

**Prognosis Factors of Soft-Tissue Sarcomas: A Retrospective Study of 50 Cases**

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**Abstract:** Soft tissue sarcomas (STS) are malignant tumors of mesenchymal origin that originate in any connective tissue or body support tissue. They have 1% of adult malignancies and are much less common than benign tumors developed in the soft tissue. Our study examined 50 cases of soft tissue sarcomas managed by the trauma and orthopedics department B4 at the university hospital center Hassan II Fès, over a period of 05 years between 2013 and the end of 2017, whose purpose is to analyze different prognostic factors determining the risk of local recurrence and metastases. The average age of patients in our series is 50 years, the sex ratio is 01. The most common types in our study were synovial sarcoma, liposarcoma and leiomyosarcoma. High grades (II and III) are the most common. The localization in the lower limb is the most frequent and concern predominantly the thigh. Wide excision is the most used treatment. 24% required a therapeutic supplement by external radiotherapy. Chemotherapy was indicated in 52% of cases. The evolution finds 10% of clinical and radiological remission, 22% of local recurrences isolated, 26% of metastases mainly pulmonary, 08% of recurrences associated with metastasis. 07 patients were lost to follow-up and 10 deaths were found postoperatively in our study. The prognosis of soft tissue sarcomas is traditionally unfortunate; and may be aggravated by inadequate therapeutic management, hence the importance of multidisciplinary management. Tumor size, depth, histological type and grade, margin status, and adjuvant radiotherapy are the main prognostic factors for recurrence and metastasis of these tumors.

**Keywords:** Sarcoma, soft tissue, limbs, prognosis, resection, margins, radiotherapy.

**INTRODUCTION**

Soft tissue sarcomas (STS) are malignant tumors of mesenchymal origin that initiate in any connective tissue or supporting tissue of the body [1]. They represent 1% of adult malignant tumors and are much less common than benign tumors developed in the soft tissue. Two-thirds of soft tissue sarcomas are localised in the limbs. In order of decreasing frequency they concern the lower limbs then the upper limbs [2].

No formal etiology has been recognized till now, but several intrinsic factors (gene mutation : NF1RB1, WRN, p53, APC respectively responsible for neurofibromatosis type I, congenital retinoblastoma and Li-Fraumeni syndromes, Gardner, de Werner) or extrinsic (exposure to ionizing radiation, vinyl chloride, dioxin, chlorophenol, some viruses, etc.) have been identified [3].

Soft tissue sarcomas are a very heterogeneous group, more than 50 different histological types have been described, some with histological subtypes

according to the latest World Health Organization (WHO) classification [4].

Their diagnosis is deemed difficult. An imaging assessment including an MRI and especially a preoperative biopsy are necessary to adapt the therapeutic approach [2, 5-7].

Treatment of limb soft tissue sarcomas (STS) is currently based on conservative surgery associated with radiotherapy, with the goal of maximizing function while ensuring optimal oncologic safety. Chemotherapy finds its place in locally advanced tumors and / or high grade malignancies with high metastatic potential. therefore, The great difficulty of the treatment is in the balance between function and safety, that it is up to the Multidisciplinary Consultation Meetings (RCP) to define it for each patient [9]. Post-therapeutic follow-up is clinico-radiological, based on MRI control.

The prognosis of soft tissue sarcomas is poor; and may become worse with inadequate management.

Our work aims to determine the epidemiological, clinical, radiological and anatomopathological peculiarities of these tumors; evaluate their diagnostic and therapeutic management in order to detail the prognostic factors implicated in this pathology.

#### PATIENTS AND METHODS

This is a retrospective descriptive analytic study, which focuses on patients with soft-tissue sarcomas of limbs who were followed at the osteo-articular surgery II, oncology and radiotherapy departments of University Hospital hassan II in Fez during the period from January 2013 to December 2017; a duration of 5 years.

It included any patient managed in the departement of Traumatology and Orthopedic Surgery II during the study period, hospitalized with the intention of being treated and having a tumor located at the extremities or the trunk with obligatorily histological evidence and an exploitable medical record.

The data were collected from the hospital registers of the osteo-articular surgery II and onco-radiotherapy departments and those of the central operating theater of the CHU Hassan II of Fès and then established and analyzed on previously established case report form. The data entry was done using the Excel software and their statistical analysis was done using the SPSS20 software. Quantitative variables were expressed as mean, standard deviation and qualitative variables in numbers and percentages. Characteristics comparison was performed by Khi2 tests, Student's t test and Mann-Whitney U test. Statistical significance was defined by a p value <0.05.

In order to complete this study and to have more relevant and detailed information, we have used other hospital structures including the radiology, pathology and onco-radiotherapy departments of the CHU Hassan II of Fez.

Thus, after excluding patients who did not meet the criteria of the study (benign tumors of the soft tissues, cutaneous tumors, non-exploitable record, refusal of treatment), we selected 50 out of 65 cases initially collected.

#### RESULTS

Over a period ranging from January 2013 to December 2017, we collected 50 patients with soft tissue sarcoma. The average age was 50, and sex ratio 1. The peak frequency is between 31 and 45 years old. 84% of the patients had no history, 02% a traumatism of the affected limb, 06% an active smoking, 08% a notion of familial cancer. The study of the distribution of STM shows that synovial sarcoma (30%) is the predominant histological type in our series, followed by liposarcoma (28%), leiomyosarcoma (16%), and Ewing extra-skeletal sarcoma (6%). %, myxofibrosarcoma (6%), rhabdomyosarcoma (4%), chondrosarcoma (4%), histiofibrosarcoma (2%), pleomorphic cell sarcoma (2%) and Dermatofibrosarcoma Darrier and Ferrand (2%) are less common. In our series, the tumor is located mainly in the lower limbs with a rate of 76%, of which 56% in the thigh. Localization in the upper limb was founded in 24% of patients. The delay in consultation ranged from 1 to 60 months (5 years), with an average of 22 months. Only two cases consulted before 3 months. The discovery by the patient of a mass at the level of his limb, which gradually increases in volume, is the main reason for consultation.



**Fig-1: Sarcoma located at popliteal fossa**



**Fig-2: Sarcoma located at leg**



**Fig-3: Sarcoma of shoulder**



**Fig-4: Sarcoma located at the posterior thigh**

The size of the tumor ranged from 3 to 30 cm, 78% of the patients presented with voluminous swelling and only 22% consulted for masses of less than 5 cm. 76% of sarcomas were deep seated, while only 24% was superficial.

Standard radiography of affected limb was requested in all patients. 03 patients underwent soft tissue ultrasound. The CT of the affected limb was performed in 10 patients. Magnetic resonance imaging was performed in 37 patients (74%). 11 of our patients had a deep or sub fascial lesion process, whereas in 8

patients, the mass was superficial on MRI. MRI showed voluminous processes (above 5 cm) in 17 patients, the mass was small in 04 patients.

The locoregional extension assessment showed involvement of the neighboring vascular pedicle in 02 cases. The tumor was in contact with the vascular pedicle without invasion in 04 cases. In 04 cases, an intimate contact of the tumor with the adjacent bone was found, with bone lysis in 03 of them. There was only one involvement of the adjacent joint.



**Fig-5: MRI of the right thigh : (a) coronal (T1) (b) coronal (T2) fat sat (c) sagittal T1 C+ slices – synovial sarcoma in 28 years old patient**



**Fig-6: MRI of the left thigh: (b) axial T2 (c) coronal T2 (d) coronal T2 FAT SAT slices. Rhabdomyosarcoma in 22 years old patient**

The remote extension assessment was carried out. The standard chest radiography showed a cannonballs appearance related to pulmonary metastases with a pleural effusion of great abundance in a single patient. An abdominal ultrasound was performed in 02 patients, with normal results. Thoracic CT was performed in only 2 patients and showed suspicious-looking pulmonary micronodules in one patient. Thoracoabdominopelvic CT was performed in 40 patients and showed a nodule and pulmonary micronodule in 13 patients, a pleural nodule with pleural effusion in 03 patients, suspicious liver lesions in 04 patients, Suspicious bone lesions in 2 patients, vertebral lesions in 2 patients, metastatic adenopathy in 2 patients and metastasis in the contralateral limb in 1 patient.

The biopsy was performed in all our patients. In 72% of cases, a surgical biopsy was performed, while 04 patients (8%) underwent an imaging guided biopsy. In 01 patients, the diagnosis was made on a percutaneous biopsy. In 7 cases the diagnosis was confirmed on the operative specimen. An immunohistochemical study was performed in 29 patients confirming the histological diagnosis. The technique of molecular biology: fluorescence in situ hybridization [FISH], was used in 13 patients. 38 patients were discussed in multidisciplinary consultation meeting. The included patients benefited

from conservative or mutilating surgical treatment, depending on the stage, grade and general condition of the patient. Additional radiotherapy or chemotherapy has been required in some cases. Conservative surgical treatment was performed in 28 patients. 01 patient underwent reconstruction after extensive resection and 01 patient underwent bypass. 12 patients did not benefit from surgical treatment given the advanced stage of the disease. 09 patients underwent a surgical revision: either in the context of a recurrence or in the context of a recovery of the tumoral bed considering the non-healthy margins R2 of the first surgery (06 among them benefited from a conservative treatment). Therapeutic supplementation with external radiotherapy was performed in 24% of patients. Chemotherapy was indicated in 26 patients, or 52%. It is a neoadjuvant chemotherapy for 07 patients with a locally advanced tumor, and a palliative adjuvant chemotherapy for 19 patients with metastatic secondary localization. 02 patients received both adjuvant and neoadjuvant chemotherapy.

We found that 30% of patients had recurrences, of which 01 cases had a recurrence in a different site (initial thigh tumor, recurrence in the shoulder). The duration of recurrence varies between 6 months and 36 months (3 years) with an average of 19 months. Only 1 recurrence was noted in 13 cases, 2 recurrences in 2 cases.



**Fig-7: wide resection of a myxoid liposarcoma in 31 years old patient**



**Fig-8: Shoulder disarticulation**

## DISCUSSION

Soft tissue sarcomas are rare [8-10], they present 0.5 to 1% of malignant tumors in adults whose annual incidence is estimated at 3 to 8 / 100,000 [2]. STMs represent only 1.4% of all cancers according to data from the Cancers Registry of Casablanca Region

The prognostic factors of local recurrence are:

### Age

Gronchi *et al.* [14] and S. Bonvalot *et al.* [2] reported no association with local recurrence. While Gunar K. Zagars M.D *et al.* [15], P W Pisters *et al.* [16] and Biau *et al.* [13] showed that the patient's advanced age is an unfavorable prognostic factor for local recurrence. In our study: 40% of patients with an age >

2005-2007 [11]. At the University Hospital of Fès, STMs represent 2.15% of all cancers diagnosed in anatomopathology department [12]. The prognosis of soft tissue sarcomas is traditionally unfortunate; and may become worse with inadequate management.

50 years developed a local recurrence VS 30.7% of patients <50 years. Comparing the percentages with a KHI2 test; age has no prognostic value in this study.

### Sex

No study has shown the prognostic value of sex. According to the studies, the distribution between the two sexes is balanced, sometimes it shows a slight male predominance [2]. In our series, we note a discreet female predominance that remains insignificant.

### The site of the tumor

Gunar K. Zagars M.D *et al.* [15] showed that the localization of the tumor has a prognostic value on local recurrence, in decreasing order of significance: deep regions of the trunk; head and neck; upper extremities; superficial wall of the trunk; lower extremities, with a relative risk of 2.6 (95% CI, 1.8-3.6,  $P < 0.001$ ). There were no differences in local control rates depending on the location of the tumor in the extremities. Patients with proximal lower extremity lesions (groin and thigh) had control rates of 5 and 15 years respectively of 88% and 85%; and patients with distal lower extremity (knee and leg) lesions had 5-year and 15-year control rates of 84% and 79%, respectively ( $p = 0.084$ ). Patients with proximal upper extremity (shoulder and arm) lesions had 5 and 15 year control rates of 81% and 80%, respectively; and patients with distal upper extremity (elbow and forearm) lesions had control rates at 5 and 15 years of 80% and 77%, respectively ( $p = 0.772$ ).

In our series, the location of STS was 84% in the lower limbs, 80% of whom were sitting in the thigh; of these, half developed recidive. We can not decide on the value of the seat in local recurrence since only the soft tissue sarcomas of the extremities have been treated.

### The size of the tumor

Gunar K. Zagars M.D *et al.* [15] showed that the tumor size had a relative risk of 1.7 (95% CI, 1.2-2.4,  $P = 0.002$ ). P W Pisters *et al.* [16] showed that the size of the tumor was one of the prognostic factors in distant recurrence. In our study, patients who developed a tumor recurrence, the size of the initial tumor varies between 6cm and 20cm (35% between 5cm and 10cm and 65% higher than 10cm) and we thus join the other studies.

### The depth of the tumor: [15-17]

P W Pisters *et al.* Coindre *et al.* S Bonvolat *et al.* Considered that the depth of the tumor is significant in the local recurrence especially distant. In our study, 9 patients / 13 patients with deep tumors developed a recurrence, while 03 patients / 08 patients with superficial tumors presented a recurrence. Comparing the results with the KHI2 test we find that the depth of the tumor is significant as a prognostic factor.

### The histological type

The histological type has a prognostic value according to Gunar K. *et al.* [15] who considered histyofibrosarcomas, neurogenic sarcomas and epitheloid sarcomas to be factors of poor prognosis compared with other histological types. P W Pisters *et al.* [16] also consider that HFM and neurogenic

sarcomas are significant adverse prognostic factors for local recurrence.

### The histological grade: [2,15,17]

According to JM Coindre, among the unfavorable characteristics for the development of distant metastases, grade 3 had a value ( $P = 4 \times 10^{-12}$ ). S. Bonvalot *et al.* determined the histologic grade as the most important prognostic factor with a 5-year survival rate of 90%, 60% and 35% respectively for grades 1, 2 and 3. Gunar k. showed that the intermediate grade had a relative risk of 8.9 (95% CI: 1.2-64.1,  $P < 0.001$ ) and that high-grade tumors had a relative risk of 22.5 (CI to 95%, 3.2-160.1,  $P < 0.001$ ). Our study aligns with the literature and shows that Grade III has a significant risk of metastasis compared to other histological grades.

### CONCLUSION

We were able to show that local control was affected by many factors: radical excision, tumor size less than 5 cm, depth, histological grade, margin status, adjuvant radiotherapy, whereas recurrence metastatic was determined by only four independent factors: tumor depth versus fascia, tumor size, tumor grade, and histological type.

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