

Synovial sarcoma of the limbs: clinical features, imaging, and treatment- A retrospective study of 19 cases

Dr OMAR HABIB ALLAH, Dr AYOUB MIKOU, Pr MOHAMMED BENSAKA, Pr HATIM ABID, Pr MOHAMMED ELIDRISSI, Pr ABDELMAJID ELMRINI

Service de Traumatologie-Orthopédie B4

CHU Hassan II – Fes, Morocco

Corresponding author : Dr Omar Habib Allah

Email : omarhabiballah2017@gmail.com

Abstract: Synovial sarcoma (SS) is a rare malignant soft tissue tumor of mesenchymal origin with variable epithelial differentiation, accounting for 5–10% of all soft tissue sarcomas. It carries a reputation for diagnostic difficulty and a guarded long-term prognosis. We conducted a retrospective descriptive study of 19 cases of limb synovial sarcoma managed in the Department of Traumatology and Orthopedic Surgery B4 at CHU Hassan II, Fes, Morocco, between January 2020 and December 2025. The mean patient age was 36.68 years (range: 17–77), with a male predominance (M/F = 1.7). Lower limb localization predominated (79%), particularly the thigh (32%). The mean diagnostic delay was 18 months, reflecting the indolent and nonspecific clinical presentation of this tumor. MRI was performed in 84% of patients and constituted the reference imaging modality. Histological confirmation was achieved in all cases, primarily through surgical biopsy (52.5%). Surgical resection was the cornerstone of treatment: limb-sparing surgery was feasible in 56% of patients, while 44% required amputation or disarticulation due to locally advanced disease. Chemotherapy was administered in 63% of cases and adjuvant radiotherapy in 15.7%. Local recurrence was observed in 26.3% and distant metastases in 58% of patients, predominantly pulmonary. The overall mortality rate reached 31.5%. Our series confirms the aggressive biological behavior of SS and underscores the necessity of early diagnosis, rigorous staging, and coordinated multidisciplinary oncological management.

Keywords—Synovial sarcoma; soft tissue tumors; MRI; limb surgery; chemotherapy; local recurrence; metastasis

1. INTRODUCTION

Synovial sarcoma is a high-grade malignant neoplasm of uncertain histogenesis, classified among soft tissue sarcomas despite its longstanding and now recognized as misleading designation suggesting a synovial origin. It accounts for approximately 5–10% of all soft tissue sarcomas and represents the second most common sarcoma in the pediatric and young adult population [1]. In the vast majority of cases, SS arises in a periarticular location, in close proximity to tendons, bursae, or joint capsules, but without arising from the synovium itself [2,3].

Clinically, SS is notorious for its insidious onset. Patients typically present with a slowly enlarging soft tissue mass, often painless in the early stages, which may go unnoticed or be misattributed to a benign process such as a ganglion cyst, lipoma, or post-traumatic hematoma. This diagnostic pitfall is compounded by the fact that the tumor predominantly affects adolescents and young adults in the third decade of life, in whom soft tissue malignancy is not the first diagnostic consideration [4]. As a consequence, diagnostic delays of months to years are commonly reported in the literature, and our own series is no exception.

From a histopathological standpoint, SS is classified into three variants: the monophasic form, composed exclusively of spindle cells; the biphasic form, which additionally contains epithelial glandular elements; and the poorly differentiated

form, which carries the worst prognosis. All three variants share a characteristic cytogenetic hallmark: the t(X;18)(p11;q11) chromosomal translocation, generating the SYT–SSX fusion oncogene, which is now considered pathognomonic and detectable in over 95% of cases by molecular methods [5].

Imaging, and MRI in particular, occupies a central position in the management of SS. It delineates the tumor's relationship to adjacent neurovascular structures, characterizes its internal architecture, and guides the choice of biopsy site and surgical approach. The so-called “triple sign” on T2-weighted sequences the simultaneous presence of hyperintense, isointense, and hypointense areas has been described as a distinctive, though not pathognomonic, MRI feature of SS [6].

Therapeutic management of SS is multimodal and requires coordination within a dedicated sarcoma team. Wide surgical resection with clear margins remains the definitive local treatment. The role of perioperative chemotherapy in adults remains a subject of ongoing debate, whereas radiotherapy has demonstrated clear benefit in terms of local control [5]. Despite advances in systemic treatment, the prognosis of SS remains heavily influenced by tumor size, histological grade, and the quality of surgical margins, with 5-year overall survival rates ranging between 36% and 76% across published series [7].

Through this retrospective analysis of 19 cases managed at CHU Hassan II, Fes, we aim to describe the

epidemiological, clinical, radiological, histopathological, and therapeutic characteristics of limb SS in our institutional context, and to compare our findings with current international data.

2. MATERIALS AND METHODS

2.1 Study Design and Setting

We conducted a retrospective descriptive and analytical study in the Department of Traumatology and Orthopedic Surgery B4 at CHU Hassan II, Fes, Morocco, the principal tertiary referral center for the Fez-Meknes region, over a six-year period from January 2020 to December 2025. Patient data were retrieved from the hospital information system (HOSIX), operative room registers, ward files, and radiology archives, and subsequently compiled onto standardized data collection forms.

2.2 Inclusion Criteria

- Patients managed in the department during the study period
- Tumor located on the limbs
- Mandatory histological proof of synovial sarcoma
- Exploitable medical record

2.3 Exclusion Criteria

- Absence of histological proof
- Non-exploitable medical record
- Tumors of the face, trunk, skull, or neck

3. RESULTS

3.1 EPIDEMIOLOGICAL DATA

Over the study period, 19 patients with histologically confirmed limb synovial sarcoma were included: 16 newly diagnosed cases and 3 presenting with local recurrence of a previously treated tumor, yielding an incidence of approximately 3 cases per year at our institution. The mean age at presentation was 36.68 years (range: 17–77). As illustrated in Table 1 and Fig. 1, the majority of patients were young adults aged 10–30 years (47.4%), consistent with the well-recognized predilection of this tumor for the second and third decades of life.

Table 1: Age Distribution of Patients (n = 19)

Age Group	Number of Patients	Percentage (%)
10–30 years	9	47.4
30–50 years	5	26.3
>50 years	5	26.3

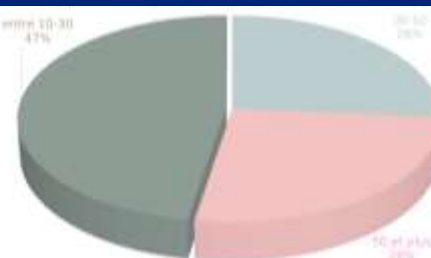


Fig. 1. Age distribution of patients in our series.



Fig. 2. Sex distribution of patients in our series (M/F ratio = 1.7).

Male sex predominated, with 12 men (63%) and 7 women (37%), yielding an M/F sex ratio of 1.7 (Fig. 2). With respect to anatomical localization (Fig. 3), the lower limbs were involved in 79% of cases, the thigh being the single most common site (32%), followed by the leg (21%) and foot (21%). Upper limb tumors accounted for 21% of the series, distributed equally across the shoulder, arm, forearm, and hand (5% each). One case was centered on the knee (5%).

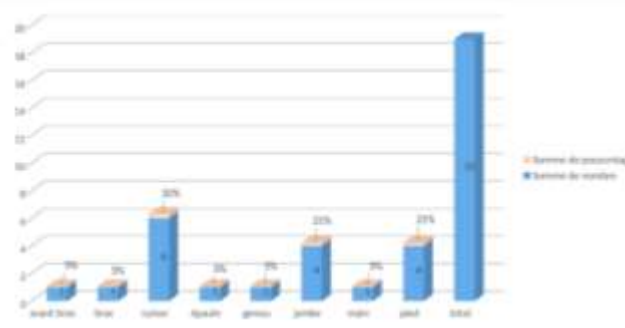


Fig. 3. Anatomical distribution of synovial sarcomas by limb location.

3.2 Clinical Presentation

The mean delay from onset of symptoms to first specialist consultation was 18 months (range: 2 months to 6 years), and could be ascertained in 17 of the 19 patients. This prolonged delay reflects the characteristically indolent and nonspecific nature of SS. A progressively enlarging soft tissue mass was the dominant presenting complaint, documented in 17 patients (96%), with associated pain in 3 of these cases (17%). One

patient presented with isolated pain in the absence of a palpable mass (6%), and two patients were referred on account of general deterioration.

Physical examination revealed a soft tissue swelling as the principal finding in all 17 patients who presented with a mass. Inflammatory signs were present in only 2 cases (11%). Tumor dimensions ranged from 6 to 20 cm in greatest diameter; the majority of lesions exceeded 10 cm (67%), indicating advanced local disease at the time of diagnosis in a significant proportion of our cohort. Firmness of the mass was noted in 3 patients (15%), with 2 tumors assessed as fixed to deeper planes. Regional lymphadenopathy was identified in 1 patient (5%), and cutaneous ulceration was observed in 2 patients (11%), including the case illustrated in Fig. 4.



Fig. 4. Clinical presentation of a synovial sarcoma of the foot at admission: medial (A) and lateral (B) views, showing a large ulcerated soft tissue mass with skin involvement.

3.3 Paraclinical Investigations

Plain radiographs were obtained in all patients and demonstrated soft tissue opacification as the most frequent finding, occasionally associated with calcifications (Fig. 5). Ultrasonography provided useful initial characterization of tissue consistency and vascularity. CT scanning was performed in 4 patients (21%) for precise local staging or when MRI was contraindicated.

MRI was performed in 16 patients (84%) and represented the reference imaging modality. It consistently demonstrated the heterogeneous intratumoral signal characteristic of SS, with cystic areas, recent or old hemorrhage, and fluid-fluid levels. The “triple sign” on T2-weighted sequences the simultaneous coexistence of hyperintense, isointense, and hypointense areas corresponding to the mixed cystic, myxoid, and fibrous components of the tumor was identified in several cases and is illustrated in Fig. 6. MRI also proved essential for defining the relationship of the tumor to adjacent neurovascular bundles and for planning the surgical approach.



Fig. 5. Plain radiographs demonstrating soft tissue opacity with calcifications in two different patients with limb synovial sarcoma.

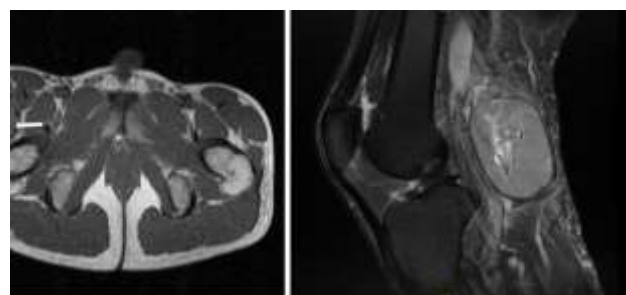


Fig. 6. MRI features of synovial sarcoma: (A) sagittal FAT-SAT sequence of the left knee; (B) axial T1 sequence of both thighs note the heterogeneous signal with the characteristic triple sign on T2 sequences.

Table 2: Imaging and Histological Findings

Investigation	Patients (n)	Rate (%)
Standard radiography	19	100
MRI	16	84
CT scan (local)	4	21
Systemic CT (extension)	All	100
Surgical biopsy	10	52.5
CT-guided biopsy	9	47.5
FISH (t(X;18) confirmed)	Selected	N/A

3.4 Treatment

Sixteen patients (84.21%) underwent surgical treatment. Three patients did not receive specific treatment: two were diagnosed at the metastatic stage and one died before a therapeutic plan could be established. Among surgical patients, 9 (56%) had limb-sparing resection and 7 (44%)

required amputation or disarticulation. Wide resection was the most common conservative approach (50% of surgical cases); radical resection was performed in 1 patient (6%). No marginal resections were carried out.

Chemotherapy was administered to 12 patients (63%): neoadjuvant in 6 (50%), adjuvant in 7 (58.3%), and palliative in 2 (16.6%); 3 patients received both neoadjuvant and adjuvant chemotherapy. The MAI protocol (Doxorubicin + Ifosfamide + Mesna) was the most used polychemotherapy regimen. Second and third line agents included high-dose Ifosfamide, Gemcitabine, and Dacarbazine. Adjuvant external beam radiotherapy was administered to 3 patients (15.7%). Table 3 summarizes the therapeutic approaches.

Table 3: Summary of Therapeutic Approaches (n = 19)

Treatment	n	% of Total Cohort
Limb-sparing surgery	9	47.4%
Amputation / disarticulation	7	36.8%
No surgery (metastatic/deceased)	3	15.8%
Neoadjuvant chemotherapy	6	31.6%
Adjuvant chemotherapy	7	36.8%
Palliative chemotherapy	2	10.5%
Adjuvant radiotherapy	3	15.7%

3.5 Outcomes and Follow-up

Radiological surveillance combining local MRI and systemic CT was carried out in 13 patients (68%). Three patients (15.7%) were lost to follow-up after completing initial treatment. Local recurrence was documented in 5 patients (26.3%), arising almost exclusively in patients who had undergone conservative resection. In each case, recurrence was suspected on follow-up imaging and confirmed histologically on biopsy. The case illustrated in Fig. 7 is representative: axial T2 and coronal STIR sequences of both thighs revealed a recurrent mass at the right inguinal fold in a patient who had previously undergone wide resection of a right thigh SS.



Fig. 7. MRI of both thighs in a patient with prior right thigh synovial sarcoma: (A) axial T2; (B) coronal STIR local recurrence at the inguinal fold confirmed on subsequent biopsy.

Distant metastatic spread was observed in 11 patients (58%). The lung was overwhelmingly the most frequent site, affected in 9 of the 11 metastatic patients (82%), consistent with the haematogenous dissemination pattern typical of high-grade soft tissue sarcomas. Pleural involvement was noted in 5 patients (45%), lymph node metastases in 4 (36%), and isolated cutaneous, hepatic, and cerebral localizations in one patient each. Six deaths were recorded during the observation period, yielding an overall mortality rate of 31.5% (Table 4).

Table 4: Distribution of Distant Metastatic Sites (n = 11 metastatic patients)

Metastatic Site	n	% of Metastatic Cases
Pulmonary	9	82%
Pleural	5	45%
Lymph node	4	36%
Cutaneous	1	9%
Hepatic	1	9%
Cerebral	1	9%

4. DISCUSSION

4.1 Epidemiology

Synovial sarcoma is an uncommon malignancy, with a reported annual incidence of approximately 2.75 cases per million population worldwide [7]. Our institutional rate of roughly 3 cases per year over six years is coherent with this figure and reflects the regional referral activity of CHU Hassan II as the main tertiary oncological center for north-central Morocco. The mean age of 36.68 years, predominantly affecting individuals in the second and third decades, is consistent with virtually all published series [8,9]. The male predominance we observed (M/F = 1.7) mirrors international

data and, although its biological basis remains unexplained, has been a consistent finding across large multicentric studies. Lower limb predilection with the thigh as the leading site is equally well established: major series report 60–70% of SS arising in the lower extremities [7,8], a figure that our cohort (79%) slightly exceeds, possibly reflecting referral patterns.

4.2 Diagnostic Delay and Clinical Presentation

The 18 month mean consultation delay documented in our series is a striking finding that deserves emphasis. This protracted interval between symptom onset and specialist referral is not an isolated observation: it is a recurrent theme in SS literature, particularly in settings where awareness of soft tissue sarcomas among general practitioners and first line clinicians is limited [9]. The clinical mimicry of SS a painless, slow-growing mass that may wax and wane readily invites misdiagnosis as a benign entity. The finding that 67% of our patients harboured tumours exceeding 10 cm at presentation is a direct and sobering consequence of this delay. We wish to draw attention to a simple but often overlooked clinical rule: any soft tissue mass in a young adult that has been present for more than four weeks, exceeds 5 cm, or is located deep to the fascia should be considered malignant until proven otherwise, and warrants urgent MRI and oncological referral [12].

4.3 Imaging

MRI remains the uncontested first-line imaging modality for the local assessment of suspected soft tissue sarcomas [6,10]. In our series, 84% of patients underwent MRI prior to treatment, and it proved indispensable in all cases for delineating tumor extent, identifying compartmental involvement, assessing neurovascular proximity, and guiding biopsy planning. The “triple sign” on T2-weighted sequences reflecting the simultaneous presence of solid high-signal myxoid tissue, intermediate-signal cellular areas, and low-signal fibrous or calcified components was a recurrent and diagnostically suggestive feature in our cohort, as illustrated in Fig. 6 [10]. While not pathognomonic in isolation, this MRI pattern in the appropriate clinical context (young adult, periarticular lower limb mass) should raise strong suspicion for SS and prompt expedited histological confirmation. Chest CT for pulmonary staging was performed systematically given the predilection of SS for haematogenous pulmonary dissemination.

4.4 Histopathology and Molecular Diagnosis

Histological confirmation is mandatory before any therapeutic decision. In our practice, surgical biopsy under general anaesthesia was preferred in 52.5% of cases, allowing for larger and more representative tissue samples, particularly when CT-guided percutaneous biopsy was not feasible due to tumour consistency or location. The monophasic spindle cell variant predominated in our series, as is typically reported [5,11]. Immunohistochemistry with diffuse nuclear TLE1 positivity, BCL-2 expression, and variable CD99 staining — remains the cornerstone of diagnostic workup in most

institutions. FISH detection of the t(X;18)(p11;q11) SYT–SSX translocation provides molecular certainty in diagnostically challenging cases and was performed selectively in our series [5,11].

4.5 Surgical Strategy

Wide en-bloc resection with histologically clear margins of at least 1–2 cm remains the gold standard for localized SS [12]. Achieving negative margins is the single most powerful modifiable determinant of local control and long-term survival. In our series, 56% of surgical patients benefited from limb-sparing resection, while 44% required amputation or disarticulation. This amputation rate, higher than that reported in specialized sarcoma centres from high-income countries, reflects two converging factors: the advanced local tumor size at presentation and the limited availability of plastic reconstructive resources required for complex limb-salvage procedures following wide excision. When oncologically equivalent, limb-sparing surgery is always to be preferred, as it has demonstrated comparable survival outcomes to amputation without compromising oncological principles [12,13]. The systematic preoperative discussion of each case in a multidisciplinary oncological board is therefore non-negotiable.

4.6 Chemotherapy

Synovial sarcoma is one of the more chemosensitive subtypes of soft tissue sarcoma, and the MAI regimen (Doxorubicin + Ifosfamide + Mesna) was the most frequently employed protocol in our series, consistent with standard international practice [13,14]. Sixty-three percent of our patients received chemotherapy in some form a proportion that reflects both the aggressive biology of the tumors and the locally advanced stage at presentation. The precise survival benefit of neoadjuvant or adjuvant chemotherapy in adult SS nevertheless remains a matter of ongoing controversy. Neoadjuvant chemotherapy may offer the theoretical advantages of rendering borderline resectable tumors operable and testing in vivo chemosensitivity, but no randomized controlled trial has definitively established its superiority over immediate surgery in adults. Adjuvant chemotherapy is generally reserved for high-grade, large (>5 cm), or margin-positive tumors and should be decided collectively at multidisciplinary tumor board meetings [14,15].

4.7 Radiotherapy

External beam radiotherapy was delivered as an adjuvant to surgery in 3 patients (15.7%). Perioperative radiotherapy whether pre- or postoperative has demonstrated a consistent benefit in terms of local control in soft tissue sarcomas of the extremities, even in the absence of a proven overall survival advantage [16]. Its relatively limited use in our series is attributable to resource availability and competing therapeutic priorities in patients with widespread metastatic disease. In locally advanced or margin-positive cases, radiotherapy

should be systematically considered as part of the multimodal treatment plan.

4.8 Emerging Therapeutic Perspectives

The management of recurrent and metastatic SS remains a formidable challenge. Beyond first-line doxorubicin- and ifosfamide-based regimens, several avenues are under active investigation. Trabectedin has demonstrated activity as a second-line agent in relapsed soft tissue sarcomas and is approved for this indication in several countries; its mechanism of action in translocation-driven sarcomas such as SS involves disruption of the SS18-SSX fusion oncoprotein's transcriptional activity, which is thought to underlie its particular relevance in this histotype [17]. Isolated limb perfusion with TNF- α and melphalan offers a viable limb-salvage strategy in patients with unresectable extremity disease. Targeted molecular therapies, including multi-kinase inhibitors such as pazopanib and regorafenib, have shown modest but reproducible activity in phase II trials involving SS patients. Immunotherapy with PD-1/PD-L1 checkpoint inhibitors has been evaluated in soft tissue sarcomas, with overall modest results across histotypes; however, adoptive T-cell receptor therapies targeting cancer testis antigens such as NY-ESO-1 and MAGE-A4 have demonstrated more meaningful and durable responses specifically in synovial sarcoma, and represent a rapidly evolving therapeutic frontier [18]. As our understanding of the SYT-SSX oncogenic pathway deepens, rational targeted approaches directed at this fusion protein represent a compelling research priority.

4.9 Prognosis

The overall prognosis of SS remains guarded. Published 5-year overall survival rates range from 36% to 76% across series, with this wide range reflecting differences in tumor size, histological subtype, margin quality, and metastatic status at presentation [7,11]. In our cohort, the 31.5% mortality rate over a six-year observation period, combined with a 26.3% local recurrence rate and a 58% distant metastasis rate, attests to the aggressive biological behaviour of this tumor. The predominance of pulmonary metastases (82% of metastatic patients) reinforces the necessity of systematic thoracic CT surveillance at regular intervals throughout the follow-up period. Factors consistently associated with poor prognosis in the literature include tumour size >5 cm, poorly differentiated histology, positive or close resection margins, and the presence of metastatic disease at diagnosis — all of which were prevalent in a significant proportion of our patients, largely as a consequence of delayed diagnosis.

5. CONCLUSION

Synovial sarcoma of the limbs is a rare but biologically aggressive malignancy whose deceptive clinical presentation as a benign-appearing soft tissue mass represents its greatest diagnostic pitfall. Our institutional experience of 19 cases over six years confirms the characteristic epidemiological and clinicopathological profile of this tumor: a predilection for

young men, lower limb predominance, and a disturbingly prolonged diagnostic delay that results in large, locally advanced tumors at the time of first oncological contact.

MRI is indispensable and should be obtained without delay in any patient with a soft tissue mass suspected of malignancy. The “triple sign” on T2 sequences, when present in the appropriate clinical context, should orient the clinician towards SS and prompt urgent multidisciplinary evaluation. Histological confirmation — supported by immunohistochemistry and molecular analysis — remains the diagnostic gold standard.

Therapeutic management must be conducted within a dedicated sarcoma multidisciplinary team. Wide oncological resection with clear margins is the definitive treatment for localized disease and represents the most important prognostic variable that is within the surgeon's control. The role of perioperative chemotherapy and radiotherapy should be individualized on the basis of tumor stage, grade, and margin status. In metastatic disease, palliative systemic chemotherapy remains the first-line option, with emerging targeted and immunological approaches offering cautious optimism for the future.

The high rates of local recurrence and pulmonary metastasis observed in our series underscore the imperative of long-term, protocol-based follow-up. Reducing diagnostic delays through heightened clinical awareness at all levels of the healthcare system remains, in our view, the most impactful intervention available to improve outcomes for patients with synovial sarcoma in resource-limited settings.

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7. CONFLICT OF INTEREST

The authors declare no conflict of interest.

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