal for every tumor [13]. Large size at presentation (>5 cm), rapid growth, deep location, and hyperemic chaotic-type vascular on Doppler imaging [14,15] are all more common in malignant tumors, and further evaluation is needed. The most frequent lesion in our lot was liposarcoma. According to the World Health Organization, liposarcomas are divided into 5 subtypes: well-differentiated, myxoid, round cell, dedifferentiated and pleomorphic [16]. Well-differentiated liposarcoma represent a locally aggressive tumor with no risk of metastatic disease [17].

The highest survival rate has been recorded in synovial sarcomas. The cases of synovial sarcomas included in our study are described as biphasic type, with spindle cells arranged in fascicles and hyalinization, and surrounded by an inflammatory area with increased vascularity, fibrin deposition, and diffuse lymphocytic infiltrate [18].

Most important prognostic factors for

overall survival rate in patients with soft tissue tumors are primary site, size, histological type, grade, and stage at presentation [18]. Based on these criteria, some specialist centers have made online calculators available [19,20].

## Conclusions

Although they share biological characteristics, and are treated in a similar manner, each of the various soft-tissue sarcomas has a unique morphology, biological behavior, and prognosis.

Pathologic grading is at times difficult. In general, the extent of pleomorphism, atypia, mitosis, and necrosis correlates with the grade of malignancy.

The five-year survival is inversely proportional to the extent of the tumor and the local invasion, as well as the age of the patient.

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