

# Cancer Association of South Africa (CANSA)



## Fact Sheet on Leiomyosarcoma

### Introduction

Leiomyosarcoma (LMS) is a type of soft tissue sarcoma. Soft tissue sarcoma is a cancer that starts in soft tissues of the body, including muscle, tendons, fat, lymphatic vessels, blood vessels, nerves, and tissue around joints. The tumours can be found anywhere in the body but often form in the arms, legs, chest, or abdomen.

[Picture Credit: Subcutaneous Leiomyosarcoma]



Both children and adults can develop soft tissue sarcoma. Treatment often works better in children and they may have a better chance of being cured than adults. There are many types of soft tissue sarcoma, based on the type of soft tissue cell in which the cancer formed. Different types may be treated differently.

Leiomyosarcoma (LMS) is one of the more common types of soft tissue sarcoma to develop in adults. The exact cause of LMS is not yet known.

**Mestiri, S., Elghali, M.A., Bourigua, R., Abdessayed, N., Nasri, S., Amine, B.A., Missaoui, N., Ben Maitig, M., Hmissa, S., Sriha, B. & Mokni, M. 2019.**

**BACKGROUND:** Soft tissue leiomyosarcomas are rare, accounting for almost 5%-10% of all soft tissue sarcomas; they account for almost 1% of all sarcomas. They are aggressive tumors where location, size, and management require a multidisciplinary approach. Since there are few series published, we here analyze epidemiological pattern, clinical and pathologic features of soft tissue leiomyosarcomas.

**METHODS:** We conducted a retrospective study of 29 consecutive cases of histologically proven soft tissue leiomyosarcoma extracted from the database of the Cancer Registry of the Center of Tunisia and the Department of Pathology of Farhat Hached University Hospital of Sousse of Tunisia, during a 10-year period (from January 1996 to December 2005). Epidemiologic details, clinico-pathological features, and treatment modalities were assessed with focus on patients' 5-year overall survival, tumor relapse, and metastases.

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**RESULTS:** Soft tissue leiomyosarcoma accounted for 17.5% of all soft tissue sarcomas diagnosed at our pathology department. Most of patients were of advanced age (median: 52 years), with extremes ranging from 12 and 87 years. There was a slight male predominance (sex-ratio = 1.07). Tumors were located mostly in the lower limbs (45%). Deep sites as retroperitoneum was found only in two cases. Tumor size was more than 5 cm in 83% of cases (average size = 9.4 cm). Five cases had metastasis on initial staging. For 24 patients, the disease was locally limited at the moment of diagnosis. Palliative chemotherapy was indicated for four patients and surgery was performed for 20 patients. Local recurrence occurred in 11 patients (55% of operated patients) and metastasis in 6 patients. Overall, 5-year survival was about 24%.

**CONCLUSION:** Our study results highlight the scarcity of soft tissue leiomyosarcoma. Unfortunately, unusual tumor sites, disease's advanced stages, and intralesional resection made the prognosis poorer than in other series. Clinical course of soft tissue leiomyosarcoma was highly marked by local recurrence and metastasis.

### **Types of Leiomyosarcoma (LMS)**

Leiomyosarcoma, or LMS is a rare condition and yet there are a few thousand cases each year all over the world. It is a form of soft tissue cancer and appears specifically in the involuntary muscles.

There are three types of LMS:

Somatic Soft Tissue LMS - the words "somatic soft tissue" are another way of describing the body's connective tissue. This is the most common location for LMS to appear, and so almost everyone diagnosed with LMS may be said to have LMS of the somatic soft tissue. Interestingly enough, the somatic soft tissues hold the body together, but they are not the same tissues as those of the organs (such as the kidneys). Although one's liver or kidneys can be called soft tissue, when cancers are due to something malfunctioning in the actual cells that make up one's visceral organs, they are not sarcomas. Those are known as carcinomas instead. So, someone who has liver cancer is not, necessarily, someone with LMS.

Cutaneous or Subcutaneous LMS - this is a very rare form of LMS and is when the "pilo erector" muscles in the skin develop the condition. It is often viewed as a dermatological condition in addition to something for an oncologist. Fortunately, for someone diagnosed with the cutaneous version there is an "excellent outcome with rare recurrence". For the subcutaneous variants, though, treatment can be challenging.

LMS of a Vascular Origin - noted as truly rare, however, it has occurred. This is when LMS comes directly from a major blood vessel such as the inferior vena cava. Additionally, the pulmonary artery can be involved along with peripheral arteries. There are formal syndromes that arise from some of these variants of LMS due to the symptoms and issues they may cause. For example, Budd-Chiari syndrome is what presents in those with LMS in the inferior vena cava.

Other LMS Variants - experts indicated that there are also cases of LMS in those with immunocompromised conditions and even LMS of the bone. Additionally, the patient with gastrointestinal tumours once cited as a form of LMS will no longer be identified as such. Instead, this is now known as GISTs or Gastrointestinal Stromal Tumours. These are no longer viewed as a form of LMS and though they are tumours of the smooth tissue and muscles of the stomach, they are treated with a unique and initially successful new drug protocol.

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**Llombart, B., Serra-Guillén, C., Requena, C., Alsina, M., Morgado-Carrasco, D., Machado, I. & Sanmartín, O. 2019.**

“There are 3 types of leiomyosarcoma of the skin: dermal, subcutaneous, and metastatic cutaneous. Dermal leiomyosarcoma arises from smooth muscle fibers in arrector pili muscles, genital dartos muscles, and the nipple-areola complex. It is an intermediate-grade tumor associated with a tendency for local recurrence (24%) and low metastatic potential (4%). Subcutaneous leiomyosarcoma originates from smooth muscle in blood vessel walls and has higher rates of local recurrence (37%) and metastasis (43%). Pleomorphic dermal sarcoma typically affects elderly patients and arises in sun-exposed areas (e.g., the scalp). Its histologic and immunohistochemical characteristics are similar to those of atypical fibroxanthoma, but it is more aggressive (metastasis rate of 10-20%). Histologically, it can be distinguished from atypical fibroxanthoma by the observation of subcutaneous tissue invasion, perineural invasion, and foci of necrosis.”

### **Incidence of Leiomyosarcoma in South Africa**

The National Cancer Registry (2014) does not make any mention of the incidence of Leiomyosarcoma in South Africa.

### **General Clinical Features of LMS**

There are no specific clinical features diagnostic of leiomyosarcoma of soft tissue that distinguish these tumours from other soft tissue sarcomas. Women are affected more than men, with the disease typically occurring in the 5th and 6th decades of life. This gender distribution may reflect the proliferation of smooth muscle that can occur in response to oestrogen. Prognosis and treatment varies on the location, stage and grade of the primary tumour as well as the presence of metastatic disease.

The most common site of involvement of leiomyosarcoma is the retroperitoneum, accounting for approximately 50% of occurrences.<sup>8</sup> In the case of retroperitoneal tumours, presenting signs and symptoms can include an abdominal mass, pain, swelling, weight loss, nausea or vomiting. Leiomyosarcoma of somatic soft tissues, like other soft tissue sarcomas, often present as an enlarging, painless mass.

Although these tumours are generally associated with small blood vessels, they usually do not present with signs or symptoms of vascular compression. However, when leiomyosarcoma arises from a major blood vessel, symptoms of vascular compromise or leg oedema may be present, as well as neurologic symptoms such as numbness from compression of an adjacent nerve. Soft tissue leiomyosarcoma typically affects adults, however it can present in childhood.

**Juhasz-Böss, I., Gabriel, L., Bohle, R.M., Horn, L.C., Solomayer, E.F. & Breitbach, G.P. 2018.**

“Uterine leiomyosarcoma (uLMS) is a rare entity among malignant gynecologic tumors with a very unfavorable prognosis and the highest prevalence in the pre- and peri-menopause. Only early-stage tumors have an acceptable prognosis, provided the patient has been treated without injuring the uterus. uLMS is often diagnosed accidentally and the correct diagnosis is hampered by equivocal features similar to the far more frequent benign uterine fibroids. Surgery is the basis of therapy, and

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it should be done in order to remove the uterus intact. As vaginal, abdominal, and endoscopic surgery - possibly including morcellation - are the methods of choice for the treatment of uterine fibroids, pre-operatively undiagnosed leiomyosarcoma detected by pathologic examination will have a worsened prognosis. Systemic treatment and radiotherapy are of no proven value in the adjuvant setting. Thus, there is strong need for a reliable pre-operative risk score for leiomyosarcoma in order to justify diagnostic means beyond clinical routine and to choose the correct surgical pathway. The clinical problems in the diagnosis of leiomyosarcoma and treatment are exemplified by a case report of a 30-year-old childless patient. Diagnostic tools as well as treatment options in adjuvant and palliative situations are reviewed.”

### **Diagnosis of Leiomyosarcoma (LMS)**

Ultrasound examination, magnetic resonance imaging (MRI), or computed tomography (CT) do not reliably distinguish between sarcoma, leiomyoma, endometrial cancer, lymphoma, intravenous leiomyomatosis, or adenomyosis.

The following tests are commonly used to diagnose a leiomyosarcoma. The tests one has will depend on the part of the body being investigated. One may have had some of these tests already.

Hysteroscopy - this test is used to diagnose problems in the uterus (womb). One may have this test as an outpatient under local anaesthetic, but sometimes a general anaesthetic is needed. A hysteroscopy may be uncomfortable but should not be painful. Some women may have mild cramping during the procedure and for a few days afterwards. It is advised to take mild painkillers, such as paracetamol, 30 minutes before the procedure.

Ultrasound scan - this test uses sound waves to create a picture of the abdomen and surrounding organs. It is done in the hospital's scanning department. One will be asked not to eat, and to drink only clear fluids (nothing fizzy or milky) for 4-6 hours before the scan. Ultrasound may also be used to look for a suspected cancer in a limb.

CT (computerised tomography) scan - a CT scan takes a series of x-rays, which build up a three-dimensional picture of the inside of the body. The scan takes 10–30 minutes and is painless. It uses a small amount of radiation, which is very unlikely to harm either the patient nor harm anyone he/she comes into contact with. The patient is asked not to eat or drink for at least four hours before the scan.

Before a CT scan one may be given an injection of a dye, which allows particular areas to be seen more clearly. This may make one feel hot all over for a few minutes. It is important to let the doctor know if one is allergic to iodine or have asthma, because one could have a more serious reaction to the injection.

MRI scan - this test uses magnetism to build up a detailed picture of areas of the body. The scanner is a powerful magnet so one is asked to complete and sign a checklist to make sure it is safe. The checklist asks about any metal implants one may have, such as a pacemaker, surgical clips, bone

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pins, etc. One should also tell the doctor if one has ever worked with metal or in the metal industry as very tiny fragments of metal can sometimes lodge in the body. If one does have any metal in one's body it is likely that one will not be able to have an MRI scan. In this situation another type of scan can be used.

[Picture Credit: MRI Scan]



**Tong, A., Kang, S.K., Huang, C., Huang, K., Slevin, A. & Hindman, N. 2019.**

**BACKGROUND:** Uterine fibroids are a common benign tumor and can be symptomatic, necessitating resection. Surgical myomectomy is an effective treatment option with a risk of disseminating occult uterine leiomyosarcoma (LMS), creating a need for an effective presurgical screening protocol. Clinical collaboration with contrast-enhanced MRI including T<sub>2</sub> and diffusion-weighted imaging (DWI) can be utilized as a screening exam.

**PURPOSE:** To review the accuracy and feasibility of an interdisciplinary prospective contrast-enhanced MRI pelvis with DWI screening system for LMS prior to fibroid resection.

**STUDY TYPE:** Retrospective cohort study.

**POPULATION:** In all, 1960 adult female patients aged 18-87 undergoing screening MRI pelvis prior to uterine fibroid resection.

**FIELD STRENGTH/SEQUENCE:** T<sub>1</sub> and T<sub>2</sub>-weighted imaging, DWI, and contrast-enhanced images were acquired at 1.5 T and 3.0 T.

**ASSESSMENT:** Each radiologist at the time of clinical study prospectively designated a confidence level of presence of LMS in the impression, which was reviewed retrospectively. A separate retrospective evaluation of the histologically proven LMS and the false positives was performed for the presence of five MRI features of LMS including low ADC values, intermediate/high T<sub>2</sub> signal intensity, irregular margins, hemorrhage, and necrosis. A preliminary cost-effectiveness analysis was performed, comparing the costs of treatment of uterine fibroids with vs. without a collaborative screening protocol using MRI.

**STATISTICAL TESTS:** Sensitivity, specificity, positive predictive value, and negative predictive value were obtained from the prospective evaluations. Student's t-tests were used to compare demographics and apparent diffusion coefficient values between LMS and false-positive results.

**RESULTS:** We prospectively identified LMS patients with 100% sensitivity and 97% specificity. Preliminary cost analysis demonstrated that the MR screening protocol increased life expectancy by 0.04 years at a cost of \$12,937 per life-year gained.

**DATA CONCLUSION:** MRI is an effective and potentially economic screening test, especially with standardized reporting and coordination with clinicians.

**Biopsy** - the results of the previous tests may make the doctor strongly suspect the patient has cancer. The only way to be sure is to take some cells or a small piece of tissue from the affected area to look at under a microscope. This is called a biopsy.

**Mulani, S.R., Stoner, P., Schlachterman, A., Ghayee, H.K., Lu, L. & Gupte, A. 2018.**

“Primary adrenal leiomyosarcoma (PAL) is an extremely rare mesenchymal tumor with only a few isolated case reports in the medical literature. Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) or endoscopic ultrasound-guided core biopsy (EUS-CB) is a safe, effective modality for

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sampling lesions in the gastrointestinal tract and adjacent organs, including the adrenal glands. We describe the case of a 50-year-old male presenting with abdominal pain and unintentional weight loss over the course of one year. CT imaging revealed an 8.1 cm heterogeneous left adrenal mass with PET-confirmed metastases to the liver and lung. Pheochromocytoma was ruled out. Adrenal cortical carcinoma was the other critical differential diagnosis. As the patient was not a candidate for surgery, an EUS-FNA and CB were performed on this left adrenal mass revealing a spindle cell neoplasm with extensive necrosis confirming the diagnosis of primary leiomyosarcoma. The patient was treated with chemotherapy with palliative radiation. This case demonstrates the utility of EUS-FNA or CB as modalities that can aid in the diagnosis of adrenal lesions in specific circumstances.”

### **Treatment of Leiomyosarcoma (LMS)**

Due to the rarity of these tumours, and the need for a multi-specialty treatment team, treatment is best carried out in a specialised centre with expertise in sarcoma care.

Surgery - Local control of soft tissue sarcomas is usually achieved with surgical resection. Achieving wide surgical margins is important in preventing local recurrence.

**Nathenson, M.J., Barysaukas, C.M., Nathenson, R.A., Regine, W.F., Hanna, N. & Sausville, E. 2018.**

**BACKGROUND:** Retroperitoneal soft tissue sarcomas (STS) include a number of histologies but are rare, with approximately 3000 cases in the USA per year. Retroperitoneal STS have a high incidence of local and distant recurrence. The purpose of this study was to review the University of Maryland Medical Center's (UMMC) treatment experience of retroperitoneal STS, where the patient population served represents a diverse socioeconomic and ethnic catchment.

**METHODS:** IRB approval was obtained. We constructed a de-identified database of patients diagnosed with retroperitoneal liposarcomas (LPS) or leiomyosarcomas (LMS) treated at UMMC between 2000 and 2013. A total of 49 patients (Pts) with retroperitoneal STS met our eligibility criteria. Kaplan-Meier plots were used to graphically portray progression-free survival (PFS) and overall survival (OS). The log-rank test was used to compare time-to-event distributions.

**RESULTS:** The median OS for all patients (Pts) was 6.3 years, and the 2-year OS rate was 81%. The median PFS for all Pts was 1.8 years, and the 2-year PFS rate was 45%. There was no difference in OS and PFS among LMS and LPS patients; the median OS for LMS was 3.8 years vs. LPS 6.4 years ( $p = 0.33$ ), and the median PFS for LMS was 1.2 years vs. LPS 2.5 years ( $p = 0.28$ ). There was a significant difference between histology and race ( $p = 0.001$ ). LPS were primarily Caucasian 86% vs. 14% black, whereas LMS were primarily black 52% vs. 33% Caucasian. OS was influenced by functional status, gender, American Joint Committee on Cancer (AJCC) stage, grade, histology, tumor size, and extent of resection. PFS was influenced by AJCC stage, grade, and extent of resection. Neither adjuvant chemotherapy (1 Pt) nor neoadjuvant/adjuvant radiation therapy (18 Pts) influenced OS or PFS. There was a non-significant difference that Pts who could undergo resection of local recurrence had improved 2-year OS, with 100% LMS and LPS compared to 2-year OS of 71% (LMS) and 78% (LPS) not undergoing resection of local recurrence.

**CONCLUSIONS:** This study suggests a higher incidence of leiomyosarcoma in the African-American population. This study confirms the prognostic importance of grade, tumor size, AJCC stage, histology, and extent of resection in patient outcomes, at a large substantially diverse academic medical center. Future research into the biological features of liposarcoma and leiomyosarcoma Pts imparting these characteristics will be important to define.

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Radiation Therapy - Many tumours involve or are directly adjacent to vital structures. In these cases achieving a wide surgical margin is impossible. Radiation therapy is an important additional treatment for improving rates of local control when surgical margins are close, especially in high-grade sarcomas. Radiation therapy can be delivered either pre-operatively (neoadjuvant) or post-operatively (adjuvant). Radiation therapy can also be utilised as a means of palliative local control in cases where extensive metastasis has already occurred.

Chemotherapy - The primary role of chemotherapy is in the treatment of metastatic disease. While not curative, it may slow the progression of systemic disease.

### **About Clinical Trials**

Clinical trials are research studies that involve people. They are conducted under controlled conditions. Only about 10% of all drugs started in human clinical trials become an approved drug.

Clinical trials include:

- Trials to test effectiveness of new treatments
- Trials to test new ways of using current treatments
- Tests new interventions that may lower the risk of developing certain types of cancers
- Tests to find new ways of screening for cancer

The South African National Clinical Trials Register provides the public with updated information on clinical trials on human participants being conducted in South Africa. The Register provides information on the purpose of the clinical trial; who can participate, where the trial is located, and contact details.

For additional information, please visit: [www.sanctr.gov.za/](http://www.sanctr.gov.za/)

### **Medical Disclaimer**

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### MacMillan Cancer Support

<http://www.macmillan.org.uk/information-and-support/soft-tissue-sarcomas/leiomyosarcomas>

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### National Cancer Institute

<https://www.cancer.gov/types/soft-tissue-sarcoma>

<http://www.cancer.gov/about-cancer/treatment/clinical-trials/what-are-trials>

### Sarcoma.org

<http://www.leiomyosarcoma.org/types/>

<http://www.leiomyosarcoma.org/stages/>

### Sarcomahelp.org

<http://sarcomahelp.org/leiomyosarcoma.html>

### Subcutaneous Leiomyosarcoma

<http://www.pcids.org.uk/clinical-guidance/leiomyosarcoma>

### The Liddy Shriver Sarcoma Initiative

<http://sarcomahelp.org/leiomyosarcoma.html>

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