Cancer Association of South Africa (CANSA)

Research • Educate • Support

Fact Sheet
on
Uterine Leiomyosarcoma

Introduction

Uterine leiomyosarcoma (uLMS) is a rare entity among malignant gynaecologic tumours with a very unfavourable prognosis and the highest prevalence in the pre- and peri-menopause. Only early-stage tumours 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 it should be done in order to remove the uterus intact.

[Picture Credit: Uterine Leiomyosarcoma Graphic]

Uterine Leiomyosarcoma

Uterine leiomyosarcoma is a rare malignant (cancerous) tumour that arises from the smooth muscle lining the walls of the uterus (myometrium). There are essentially two types of muscles in the body: voluntary and involuntary. Smooth muscles are involuntary muscles; the brain has no conscious control over them.

Uterine leiomyosarcomas are malignant and may spread (metastasize) locally and to other areas of the body, especially the lungs and liver often causing life-threatening complications. Leiomyosarcomas recur in more than half of the cases sometimes within eight to 16 months of the initial diagnosis and treatment.

Incidence of Uterine Leiomyosarcoma

The National Cancer Registry does not provide any information regarding the incidence of uterine leiomyosarcoma.

Risk Factors for Uterine Leiomyosarcoma

Leiomyosarcomas are associated with specific genetic and environmental risk factors.

Certain inherited conditions may increase the risk of developing a leiomyosarcoma:

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- Gardner syndrome
- Li-Fraumeni syndrome
- Werner syndrome
- Neurofibromatosis
- Several of theimmune deficiency syndromes.

Some sources also identify exposure to the following as possible risk factors although definitive links have not been established:
- High dose radiation
- Certain chemicals (e.g., herbicides).

Signs and Symptoms of Uterine Leiomyosarcoma
Symptoms of uterine leiomyosarcoma may vary from case to case depending upon the exact location, size and progression of the tumour. Many women will not have any apparent symptoms (asymptomatic).

The most common symptom is abnormal bleeding from the vagina and the uterus.

Postmenopausal bleeding is another important factor that may indicate a uterine leiomyosarcoma.

Diagnosis of Uterine Leiomyosarcoma
Often, the diagnosis of a uterine leiomyosarcoma is made incidentally when affected individuals are operated on for benign smooth muscle tumours of the uterus.

Other diagnostic procedures may include imaging techniques such as:
- Computerised tomography (CT) scanning
- Magnetic resonance imaging (MRI)
- Ultrasound.

Lawlor, H., Ward, A., Maclean, A., Lane, S., Adishesh, M., Taylor, S., DeCruze, S.B. & Hapangama, D.K. 2020.
”Early diagnosis of the rare and life-threatening uterine leiomyosarcoma (LMS) is essential for prompt treatment, to improve survival. Preoperative distinction of LMS from benign leiomyoma remains a challenge, and thus LMS is often diagnosed post-operatively. This retrospective observational study evaluated the predictive diagnostic utility of 32 preoperative variables in 190 women who underwent a hysterectomy, with a postoperative diagnosis of leiomyoma (n = 159) or LMS (n = 31), at the Liverpool Women's National Health Service (NHS) Foundation Trust, between 2010 and 2019. A total of 7 preoperative variables were associated with increased odds of LMS, including postmenopausal status ($p < 0.001$, OR 3.08), symptoms of pressure ($p = 0.002$, OR 2.7), postmenopausal bleeding ($p = 0.001$, OR 5.01), neutrophil count $\geq 7.5 \times 10^9$/L ($p < 0.001$, OR 5.72), haemoglobin level <118 g/L ($p = 0.037$, OR 2.22), endometrial biopsy results of cellular atypia or neoplasia ($p = 0.001$, OR 9.6), and a mass size of ≥10 cm on radiological imaging ($p < 0.0001$, OR 8.52). This study has identified readily available and easily identifiable preoperative clinical variables that can be implemented into clinical practice to discern those with high risk of LMS, for further specialist investigations in women presenting with symptoms of leiomyoma.”

Virarkar, M., Diab, R., Palmquist, S., Bassett, R. Jr, & Bhosale, P. 2020.
Purpose: To perform a meta-analysis comparing the diagnostic performance of increased signal intensity on T1- and T2-weighted magnetic resonance images and apparent diffusion coefficient (ADC) values in differentiating uterine leiomyosarcoma (LMS) from benign leiomyoma (LM).
Methods: A systematic literature search for original studies was performed using PubMed/MEDLINE, the Cochrane Library, Embase, and Web of Science. Data necessary for the meta-analysis was extracted from the selected articles and analyzed.
Results: Eight studies with 795 patients met our predefined inclusion criteria and were included in the analysis. Increased signal on T1-weighted imaging had a pooled sensitivity of 56.8% (95% CI: 20%-87.4%) for LMS (n = 60) which was significantly higher than 7.6% (95% CI: 2.2%-22.7%) for LM (n = 1272) (p = 0.0094). Increased signal analysis on T2-weighted imaging had a pooled sensitivities of 93.2% and 93.2% (95% CI: 45.7%-99.6% and 42.9%-99.6%) for LMS (n = 90), which were not significantly different from the 54.5% and 53.9% (95% CI: 33.6%-74%, 32%-74%) for LM (n = 215) (p = 0.102 and 0.112). On ADC value analysis, LMS (n = 43) had a weighted mean and standard deviation of 0.896 ± 0.19 10^{-3} mm^2/s, 0.929 ± 0.182 10^{-3} mm^2/s, which were significantly lower from 1.258 ± 0.303 10^{-3} mm^2/s, 1.304 ± 0.303 10^{-3} mm^2/s for LM (n = 159) (p = < 0.0001, < 0.0001).
Conclusion: Our meta-analysis demonstrated that high signal intensity on T1-weighted images and low ADC values can accurately differentiate LMS from LM. Although, LMS had a higher pooled sensitivity for T2-weighted increased signal intensity compared to LM, there was no statistical significance.

Treatment of Uterine Leiomyosarcoma
Total hysterectomy is the cornerstone of management of early disease.

Other treatments may include:
- Adjuvant pelvic radiotherapy
- Adjuvant chemotherapy

The above is often not associated with an overall survival benefit.

Matsuzaki, S., Matsuzaki, S., Chang, E.J., Yasukawa, M., Roman, L.D. & Matsuo, K. 2021.
Objective: To examine the perioperative and survival outcomes in women with disseminated peritoneal uterine leiomyosarcoma (uLMS) who underwent cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC).
Methods: A comprehensive systematic review of literature was conducted using multiple public search engines, PubMed, Scopus, and the Cochrane Library, in compliance with the PRISMA guidelines. Women with disseminated peritoneal uLMS treated with CRS-HIPEC were analyzed. Perioperative morbidity and mortality rate as well as oncologic outcomes related to CRS-HIPEC were assessed.
Results: Ten studies met the inclusion criteria from 2004 to 2020, including 8 case series (n=28) and 2 original articles (n=47). Of the 75 patients, 68 (90.7%) were women with uLMS whereas 7 women were non-uLMS. Of these, 64 (85.3%) had recurrent disease, and 39 (52.0%) received chemotherapy or radiotherapy prior to CRS-HIPEC. The perioperative mortality rate was 4.0% (intraoperative 1.3%, and postoperative 2.7%), and postoperative complications (grade ≥3) rate ranged 21.4-22.2%. With regard to HIPEC regimens (n=75), cisplatin was most frequently used (n=55, 73.3%) followed by melphalan (n=17, 22.7%) and others (n=3, 4.0%). Among the two observational studies, the median overall survival after CRS-HIPEC treatment was 29.5-37 months. In one limited comparative effectiveness study (n=13), albeit statistically non-significant CRS-HIPEC was associated with higher progression-free survival versus CRS alone (3-year rates, 71.4% versus 0%, P=0.10). When the HIPEC regimens were compared, melphalan use was associated with

decreased uLMS-related mortality compared to a cisplatin-based regimen, but the association was not statistically significant (hazard ratio 0.35, 95% confidence interval 0.04-3.05, P=0.35).
Conclusion: Effectiveness of CRS-HIPEC for disseminated peritoneal uLMS is yet to be determined. As interpretation of the available data on survival is limited due to small sample sizes or the lack of an active comparator, further study is warranted to examine the safety and survival effect of CRS-HIPEC in disseminated peritoneal uLMS.

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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Uterine Leiomyosarcoma Graphic
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