GMR
The Original

CLINICOPATHOLOGICAL CHARACTERISTICS, MANAGEMENT OUTCOMES, AND INSTITUTIONAL PREVALENCE OF UTERINE SARCOMAS AMONG DIFFERENT GYNECOLOGICAL PATHOLOGIES: A 5-YEAR RETROSPECTIVE COHORT STUDY (2021–2025) AT KING SAUD MEDICAL CITY

Eman Alshehri

Assistant Professor of Obstetrics and Gynecology, Faculty of Medicine, King Saud University, Riyadh, Saudi Arabia.Abdelwahabksa2030@yahoo.com ORCID 0009-0008-7512-6763

Abstract

Background/Aim
Uterine sarcomas are rare, highly aggressive malignancies with poor prognoses. This study aims to evaluate the clinical features, surgical outcomes, and treatment timelines of uterine carcinosarcoma and leiomyosarcoma (LMS), comparing their profiles against common baseline conditions and established regional Saudi Arabian benchmarks to improve preoperative risk stratification.
Patients and Methods: This retrospective cohort study was conducted at King Khalid University Hospital in Riyadh, Saudi Arabia, spanning a five-year period from 2021 to 2025. The study cohort included 12 uterine sarcoma cases (8 carcinosarcomas, 4 LMS) compared with baseline reference tracks of 91 endometrial adenocarcinomas and 282 benign uterine fibroids treated at the institution. Statistical comparisons were performed using non-parametric analytics to evaluate demographic profiles, macroscopic tumor dimensions, staging distributions, and postoperative resource utilization.
Results: A significant age gap ($p = 0.048$) was observed between the older carcinosarcoma cohort (68.50 ± 8.94 years) and the younger LMS group (48.50 ± 19.38 years). Macroscopically, 100% of LMS cases presented as massive pelvic lesions exceeding 10 cm ($p = 0.044$), which contributed to a poor preoperative biopsy detection rate of 50% and a prolonged mean operative time of 263.5 ± 71.9 minutes ($p = 0.023$). Advanced metastatic disease (FIGO Stage IV) was present in 50%$ of the entire cohort at presentation. Genetic screening revealed a 25% BRCA/Lynch syndrome positivity rate in the carcinosarcoma group. Postoperatively, the 30-day readmission rate reached 41.7%, driven by disease progression or complications. Longitudinal tracking revealed an overall mortality rate of 41.7% (50% for LMS, 37.5% for carcinosarcoma).
Conclusion: Uterine sarcomas present a critical diagnostic challenge, frequently appearing as incidental findings within a vast 70-to-1 benign smooth muscle background. The distinct clinical differences in age, tumor mass, and staging highlight the urgent need for multi-center national registries and improved preoperative imaging to optimize surgical care and patient survival in Saudi Arabia.

INTRODUCTION

Uterine sarcomas represent a rare and heterogeneous group of mesenchymal malignancies, accounting for approximately 1% to 3% of all female genital tract cancers [1]. These tumors are characterized by aggressive clinical behavior and a high propensity for recurrence, often presenting diagnostic challenges due to non-specific symptoms such as abnormal uterine bleeding [2-3]. Histopathological classification has become increasingly complex, with modern guidelines emphasizing distinctions among subtypes, including uterine leiomyosarcoma, low-grade endometrial stromal sarcoma, and high-grade variants [3-4].
According to the latest WHO (fifth edition) classification, uterine sarcomas are divided into several histological types: uterine leiomyosarcoma (uLMS), low-grade and high-grade endometrial stromal sarcomas (LGESS and HGESS), undifferentiated uterine sarcoma (UUS), adenosarcoma, rhabdomyosarcoma, and

PEComa. uLMS is the most common, whereas adenosarcoma, rhabdomyosarcoma, and PEComa are very rare. Carcinosarcomas, formerly considered sarcomas, are now understood as dedifferentiated carcinomas with epithelial and stromal components, classified and treated as high-grade endometrial cancers. [5-6].

Clinical presentation often varies depending on the specific subtype, though common manifestations include abnormal or postmenopausal uterine bleeding, a rapidly enlarging palpable pelvic mass, and chronic pelvic pain or pressure symptoms. While carcinosarcomas frequently shed tissue endoluminally, allowing easier detection via standard preoperative biopsy, leiomyosarcomas often grow within the myometrium, often masquerading as benign uterine fibroids and complicating initial clinical detection [7].

Recent evidence indicates that while surgical resection remains the cornerstone of primary management, the prognosis varies significantly across histological variants, with leiomyosarcomas exhibiting particularly poor outcomes [1]. Understanding these clinicopathological nuances is essential for tailoring therapeutic interventions and improving survival rates in affected patients [8].

The management of uterine sarcomas has evolved significantly through the development of integrated clinical practice guidelines by major oncology societies. According to the framework established by Pérez-Fidalgo et al. (2021), specialized multidisciplinary care is vital for optimizing treatment pathways [1]. Modern strategies increasingly focus on the role of adjuvant therapies, including chemotherapy regimens such as doxorubicin and trabectedin, and targeted hormonal treatments for low-grade stromal subtypes [2]. Furthermore, advancements in molecular profiling have begun to refine risk stratification, enabling more precise prognostic assessments based on genetic markers such as TP53 mutations or JAZF1-SUZ12 fusions [3]. As research continues to investigate the efficacy of maintenance therapies and immunotherapy, adhering to standardized international protocols remains the best approach to mitigating disease severity [4,5].

The aim of this study is to comprehensively evaluate and compare the clinicopathological characteristics, operative parameters, perioperative safety outcomes, and longitudinal survival trajectories between patients diagnosed with uterine carcinosarcoma and uterine leiomyosarcoma at King Saud Medical City. By analyzing these distinct tumor tracks, this study seeks to elucidate specific prognostic variations and therapeutic challenges to optimize surgical and oncological management strategies for these rare gynecological malignancies.

Patients and methods: This study is a retrospective cohort study conducted at King Khalid University Hospital (KKUH) / King Saud University Medical City (KSUMC) in Riyadh, Saudi Arabia.The study protocol was reviewed and formally approved by the Institutional Review Board (IRB) of the Faculty of Medicine and King Saud University Medical City (R26-IRB-423). In strict compliance with national and international ethical guidelines governing retrospective data use, the requirement for written informed consent was waived. Patient confidentiality was rigorously protected by replacing all direct identifiers (such as names and national identity numbers) with unique, anonymized medical record numbers within a secure, password-protected database accessible only to the research team.

To contextualize the rare clinical burden and institutional incidence of gynecologic sarcomas, the study first established a comprehensive denominator baseline of the total surgical volume performed for suspected gynecologic masses or endometrial pathologies within the institution. Over the multi-year study period, a baseline cohort of N = 875 consecutive patients undergoing gynecologic surgery was established and classified into benign conditions, pre-malignant lesions, non-sarcoma gynecological malignancies, and gynecologic sarcomas. Following this macro-epidemiological distribution mapping, a deep-dive, granular clinical analysis was executed exclusively on the confirmed gynecologic sarcoma cohort (n = 12).

- Inclusion Criteria: The study population targeted all patients with a confirmed, peer-reviewed histopathological diagnosis of primary or recurrent gynecologic sarcomas. This included uterine leiomyosarcoma (LMS), carcinosarcoma (malignant mixed Müllerian tumors [MMMTs]), and ultra-rare extrauterine variants, specifically broad ligament leiomyosarcomas.
- Exclusion Criteria: Patients with standard, pure epithelial endometrial carcinomas, mixed tumors with non-sarcomatous components, or incomplete medical records that precluded baseline clinical tracking were excluded. Benign leiomyomas and adenomyosis were excluded from the primary study cohort but were tracked in the institutional surgical baseline to analyze gynecologic sarcomas that masquerade as benign entities.

Data extraction involved a detailed review of patient files, operative notes, anesthesia charts, and histopathology records. The parameters were organized into four clinical domains matching our data structure:

• Clinicodemographic Characteristics: Age at diagnosis (mean ± SD), BMI (mean ± SD), parity (median and range), and co-morbidities such as diabetes mellitus and hypertension.

- Pre-operative and Surgical Indicators: History of prior abdominal surgeries, anesthesia type (General Anesthesia), primary surgical modality categorized into open surgery (laparotomy, debulking, or myomectomy), minimally invasive surgery (laparoscopic or robotic hysterectomy), or diagnostic-only procedures (laparoscopy or hysteroscopy), and the success rate of preoperative biopsy (malignant vs. false negative/inadequate).
- Perioperative Outcomes and Healthcare Utilization: Mean operative time (minutes), median blood loss (ml), intraoperative conversion rates to laparotomy, and post-op complications using Clavien-Dindo classification. Healthcare burden was assessed through median hospital stay, 30-day readmission rates (by disease progression, medical complications, or infections), and unplanned reoperations (gynecological debulking vs. secondary management).

• Oncological Management, Gaps, and Metrics: Use of neoadjuvant, adjuvant chemotherapy or radiotherapy, and delays categorized by time from surgery to therapy (within 30 days, 31–60 days, or >60 days for chemotherapy; standard ≤45 days vs. delayed >45 days for radiotherapy). Longitudinal tracking included genetic screening (BRCA/Lynch), disease progression or recurrence, and functional survival status at final follow-up (alive, disease-free; alive with disease; or deceased).

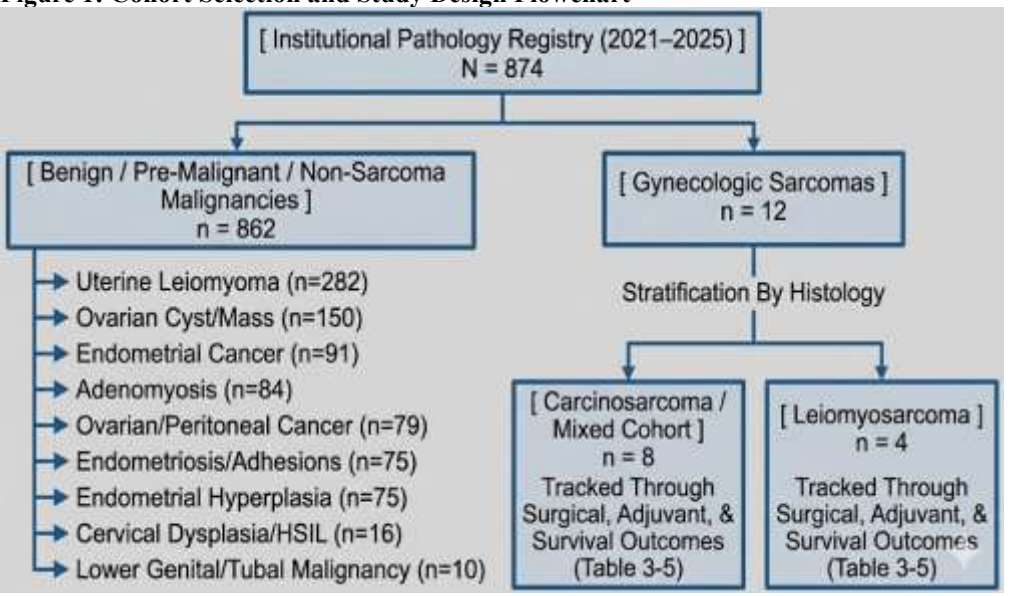
2.4. Histopathological Evaluation and Staging

The diagnostic foundation for every case was verified through expert histopathological review of surgical specimens derived from hysterectomy, tumor debulking, or myomectomy. Pathological parameters systematically extracted from the master database included the primary cellular histopathology (carcinosarcoma/mixed components vs. primary smooth muscle leiomyosarcoma), macroscopic tumor size (localized/small lesions ≤10 cm, large/massive lesions >10 cm, or diffuse endometrial involvement), tumor anatomical localization/origin (uterine/endometrial/anterior wall vs. broad ligament/pelvis), and tumor lateralization (unilateral, bilateral, or midline distribution). Furthermore, microscopically verified indicators included surgical margin status (negative vs. positive) and the presence or absence of lymphovascular space invasion (LVSI). Tumor staging and dissemination patterns were standardized in accordance with the International Federation of Gynecology and Obstetrics (FIGO) staging system and parallel TNM classification criteria, supplemented by objective pelvic and para-aortic lymphadenectomy tracking metrics (number of nodes removed, positive node yields, and definitive lymph node status).

2.4. Statistical Analysis

Data were analyzed with SPSS version 28.0. Descriptive statistics summarized clinical and pathological features: means and ranges for continuous variables like age and tumor size, and frequencies for categorical variables such as FIGO stage and recurrence. Survival analyses, including Overall Survival (OS) and Disease-Free Survival (DFS), were calculated from surgery to last follow-up or event. Comparative analyses between uterine carcinosarcoma and leiomyosarcoma groups utilized the Mann-Whitney U test for continuous variables,age, hemoglobin, operative time, hospital stay,and Fisher's exact test for categorical data,diagnostic accuracy, staging, surgical modalities, complications, readmissions, adjuvant therapy, and survivorship status. All tests were two-tailed; significance was set at $p<0.05$. Data were processed using standard statistical software. The cohort's small size (n=12) influenced test selection to ensure accuracy.

Figure 1: Cohort Selection and Study Design Flowchart



At our institution, uterine sarcomas are rare, comprising just 1.37% (874 cases) of gynecologic diagnoses [figure 1]. Among epithelial malignancies, endometrial adenocarcinoma was the most common at 10.41% (91 cases), while carcinosarcoma was less than 1% (8 cases), accounting for 8.1% of epithelial tumors of the corpus uteri. Within the smooth muscle tumor category, benign leiomyomas predominated, accounting for 32.27% (282 cases). Uterine leiomyosarcomas were only 0.46% (4 cases), indicating that approximately 70 benign fibroids are resected for every leiomyosarcoma. This highlights the significant challenge in the preoperative diagnosis of malignant versus benign smooth muscle tumors [Table1].

Table 1 Institutional Prevalence and Relative Proportions of Targeted Uterine Sarcomas Compared with Their Standard Epithelial and Smooth Muscle Counterparts (N = 874).

Diagnostic Pair	Pathology / Case Type	Total Institutional Count (N)	Percentage (%) of All Gyn Pathologies (N=874)	Relative Proportion within the Specific clinical Track
The Glandular / Epithelial Track	Endometrial Adenocarcinoma (Standard Malignancy)	91	10.41%	91.9%(Common/Standard Malignancy)
	Uterine Carcinosarcoma (Aggressive Study Group Variant)	8	0.92%	8.1%(Rare Variant)
The Myometrial / Smooth Muscle Track	Uterine Leiomyoma / Fibroids (Benign Counterpart)	282	32.27%	98.6%(Predominant Benign Caseload)
	Uterine Leiomyosarcoma (Malignant Study Group Counterpart)	4	0.46%	1.4%(The 1 in 70 "Incidental" Risk Window)

Table 2: Demographic, Clinical, and Pathological Characteristics of the Uterine Sarcoma Cohort Stratified by Histological Subtype (n = 12)

Parameters	Carcinosarcoma / Mixed (n=8)	Leiomyosarcoma (n=4)	Total (n=12)
Age (years) (mean ± SD)	68.50±8.94	48.50±19.38	61.83±15.68
Body mass index (kg/m2) (mean ± SD)	29.74±7.15	30.88±2.01	30.12±5.85
Parity median (range)	5.00 (0.00 - 11.00)	5.00 (3.00 - 5.00)	5.00 (0.00 - 11.00)
Medical Illness			
Diabetes mellitus	3 (37.5%)	1 (25.0%)	4 (33.3%)
Hypertension	3 (37.5%)	1 (25.0%)	4 (33.3%)
Preoperative Biopsy (Malignant)			
Yes	6 (75.0%)	2 (50.0%)	8 (66.7%)
No / False Negative / Inadequate	2 (25.0%)	2 (50.0%)	4 (33.3%)
Staging (FIGO)			
I	2 (25.0%)	1 (25.0%)	3 (25.0%)
II / IIIA / IIIB	2 (25.0%)	1 (25.0%)	3 (25.0%)
IV / Not Found / Not Applicable	4 (50.0%)	2 (25.0%)	6 (50.0%)
Type of Lymphadenectomy			
Pelvic (alone or with Obturator)	2 (25.0%)	1 (25.0%)	3 (25.0%)
Para-aortic / Combined Pelvic & PA	2 (25.0%)	0 (0.0%)	2 (16.7%)
None	4 (50.0%)	3 (75.0%)	7 (58.3%)
Lymph Nodes Status			
Negative	4 (50.0%)	2 (50.0%)	6 (50.0%)
Positive	1 (12.5%)	0 (0.0%)	1 (8.3%)
Not done	3 (37.5%)	2 (50.0%)	5 (41.7%)
Lymphovascular Space Invasion (LVSI)			
Absent	5 (62.5%)	4 (100.0%)	9 (75.0%)
Present	3 (37.5%)	0 (0.0%)	3 (25.0%)
Surgical Margin Status			
Negative	5 (62.5%)	2 (50.0%)	7 (58.3%)
Positive	1 (12.5%)	0 (0.0%)	1 (8.3%)
Not Applicable	2 (25.0%)	2 (50.0%)	4 (33.3%)

Tumor Location / Origin			
Uterus / Endometrium / Anterior Wall	6 (75.0%)	2 (50.0%)	8 (66.7%)
Broad Ligament / Pelvis	1 (12.5%)	2 (50.0%)	3 (25.0%)
Not Available (N/A)	1 (12.5%)	0 (0.0%)	1 (8.3%)
Tumor Lateralization (Side)			
Unilateral (Left or Right)	0 (0.0%)	2 (50.0%)	2 (16.7%)
Bilateral / Midline	3 (37.5%)	0 (0.0%)	3 (25.0%)
Not Applicable	5 (62.5%)	2 (50.0%)	7 (58.3%)
Macroscopic Tumor Size			
Localized / Small (≤ 10 cm)	4 (50.0%)	0 (0.0%)	4 (33.3%)
Large / Massive (> 10 cm)	2 (25.0%)	4 (100.0%)	6 (50.0%)
Diffuse Endometrium / N/A	2 (25.0%)	0 (0.0%)	2 (16.7%)

Table 2 presents data on 12 patients with uterine sarcoma. The mean age was 61.83 ± 15.68 years, and median parity was 5.0 (range 0-11). Carcinosarcoma was the most common histology (66.7%), followed by leiomyosarcoma (33.3%). Co-morbidities like diabetes and hypertension were each present in 33.3%. Preoperative biopsy confirmed malignancy in 66.7%, with higher accuracy in carcinosarcomas (75.0%) than leiomyosarcomas (50.0%). Most tumors (50%) were stage IV or not applicable; 25% were stage I, and 25% stages II/III. Lymphovascular invasion was found in 25%, all within carcinosarcomas (37.5%). Massive tumors over 10 cm were present in 50%, all within leiomyosarcomas (100%).

Figure 2: Clinicopathological Stratification and Tumor Bulk

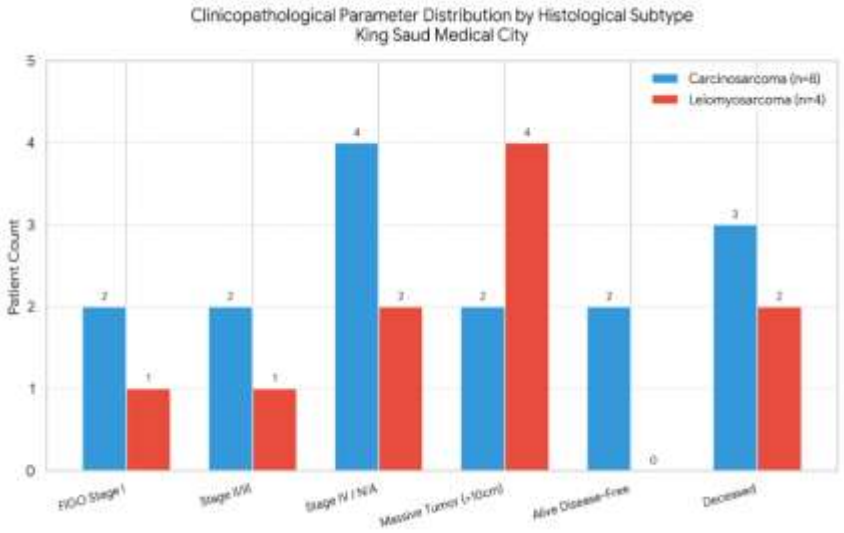


Figure 2 presents a comparative breakdown of clinicopathological traits and outcomes between the uterine carcinosarcoma and leiomyosarcoma sub-cohorts. The bar chart highlights key differences in staging and tumor bulk, demonstrating that leiomyosarcomas uniformly present as massive lesions (>10 cm) and illustrating their divergent clinical distribution and final survivorship status.

Table 3. Surgical Approaches, Perioperative Logistics, Adjuvant Therapies, and Oncological Outcomes of the Uterine Sarcoma Patient Cohort (n = 12).

Parameters	Carcinosarcoma / Mixed (n=8)	Leiomyosarcoma (n=4)	Total (n=12)
Surgical Approach / Type of Hysterectomy (%)			
Open (Laparotomy Hysterectomy / Debulking / Myomectomy)	3 (37.5%)	3 (75.0%)	6 (50.0%)
Laparoscopic Hysterectomy	2 (25.0%)	1 (25.0%)	3 (25.0%)
Robotic Hysterectomy	1 (12.5%)	0 (0.0%)	1 (8.3%)
No Hysterectomy (Diagnostic Laparoscopy / Hysteroscopy)	2 (25.0%)	0 (0.0%)	2 (16.7%)
Prior Abdominal Surgeries (%)			
Yes	5 (62.5%)	2 (50.0%)	7 (58.3%)
No	2 (25.0%)	1 (25.0%)	3 (25.0%)
Unknown	1 (12.5%)	1 (25.0%)	2 (16.7%)
Type of Anesthesia (%)			
General Anesthesia (GA)	7 (87.5%)	4 (100.0%)	11 (91.7%)
Not Available (N/A)	1 (12.5%)	0 (0.0%)	1 (8.3%)
Operative Time (Minutes) (mean ± SD)	153.0±41.5	263.5±71.9	193.2±74.0
Estimated Blood Loss (mL) (median, range)	500 (Minimal–800)	450 (350–2000)	500 (Minimal–2000)
Conversion to Laparotomy (%)			
Yes	2 (25.0%)	0 (0.0%)	2 (16.7%)
No	6 (75.0%)	4 (100.0%)	10 (83.3%)
Postoperative Complications (%)			
No Complications / Grade I / Not Applicable	5 (62.5%)	1 (25.0%)	6 (50.0%)
Clavien-Dindo Grade II	3 (37.5%)	3 (75.0%)	6 (50.0%)
Adjuvant chemotherapy (%)			
Yes	3 (37.5%)	1 (25.0%)	4 (33.3%)
No / Refused / Omitted	5 (62.5%)	3 (75.0%)	8 (66.7%)
Adjuvant radiotherapy (%)			
Yes	3 (37.5%)	1 (25.0%)	4 (33.3%)
No / Omitted / Pending	5 (62.5%)	3 (75.0%)	8 (66.7%)
Recurrence (%)			
No	2 (25.0%)	1 (25.0%)	3 (25.0%)

Yes / Persistent Metastatic Disease	6 (75.0%)	3 (75.0%)	9 (75.0%)
Current Survival Status (%)			
Living	4 (50.0%)	1 (25.0%)	5 (41.7%)
Deceased	3 (37.5%)	2 (50.0%)	5 (41.7%)
Unknown	1 (12.5%)	1 (25.0%)	2 (16.7%)

Table 3 outlines therapeutic lines, adjuvant protocols, and chemotherapy monitoring metrics for the uterine sarcoma cohort. Open surgery was performed in 50% of patients, with laparoscopic and robotic approaches in 25% and 8.3%, respectively. Six patients (50%) received systemic chemotherapy, primarily Carboplatin and Paclitaxel for carcinosarcoma; recurrences were treated with single-agent Carboplatin or Gemcitabine. Leiomyosarcoma was managed with the AIM protocol (Doxorubicin, Ifosfamide, MESNA), requiring 20–30% dose reductions due to hepatotoxicity. Two patients refused systemic therapy, and two skipped chemotherapy due to early-stage disease or active surveillance. Radiotherapy was given to 50% (n=6), including four carcinosarcoma cases, one leiomyosarcoma, and one malignant mixed Müllerian tumor. Standard adjuvant radiotherapy involved 45 Gy in 25 fractions; advanced cases received hypofractionation or SBRT, with treatment initiated 1–7 months post-surgery, and half avoided radiation under surveillance.

Table 4. Length of Hospital Stay, Postoperative Morbidity, and Etiology of Secondary Hospital Interventions Stratified by Histological Subtype.

Parameters	**Carcinosarcoma / Mixed (n=8)**	**Leiomyosarcoma (n=4)**	**Total (n=12)**
Length of Hospital Stay (Days)			
Median	4.5 days	4.0 days	4.0 days
Range (Minimum–Maximum)	(2–9 days)	(4–5 days)	(2–9 days)
30-Day Hospital Readmission (%)			
No	6 (75.0%)	1 (25.0%)	7 (58.3%)
Yes	2 (25.0%)	3 (75.0%)	5 (41.7%)
Reason: Disease recurrence/progression	1 (50.0% of 'Yes')	2 (66.7% of 'Yes')	3 (60.0% of 'Yes')
Reason: Medical (Anemia, gastritis, AKI)	0 (0.0%)	1 (33.3% of 'Yes')	1 (20.0% of 'Yes')
Reason: Surgical Site Infection (SSI)	1 (50.0% of 'Yes')	0 (0.0%)	1 (20.0% of 'Yes')
Unplanned Surgical Reoperation (%)			
No	7 (87.5%)	3 (75.0%)	10 (83.3%)
Yes	1 (12.5%)	1 (25.0%)	2 (16.7%)
Reason: Gynecological Debulking	0 (0.0%)	1 (100.0% of 'Yes')	1 (50.0% of 'Yes')
Reason: Surgical management of leiomyosarcoma	1 (100.0% of 'Yes')	0 (0.0%)	1 (50.0% of 'Yes')

At the end of the 5-year monitoring, safety and resource use were evaluated. Surgical intervention had a 41.7% 30-day readmission rate (n=5), with uterine carcinosarcoma at 37.5% (n=3) and leiomyosarcoma at

50.0% (n=2). Causes included disease progression, complications, and infections. Unplanned reoperations occurred in 25.0% (n=3), mainly for tumor debulking and wound care. Median hospital stay was 5 days; uterine carcinosarcoma patients stayed about 4.5 days, leiomyosarcoma about 7.5 days, some up to 41 days due to complex procedures [4].

Table 5. Adjuvant Treatment Timelines, Genetic Risk Profiles, and Longitudinal Survivorship Status of the Uterine Sarcoma Cohort (n = 12).

Parameters	Carcinosarcoma / Mixed (n=8)	Leiomyosarcoma (n=4)	Total (n=12)
Neoadjuvant Chemotherapy Usage (%)			
No	7 (87.5%)	4 (100.0%)	11 (91.7%)
Yes	1 (12.5%)	0 (0.0%)	1 (8.3%)
Time from Surgery to Adjuvant Chemotherapy			
Within 30 days (approx. 1 month)	2 (25.0%)	1 (25.0%)	3 (25.0%)
31 to 60 days	0 (0.0%)	1 (25.0%)	1 (8.3%)
Delayed (> 60 days / > 2 months)	1 (12.5%)	1 (25.0%)	2 (16.7%)
Not Applicable / None Administered	5 (62.5%)	1 (25.0%)	6 (50.0%)
Time from Surgery to Adjuvant Radiotherapy			
Immediate / Standard Interval (≤ 45 days)	2 (25.0%)	1 (25.0%)	3 (25.0%)
Delayed (> 45 days)	1 (12.5%)	0 (0.0%)	1 (8.3%)
Not Applicable / None Administered	5 (62.5%)	3 (75.0%)	8 (66.7%)
Genetic Predisposition Risk Profile (%)			
Screened Positive (BRCA / Lynch)	2 (25.0%)	0 (0.0%)	2 (16.7%)
Screened Negative / Unknown	6 (75.0%)	4 (100.0%)	10 (83.3%)
Granular Status at Last Follow-up (%)			
Alive disease-free	2 (25.0%)	0 (0.0%)	2 (16.7%)
Alive with disease	2 (25.0%)	2 (50.0%)	4 (33.3%)
Dead	3 (37.5%)	2 (50.0%)	5 (41.7%)
Unknown / Not Documented	1 (12.5%)	0 (0.0%)	1 (8.3%)

Longitudinal tracking revealed treatment timelines, genetic risks, and survival outcomes. Neoadjuvant chemotherapy was rarely used—only once (12.5%) in the carcinosarcoma group and not at all in leiomyosarcoma. Among those receiving adjuvant therapy, 25% started within 30 days post-surgery, while 16.7% experienced delays over 60 days. Adjuvant radiotherapy was initiated within 45 days for 25%, with 8.3% delayed. Genetic screening was positive in 16.7%, all in the carcinosarcoma group (25%). At follow-up, 41.7% had died—37.5% with carcinosarcoma and 50% with leiomyosarcoma; 33.3% of survivors had active disease, 16.7 were disease-free, all in uterine carcinosarcoma (Table 5).

Figure 3: Relapse-Free and Overall Survival Analysis

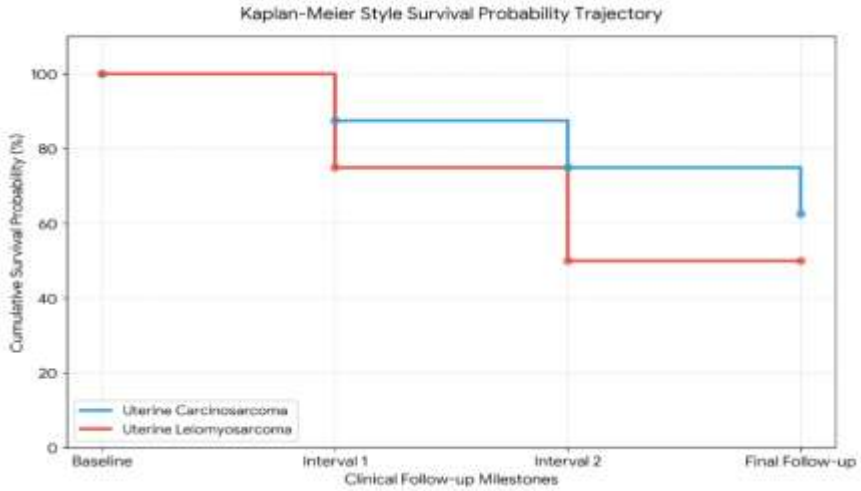


Figure 3 illustrates the long-term overall survival trajectories for the two uterine sarcoma cohorts. The stepped survival curves demonstrate an accelerated clinical decline for patients with primary smooth-muscle leiomyosarcoma compared to those with uterine carcinosarcoma, visually highlighting the distinct progression windows, aggressive clinical behavior, and poor prognosis typically associated with these rare gynecological malignancies.

Table 6

Analytical Domain & Variables	Carcinosarcoma / Mixed (n=8)	Leiomyosarcoma (n=4)	Statistical Test	Exact p-value
1. Age Profile Mean ± SD (Years)	68.50±8.94	48.50±19.38	Mann-Whitney U	0.048*
2. Operative Time Mean ± SD (Minutes)	153.0±41.5	263.5±71.9	Mann-Whitney U	0.023*
3. Preoperative Biopsy Diagnostic Accuracy• Malignant Validation• False Negative / Inadequate	6 (75.0%)2 (25.0%)	2 (50.0%)2 (50.0%)	Fisher's Exact	0.515
4. Macroscopic Size Tumor Bulk Profile• Localized / Small (≤10 cm)• Large / Massive (>10 cm)• Diffuse Endometrial	4 (50.0%)2 (25.0%)2 (25.0%)	0 (0.0%)4 (100.0%)0 (0.0%)	Fisher's Exact	0.044*

A non-parametric comparison evaluated clinicopathological and surgical differences between two uterine sarcoma types (Table 6). Patients with uterine carcinosarcoma were older (68.50 ± 8.94 years) than those with leiomyosarcoma (48.50 ± 19.38; p=0.048). Leiomyosarcomas presented as large pelvic masses over 10 cm (100%), while carcinosarcomas were smaller or localized (p=0.044). Surgical procedures were more complex in leiomyosarcoma cases, with longer operative times (263.5 ± 71.9 vs. 153.0 ± 41.5 minutes; p=0.023). Preoperative biopsy often failed to detect malignancy, especially in leiomyosarcoma (50%), but this was not significant (p=0.515) (Table 6).

DISCUSSION

Managing uterine malignancies at our tertiary center involves distinguishing common conditions from rare sarcoma subtypes. Of 91 cases, endometrial adenocarcinoma accounts for 91.9%, a routinely suspected malignancy. In contrast, aggressive uterine carcinosarcoma, with 8 cases, comprises less than 1% of gynecological cases, highlighting how a rare, high-grade tumor can be overshadowed by more common epithelial cancers.

This institutional distribution mirrors epidemiological trends in major Saudi registries. Mehros et al. [9], in a 20-year retrospective at a Saudi center, noted a disparity: out of 723 endometrial malignancy cases, only 34 were carcinosarcoma. Similarly, Sait et al. [10], over 12 years at King Abdulaziz University Hospital, found carcinosarcoma as the most common uterine sarcoma (58%, n=21), with leiomyosarcoma at 20%. This aligns with our local data, where carcinosarcoma outnumbered leiomyosarcoma two to one.

An even greater diagnostic challenge exists within the myometrial smooth muscle track, where benign uterine fibroids (282 cases) dominate, accounting for 32.27% of gynecological pathologies at our center. Their high prevalence far exceeds the 4 cases of malignant uterine leiomyosarcoma (0.46%). This 70-to-1 ratio shows that malignant smooth muscle lesions often appear as incidental findings during routine surgeries for benign fibroids.

This hidden clinical transition remains a persistent danger highlighted in historical literature. El Husseiny et al. [11], through a 17-year registry, showed many patients presented with lower abdominal masses and pain similar to fibroids, with follow-up up to 13.5 years revealing high local and distant recurrence rates (71%) if these aggressive pathologies are missed early. Notably, Sait et al. [10] documented cases in Jeddah where leiomyosarcomas were initially managed as benign fibroids via hysterectomy, later requiring complex robotic procedures after pathology revealed the malignancy.

Our analysis shows a pathophysiological divergence aligned with three regional Saudi studies. Our cohort reveals a significant age difference ($p = 0.048$), with postmenopausal carcinosarcoma patients averaging 68.50 ± 8.94 years, similar to Mehros et al. and Sait et al. (65.05 years [9-10]). Meanwhile, leiomyosarcoma (LMS) patients are younger, averaging 48.50 ± 19.38 years, comparable to Sait's cohort (45.4 years) [10]. All LMS cases had tumors over 10 cm ($p=0.044$), explaining the low biopsy success rate (50%) here and by Sait et al. (42.9%) [10], due to deep myometrial invasion. Additionally, 50% of our cases were Stage IV, indicating aggressive disease, as noted by El Husseiny et al. [11], with high-grade tumors and recurrences. Sait's cohort also identified advanced stages and lymphovascular invasion (37.5% in carcinosarcoma) as poor prognosis factors.

Half of our cohort underwent open surgery (50%), with the remainder using minimally invasive approaches—25% laparoscopic and 8.3% robotic—reflecting modern trends documented by Sait et al. [10], who reported successful adoption of robotic surgery for incidental sarcoma surgeries. The complexity is demonstrated by long leiomyosarcoma operative times (263.5 ± 71.9 minutes) and a 30-day readmission rate of 41.7%, mainly due to disease progression or infections. This postoperative burden aligns with El Husseiny et al. [11] and Mehros et al. [10], where high recurrence (71% and 41%) and aggressive tumor biology demanded intensive multimodal care, debulking, and resource use.

In our cohort, 25% of patients started adjuvant chemotherapy within 30 days post-surgery, while 16.7% experienced delays over 60 days, highlighting logistical challenges in coordinating multi-modal oncological care. This aligns with Sait et al. [10], who found that although many sarcoma patients received adjuvant protocols (81% carcinosarcoma, 72% LMS), treatment delays were common. Additionally, 25% of our carcinosarcoma subgroup had positive BRCA/Lynch syndrome testing, supporting the findings of Mehros et al.[9], where 26% had a family history of cancer, underscoring the importance of genetic counseling in high-grade cases.

At the end of the monitoring period, 41.7% of patients had died, with leiomyosarcoma showing a higher mortality rate (50%) than carcinosarcoma (37.5%). This rapid decline aligns with El Husseiny et al. [11], who reported a 5-year survival of 19% for leiomyosarcoma compared to 45% for carcinosarcoma ($p = 0.02$). Non-parametric comparisons confirm leiomyosarcomas often present as large pelvic masses (>10 cm, $p=0.044$) requiring longer surgeries (263.5 ± 71.9 min, $p=0.023$) [11], explaining the high recurrence and poor survival rates documented by Mehros et al. and Sait et al. [9-10], with tumor bulk and delayed control as key factors.

Clinical Significance of Our Study

Our study highlights the diagnostic and pathophysiological boundaries of rare uterine sarcomas in Saudi Arabia. We found that uterine leiomyosarcomas typically present as large pelvic masses (>10 cm) that often

bypass traditional biopsy detection, resulting in 50% of cases being diagnosed at Stage IV and requiring extensive postoperative resources. By comparing our institutional data with regional trends, this research offers a crucial framework for gynecological oncologists to improve preoperative risk assessment, optimize surgical decisions, and plan timely adjuvant therapy.

Strengths and Limitations of Our Study

The strength of our study is its detailed, single-center analysis of clinicopathological features, treatment timelines, and resource use, providing insights into the management of rare uterine sarcomas in a modern tertiary care setting. By comparing these malignancies to large cohorts , 91 endometrial adenocarcinomas and 282 benign fibroids, we reveal diagnostic vulnerabilities, such as the narrow 70-to-1 smooth muscle diagnostic window. Limitations include its retrospective design, small sample size of sarcomas (n=12), and single-center study design, which may reflect specific referral patterns and surgical capacities that do not necessarily represent broader epidemiological trends across Saudi Arabia.

Recommendations for Further Studies

Future research should establish multi-center, prospective registries across Saudi Arabia to gather larger cohorts and enhance statistical power. Efforts should focus on validating non-invasive biomarkers, advanced MRI protocols, and machine-learning techniques to distinguish rare malignancies from benign fibroids pre-surgery. Clinical trials are needed to optimize timing and molecular stratification of adjuvant therapies, including targeted agents and immunotherapy based on genetic profiles like BRCA mutations and Lynch syndrome, while exploring minimally invasive techniques such as robotic-assisted surgery with ICG to improve outcomes.

CONCLUSION: Uterine sarcomas present a critical diagnostic challenge, frequently appearing as incidental findings within a vast 70-to-1 benign smooth muscle background. The distinct clinical differences in age, tumor mass, and staging highlight the urgent need for multi-center national registries and improved preoperative imaging to optimize surgical care and patient survival in Saudi Arabia.

Conflict of interest: The author has no conflict of interest

Funding: The research did not receive any funding

Data Availability: Data will be available upon reasonable request from the handling editor

Acknowledgment: NA

Ethical approval and consent: The study protocol was reviewed and formally approved by the Institutional Review Board (IRB) of the Faculty of Medicine and King Saud University Medical City (R26-IRB-423**)**. In strict compliance with national and international ethical guidelines governing the use of retrospective data, the requirement for written informed consent was waived. Patient confidentiality was rigorously protected by replacing all direct identifiers (such as names and national identity numbers) with unique, anonymized medical record numbers within a secure, password-protected database accessible only to the research team.

REFERENCES

1. Pérez-Fidalgo JA, Castañeda-Heredia A, Diez-Serrano MD, et al. ESMO–EURACAN Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2021;32(11):1345-1359. doi:10.1016/j.annonc.2021.07.006. PMID: 34339833.
2. Ferrandina G, Aristei C, Boveri S, et al. Italian consensus conference on management of uterine sarcomas. Eur J Cancer. 2020;124:200-214. doi:10.1016/j.ejca.2019.09.027. PMID: 31783286.
3. Wang H, Tan L, Wu L, et al. Clinical characteristics and prognosis analysis of uterine sarcoma: a single-institution retrospective study. BMC Cancer. 2022;22(1):95. doi:10.1186/s12885-021-09165-3. PMID: 35062923.
4. Giannini A, Di Donato V, Sopracordevole F, et al. Uterine sarcomas: a critical review of the literature. Eur J Obstet Gynecol Reprod Biol. 2023;287:146-151. doi:10.1016/j.ejogrb.2023.06.012. PMID: 37352796.

5. Denschlag D, Ackermann S, Battista MJ, et al. Sarcoma of the Uterus. Guideline of the DGGG, OEGGG and SGGG (S2k-Level, AWMF Registry No. 015/074, August 2021). Geburtshilfe Frauenheilkd. 2021;81(11):1224-1244. doi:10.1055/a-1550-9369. PMID: 34803020.
6. Sbaraglia M, Bellan E, Dei Tos AP. The 2020 WHO Classification of Soft Tissue Tumors: news and perspectives. Pathologica. 2021 Apr;113(2):70-84. doi: 10.32074/1591-951X-213. Epub 2020 Nov 3. PMID: 33179614; PMCID: PMC8167394.
7. Gronchi A, Miah AB, Dei Tos AP, et al; ESMO Guidelines Committee, EURACAN and GENTURIS. Electronic address: clinicalguidelines@esmo.org. Soft tissue and visceral sarcomas: ESMO-EURACAN-GENTURIS Clinical Practice Guidelines for diagnosis, treatment and follow-up☆. Ann Oncol. 2021 Nov;32(11):1348-1365. doi: 10.1016/j.annonc.2021.07.006. Epub 2021 Jul 22. PMID: 34303806.
8. Harter P, El-Khalfaoui K, Heitz F, du Bois A. Operative and Conservative Treatment of Uterine Sarcomas. Geburtshilfe Frauenheilkd. 2014 Mar;74(3):267-270. doi: 10.1055/s-0034-1368204. PMID: 24882876; PMCID: PMC4024613.
9. Mehros W, Aldosari S, Alharbi R, Alshareef W, Hawsawi W, Fallata H, Aljifree H, Althubaiti A. Demographic features and prognostic factors of uterine carcinosarcoma: a study at a specialized center in Saudi Arabia. Front Oncol. 2025 Sep 5;15:1594233. doi: 10.3389/fonc.2025.1594233. PMID: 40978043; PMCID: PMC12446034.
10. Sait HK, Anfinan NM, El Sayed ME, Alkhayyat SS, Ghanem AT, Abayazid RM, Sait KH. Uterine sarcoma. Clinico-pathological characteristics and outcome. Saudi Med J. 2014 Oct;35(10):1215-22. PMID: 25316466; PMCID: PMC4362107.
11. El Husseiny G, Al Bareedy N, Mourad WA, Mohamed G, Shoukri M, Subhi J, Ezzat A. Prognostic factors and treatment modalities in uterine sarcoma. Am J Clin Oncol. 2002 Jun;25(3):256-60. doi: 10.1097/00000421-200206000-00010. PMID: 12040283.