Cancer Association of South Africa (CANSA)

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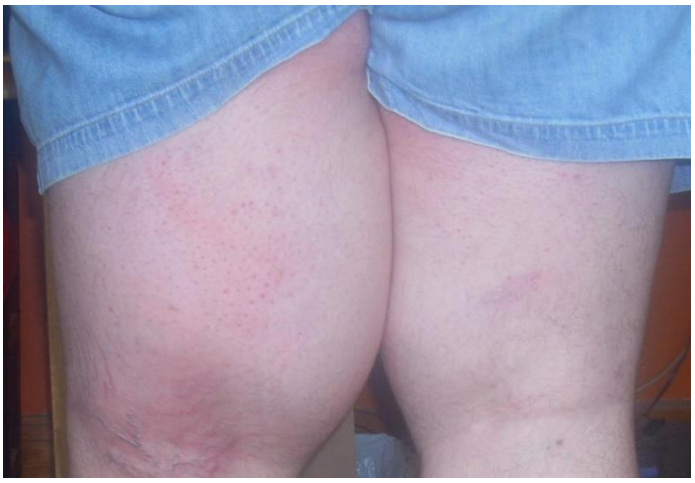
Fact Sheet on Liposarcoma

Introduction

Sarcoma is a type of cancer that can occur in various locations in the body.

Sarcoma is the general term for a broad group of cancers that begin in the bones and in the soft tissues (soft tissue sarcoma) - also called connective tissue. Soft tissue sarcoma forms in the tissues that connect, support and surround other body structures. This includes muscle, fat, blood vessels, nerves, tendons and the lining of joints.



[Picture Credit: Liposarcoma]

There are more than 70 different types of sarcoma. Treatment for sarcoma varies depending on sarcoma type, location as well as other factors.

Liposarcoma

Liposarcomas may be confused with fatty deposits of tissue, or lipomas, which are not cancerous. It is extremely rare for an existing non-cancerous lipoma to become cancerous. Instead, most liposarcomas occur as a new tumour.

Liposarcoma is a rare cancer of connective tissues that resemble fat cells under a microscope. It accounts for up to 18% of all soft tissue sarcomas. Liposarcoma can occur in almost any part of the body, but more than half of liposarcoma cases involve the thigh, and up to a third involve the abdominal cavity.

Liposarcoma tends to affect adults between the ages of 40 and 60 and occurs slightly more among men. When it does occur in children, it is usually during the teenage years.

There are five types of liposarcoma, each with its own unique characteristics and behaviours:

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Well-differentiated liposarcoma is the most common subtype and usually starts as a low-grade tumour. Low grade tumour cells look much like normal fat cells under the microscope and tend to grow and change slowly.

Myxoid liposarcoma is an intermediate to high grade tumour which occurs more in the arms and legs. Its cells look less normal under the microscope and may have a high-grade component.

Pleomorphic liposarcoma is the rarest subtype and is a high-grade tumour with cells that look very different from normal cells. It occurs more in the arms and legs.

Dedifferentiated liposarcoma occurs when a low-grade tumour changes, and the newer cells in the tumour are high grade. It tends to occur in the retroperitoneum.

Round cell liposarcoma is associated with unusual pattern of metastasis to extrapulmonary sites and occurs mostly in the arms and legs.

Sometimes liposarcoma spreads to other parts of the body. Where liposarcoma spreads to, depends on where the original tumour began. Common areas of metastasis include the lungs, soft tissue in other parts of the body, and the liver.

Liposarcoma is also known for its ability to regrow after treatment. It can come back months to decades after the initial diagnosis. That is why individuals who are diagnosed with liposarcoma should receive ongoing follow-up care and monitoring.

Zafar, R. & Wheeler, Y. 2020.
"Liposarcoma, a tumor of lipoblasts, is a rare mesenchymal neoplasm and involves deep soft tissues including retroperitoneum and popliteal fossa . The relative frequency of liposarcoma at various body sites is much dependent on the tumor subtypes. For example, dedifferentiated liposarcoma is much more common in retroperitoneal location, while myxoid liposarcoma occurs in the lower extremities . Liposarcoma is exceedingly rare in the esophagus . Esophageal liposarcoma typically behaves as a slow-growing tumor and involves the upper part of the throat. Most of them are of a well-differentiated type, confined to the esophagus with a low risk of metastasis [, and have a high rate of local recurrence (10%), even up to 25 years after the resection."

Ono, Y., Aoyama, T., Morita, J., Amano, S., Sawazaki, S., Numata, M., Hayashi, T., Yamada, T., Sato, T., Yukawa, N., Ohshima, T., Yoshikawa, T., Rino, Y. & Masuda, M. 2018. A case report of retroperitoneal liposarcoma resected sx times for 16 years. *Gan To Kagaku Ryoho*. 2018 Oct;45(10):1507-1509.
"We report of a long-surviving patient with retroperitoneal liposarcoma that required 6 surgeries in 16 years. A 62-year-old man was diagnosed with liposarcoma, which was first excised in 2001. Thereafter, we excised recurrences in the retroperitoneum with the left kidney in February 2004. We excised recurrences with the left half of the colon in November 2007 and February 2010 and recurrences with a part of the intestine in November 2014. This time, we excised recurrences under the right abdominal rectus muscle and near the left half of the colon. The pathological diagnosis was well-differentiated liposarcoma. There is currently no evidence of recurrence 16 years after the first recurrence excision. In this case, active excision of recurrences and identification of high-grade dedifferentiated-type liposarcomas were factors of long survival."

Thway, K. 2019.
"Well-differentiated liposarcoma (WDL)/atypical lipomatous tumor and dedifferentiated liposarcoma (DDL) together comprise the largest subgroup of liposarcomas, and constitute a histologic and behavioral spectrum

of one disease. WDL and DDL typically occur in middle-aged to older adults, particularly within the retroperitoneum or extremities. WDL closely resembles mature adipose tissue, but typically shows fibrous septation with variable nuclear atypia and enlargement. WDL does not metastasize, but can dedifferentiate to DDL, which is associated with more aggressive clinical behavior, with a greater propensity for local recurrence and the capacity for metastasis. Although distant metastasis is rarer in DDL compared with other pleomorphic sarcomas, behavior is related to location, with a significantly worse outcome in retroperitoneal tumors. DDL typically has the appearance of undifferentiated pleomorphic or spindle cell sarcoma, and is usually a non-lipogenic sarcoma that is adjacent to WDL, occurs as a recurrence of WDL or which can arise de novo. WDL and DDL share similar background genetic aberrations; both are associated with high-level amplifications in the chromosomal 12q13-15 region, which includes the CDK4 and MDM2 cell cycle oncogenes. In addition, DDL harbor further genetic changes, particularly 6q23 and 1p32 coamplifications. While surgical excision remains the treatment mainstay with limited medical options for patients with aggressive recurrent disease or metastases, novel targeted therapies towards the gene products of chromosome 12 are being evaluated. This review summarizes the pathology of WDL and DDL, discussing morphology, immunohistochemistry, genetics and the differential diagnosis."

Nassif, N.A., Tseng, W., Borges, Ca., Chen, O. & Eisenberg, B. 2016.
"Liposarcoma is the most common soft tissue sarcoma. With its various subtypes, the natural history of this disease can vary significantly from a locally recurrent tumor to a highly malignant one carrying a poor prognosis. Progress in the understanding of the specific molecular abnormalities in liposarcoma provides greater opportunity for new treatment modalities. Although surgical resection and radiation therapy remain the keystones for the management of primary liposarcoma, the inclusion of novel agents that target known abnormalities in advanced liposarcoma enhances the potential for improved outcomes."

Incidence of Liposarcoma
The National Cancer Registry of South Africa (2016) does not provide any information regarding the incidence of Sarcoma.

Causes and Risk Factors for Liposarcoma
Doctors are not sure exactly what causes liposarcoma. It is known that sarcomas form because of changes, called mutations, in the DNA of fat cells. But it is not clear why that happens.

Things that may make it more likely for someone to be diagnosed with liposarcoma:

- Some rare, genetic diseases or genetic syndromes, such as neurofibromatosis and Li-Fraumeni syndrome
- Previous radiation treatments another cancer
- A family history of liposarcoma or other soft-tissue cancers
- Trauma has been implicated as a possible cause
- Long-term exposure to certain chemicals, such as vinyl chloride

Signs and Symptoms of Liposarcoma
Signs and symptoms of liposarcomas vary. Many people do not feel sick or have pain. However, symptoms and signs may include the following, depending on where in the body the tumour is located:

- Painful swelling and/or a lump developing under the skin
- Numbness
- Fatigue
- Abdominal pain
- Chest pain
- Nausea
- Vomiting
- Urinary difficulties
- Swallowing difficulties
- Decreased range of motion of the limbs
- Associated episode of trauma to the region containing the mass

Liposarcoma that forms in the arms and legs can cause:
- A new lump anywhere on your body or an existing lump that keeps growing
- Pain
- Swelling
- Weakness of the affected limb

Liposarcoma that forms in the abdomen can cause:
- Abdominal pain
- Abdominal swelling
- Feeling full sooner when eating
- Constipation
- Blood in stool or vomit

Diagnosis of Liposarcoma

To diagnose a suspected liposarcoma, the doctor will most probably order a biopsy. This is a test that removes a small sample of suspicious tissue, either by surgery or with a needle and syringe. A pathologist, a doctor who examines tissue samples under a microscope, will check for cancer cells. If he or she identifies liposarcoma, the doctor may order tests to determine the extent of the sarcoma and how far it has spread.

The tests could include:
- X-rays
- MRI (magnetic resonance imaging)
- CT (computed tomography) scan
- Ultrasound
- Endoscopic Ultrasound Scan (EUS) which uses a tube-like instrument called an endoscope with an ultrasound scanner attached. This is put inside the body to look inside the gut to investigate GIST tumours.

Shimamori, N., Kshino, T., Porii, T., Okabe, N., Motohashi, M., Masushima, S., Yamasaki, S., Ohtsuka, K., Shibahara, J., Ichimura, S., Ohnishi, H. & Watanabe, T. 2019.

“Liposarcoma is the second most common malignant soft-tissue tumor. This entity is pathologically categorized into 4 subtypes: well-differentiated, myxoid, dedifferentiated and pleomorphic. Although features on magnetic resonance imaging and computed tomography for these 4 subtypes have been reported quite precisely, those on sonography have not been fully investigated. The present study was therefore aimed at clarifying the sonographic appearances of each liposarcoma subtype and assessing correlations with histopathology. The study population was made up of 35 cases, including 21 cases of well-differentiated liposarcoma, 6 cases of myxoid liposarcoma, 6 cases of dedifferentiated liposarcoma and 2 cases of pleomorphic liposarcoma. Compared with the other subtypes, well-differentiated liposarcoma was characterized by the high frequency of the following findings: isoechogenicity, tiny hyperechoic lines and hypovascularity ($p < 0.01$, in each). Myxoid liposarcomas were characterized by low echogenicity, intermingled with anechoic areas and moderate vascularity ($p < 0.01$, in each). Dedifferentiated liposarcomas showed a specific biphasic pattern of hyperechoic and hypoechoic areas and hypervascularity ($p < 0.01$, in each). Pleomorphic liposarcomas showed a specific gyrus-like mixture of hyperechoic and hypoechoic areas ($p < 0.01$). In conclusion, the present study revealed different characteristics of sonographic appearance among the 4 histopathologic subtypes of liposarcoma.”

Matthyssens, L.E., Creytens, D. & Ceelen, W.P. 2015.
Retroperitoneal liposarcoma (RLS) is a rare, biologically heterogeneous tumor that present considerable challenges due to its size and deep location. As a consequence, the majority of patients with high-grade RLS will develop locally recurrent disease following surgery, and this constitutes the cause of death in most patients. Here, we review current insights and controversies regarding histology, molecular biology, extent of surgery, (neo)adjuvant treatment, and systemic treatment including novel targeted agents in RLS.

Treatment for Liposarcoma
Surgical resection is currently the mainstay of curative treatment. Patients with large high-grade liposarcomas may benefit from multimodality treatment with chemotherapy and radiation. Radiation therapy may be a valuable adjunct to surgery, especially in those of the myxoid variant. The use of chemotherapy in liposarcomas remains experimental.

Gahvari, Z. & Parkes, A. 2020.
“Over the last several years, the systemic treatment landscape for dedifferentiated liposarcoma (DDLPS) has notably expanded. Historically, systemic therapy options have been limited to cytotoxic chemotherapy agents, including doxorubicin, ifosfamide, gemcitabine, and docetaxel, that were shown to have efficacy in unselected populations of patients with soft tissue sarcomas. More recently, however, there have been phase II and III trials establishing clinical benefit of the cytotoxic agents trabectedin and eribulin along with the tyrosine kinase inhibitor pazopanib in patients with advanced liposarcoma and DDLPS. Additionally, there are several investigational targeted therapies that have incorporated advances in the understanding of DDLPS disease biology, exploiting the fact that nearly all such tumors include highly amplified expression of MDM2 and CDK4. Recent clinical trials have supported the benefit of the CDK4 inhibitor abemaciclib and the nuclear export inhibitor selinexor and support continued development of anti-MDM2 therapies, with particular attention to the bone marrow toxicity and resultant thrombocytopenia that has thus far limited their use. In contrast, the checkpoint inhibitors pembrolizumab and nivolumab remain of questionable benefit, although these immunotherapy drugs may have a role when combined with other therapeutic agents. Ongoing phase III trials will clarify the role of these novel agents. Future directions include directly comparing current standard-of-care options and newer therapies, developing synergistic combinations of novel agents, and evaluating their role in patients with localized DDLPS.”

Yang, L., Chen, S., Luo, P., Yan, W. & Wang, C. 2020.
"Liposarcoma is a malignant tumor of mesenchymal origin with significant tissue diversity. It is composed of adipocytes with different degrees of differentiation and different degrees of heteromorphosis. It is not sensitive to traditional radiotherapy and chemotherapy and has a poor prognosis. In recent years, with the rapid development of basic immunology, molecular genetics and tumor molecular biology, the histological classification of liposarcoma has become increasingly clear. More and more new methods and technologies, such as gene expression profile analysis, the whole genome sequencing, miRNA expression profile analysis and RNA sequencing, have been successfully applied to liposarcoma, bringing about a deeper understanding of gene expression changes and molecular pathogenic mechanisms in the occurrence and development of liposarcoma. This study reviews the present research status and progress of cellular and molecular alterations of liposarcoma and corresponding clinical treatment progress."

Crago, A.M. & Dickson, M.A. 2016.
"There are 3 biologic groups of liposarcoma: well-differentiated and dedifferentiated liposarcoma, myxoid/round cell liposarcoma, and pleomorphic liposarcoma. In all 3 groups, complete surgical resection is central in treatment aimed at cure and is based on grade. Radiation can reduce risk of local recurrence in high-grade lesions or minimize surgical morbidity in the myxoid/round cell liposarcoma group. The groups differ in chemosensitivity, so adjuvant chemotherapy is selectively used in histologies with metastatic potential but not in the resistant subtype dedifferentiated liposarcoma. Improved understanding of the genetic aberrations that lead to liposarcoma initiation is allowing for the rapid development of targeted therapies for liposarcoma."

Mansfield, S.A., Polloci, R.E. & Grignol, V.P. 2018.
"Retroperitoneal sarcomas are rare tumors of which liposarcoma is the most common histology. Surgical resection remains the mainstay of therapy, particularly for the well-differentiated subtype. They can grow to massive size before causing symptoms or detection. Well-differentiated liposarcoma, while having a negligible metastatic rate, is fraught with a high local recurrence rate, despite a complete surgical resection. Reasons for this are not completely known but may be related to a field defect of the retroperitoneal fat creating a niche for recurrence. These tumors are classically chemo- and radio-resistant. Surgical therapy of recurrences can be challenging, but remains the treatment of choice for well-differentiated liposarcoma. In an attempt to improve on survival and recurrence rates for retroperitoneal liposarcoma, an extended resection approach has been promoted by a few groups. This involves the en bloc resection of contiguous organs that are not macroscopically involved. While this has improved local recurrence rates, benefit for overall survival has not been demonstrated. Interestingly, the improvement in local recurrence rate appeared to be driven by histology and was most improved in the well-differentiated subtype compared to historical data. However, for well-differentiated liposarcomas that are multifocal, this approach may be less useful. The application of this approach still requires further study in terms of balancing increased morbidity of extended resection against the potential for multiple surgeries for recurrence."

Chowdry, V., Goldberg, S., DeLaney, T.F., Cote, G.M., Chebib, I., Kim, J., Lozano-Calderon, S.A. & De Amorim Bernstein, K. 2018.
Introduction: Myxoid liposarcoma (MLS) is a subtype of liposarcoma characterized morphologically by lipomatous differentiation with a myxoid stroma. The purpose of this study was to review clinical and pathological information for patients treated for MLS at our institution to better understand neoadjuvant and adjuvant therapy.
Materials and Methods: An institutional database of sarcomas was queried for patients who were treated for MLS at our institution between 1992 and 2013. Survival curves were constructed using Kaplan–Meier analysis, and univariate and multivariate statistics were performed using the Cox-proportional hazards model and using linear regression.

Results: A total of 85 patients with myxoid liposarcoma were identified. The mean and median histologic response rate to treatment for patients who received preoperative radiation therapy was 77.6%. Five-year disease-free survival, distant metastasis-free survival, local recurrence-free survival, and overall survival were 78.6% (95% CI: 67.8–86.1), 84.7% (95% CI: 74.5–91.0), 95.6% (95% CI: 86.9–98.6), and 87.5% (95% CI: 77.2–93.3) respectively. On univariate analysis, there was a trend towards higher necrosis or treatment response rates in patients who received concurrent chemotherapy, 84.7% (95% CI: 75.9–93.4) and 69.5% (95% CI: 55.1–83.8), p=0.061. Tumor size was associated with inferior disease-free and overall survival. Hazard ratio for disease-free survival is 1.08 (per cm) (95% CI: 1.01–1.16), p=0.019.
Conclusions: Myxoid liposarcoma exhibits histological response to chemotherapy and radiation therapy. Tumor size appears to be greatest predictor of long-term disease control and overall survival. We were not able to show that chemotherapy provides a clinical benefit with regard to local control, disease-free survival, or overall survival. However, it is important to note that the selected usage of chemotherapy in the highest risk patients confounds this analysis. Further investigation is needed to help better determine the optimal use of chemotherapy in this group of patients.

Suarez-Kelly, L.P., Baldi, G.G. & Gronchi, A. 2019.
Introduction: Liposarcomas are a heterogeneous group of soft tissue tumors that arise from adipose tissue and are one of the most common soft tissue sarcomas found in adults. Liposarcomas are subclassified into four subtypes with distinct histologic and biologic features that influence their treatment and management.
Areas covered: This manuscript reviews the key clinicopathologic and cytogenic characteristics of the liposarcoma histologic subtypes and summarizes the results of recent clinical trials, treatment options, and future directions in the pharmacotherapy for the management of liposarcoma.
Expert opinion: Despite significant advancements in the management of this disease, the treatment of liposarcoma continues to be a challenge. Surgical resection remains the mainstay of treatment for localized disease; however, use of systemic therapies in conjunction with surgery may be considered in patients where tumor shrinkage could reduce surgical morbidity and in patients with high-risk of micrometastatic disease. Anthracycline-based chemotherapy regimens remain the standard first-line treatment for unresectable/metastatic liposarcoma. Trabectedin and eribulin are currently the two most promising and evidenced-based second-line treatment options for liposarcomas. However, multiple clinical trials dedicated to patients with liposarcoma evaluating novel targeted agents are ongoing. Every effort should be made to enroll patients with liposarcoma into histotype-specific clinical trials.

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/

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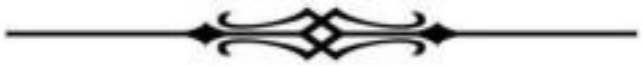

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Liposarcoma

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