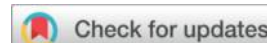


Clinical Characteristics and Prognostic Analysis of 78 Patients with Uterine Sarcoma



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Abstract

Objective: Uterine sarcoma is a rare malignant tumor of the uterus. This study aimed to identify and evaluate the prognostic factors affecting overall survival (OS) and progression-free survival (PFS) in patients with uterine sarcoma through retrospective analysis of clinical data.

Methods: This single-center retrospective study analyzed 78 patients with uterine sarcoma treated at the Affiliated Hospital of North Sichuan Medical College over the past 10 years. PFS and OS were calculated and visualized using Kaplan–Meier survival curves. Univariate and multivariate Cox regression analyses were performed to identify independent prognostic factors.

Results: Among the 78 patients, the most common histopathological subtype was uterine leiomyosarcoma (ULMS, 43/78, 55.1%), followed by low-/high-grade endometrial stromal sarcoma (LG/HG-ESS, 20/78, 25.6%) and adenosarcoma (AS, 11/78, 14.1%). Undifferentiated uterine sarcoma (UUS) was the rarest subtype (4/78, 5.1%).

Univariate analysis revealed that histological type, age, menstrual status, irregular vaginal bleeding, FIGO stage, tumor location, and incidental tumor detection were significantly associated with OS. Histological type, menstrual status, FIGO stage, and tumor location were significantly

correlated with PFS. Multivariate analysis demonstrated that histological type was significantly associated with OS ($P < 0.05$), with UUS showing the poorest PFS and OS. Tumor location and FIGO stage were significantly correlated with both PFS ($P < 0.001$) and OS ($P < 0.001$), and subserosal tumors exhibited the worst prognosis.

Conclusion: Histological type, tumor location, tumor stage, tumor size, and incidental tumor detection are significant prognostic factors influencing the overall survival of patients with uterine sarcoma.

Keywords: Uterine sarcoma; Prognostic factors; Kaplan–Meier survival analysis; Cox multivariate regression model

Introduction

Uterine sarcoma is an extremely rare, aggressive, and heterogeneous mesenchymal tumor, accounting for approximately 3%–9% of all uterine malignancies and about 1% of all female genital tract cancers. According to the 2014 World Health Organization (WHO) classification, uterine sarcomas are divided into four major histopathological subtypes: uterine leiomyosarcoma (LMS), low-grade and high-grade endometrial stromal sarcoma (LG-ESS and HG-ESS), undifferentiated uterine sarcoma (UUS), and adenosarcoma (AS) ^[1]. Carcinosarcoma has been reclassified as a metaplastic subtype of endometrial carcinoma and is now considered a high-grade carcinoma.

Compared with the more common endometrial carcinoma, uterine sarcomas generally have a poorer prognosis, with a tumor recurrence rate of approximately 70% and a 5-year overall survival rate of around 40% ^[2]. In this study, we retrospectively reviewed 78 patients diagnosed with uterine sarcoma at our hospital over the past ten years and analyzed their clinicopathological features and prognostic factors. Our findings highlight the relevance of histological type, tumor location, stage, size, and incidental detection in determining overall survival outcomes for patients with uterine sarcoma.

1. Materials and Methods

1.1 Clinical Data of Patients

Patients diagnosed with uterine sarcoma at the Affiliated Hospital of North Sichuan Medical College between January 2014 and January 2024 were retrospectively reviewed. This study was approved by the Ethics Committee of the Affiliated Hospital of North Sichuan Medical College (Approval No. 2024ER298-1). The study was conducted in accordance with the principles of the

Declaration of Helsinki and did not involve any ethical issues concerning human biological materials.

The inclusion criteria were pathologically confirmed cases of uterine sarcoma at any disease stage (FIGO 2009 staging). Carcinosarcoma was also included in this analysis. Clinical and pathological data were extracted from medical records before and after surgery. After excluding patients with incomplete data or failed follow-up, a total of 78 patients with postoperative follow-up exceeding five years were included.

Preoperative data included age at diagnosis, body weight, parity, body mass index (BMI), menstrual status, presenting symptoms, laboratory test results, and magnetic resonance imaging (MRI) or ultrasonography findings. Intraoperative data included surgical procedures and intraoperative frozen-section diagnoses. Postoperative data included histopathological results, tumor stage (according to the 2009 International Federation of Gynecology and Obstetrics [FIGO] classification), and adjuvant therapy.

Local or distant recurrence was defined as recurrence confirmed by histological or radiological evidence. Progression-free survival (PFS) was calculated from the date of initial surgery to the date of disease recurrence or progression. Overall survival (OS) was defined as the time from surgery to death from any cause (in months). The cut-off date for survival analysis was January 2024.

1.2 Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics version 27. A two-tailed P value < 0.05 was considered statistically significant. Quantitative variables were expressed as mean \pm standard deviation (SD), while qualitative variables were presented as absolute numbers and percentages. The chi-square (χ^2) test was used for comparisons of categorical variables, and the t-test or analysis of variance (ANOVA) was used for continuous variables.

Survival curves were estimated using the Kaplan–Meier method, and differences in survival rates were assessed using the log-rank test. Univariate and multivariate survival analyses were performed using the Cox proportional hazards regression model. Prognostic factors significantly associated with PFS or OS in univariate analysis were entered into a multivariate Cox regression model using a backward stepwise selection procedure. Hazard ratios (HRs) and corresponding 95% confidence intervals (CIs) were calculated from the Cox regression analysis to estimate relative risks.

2. Results

2.1 Analysis of Clinical Characteristics of Patients

The clinical characteristics of 78 patients with uterine sarcoma are summarized in Table 1. The most common histopathological subtype was uterine leiomyosarcoma (ULMS, 43/78, 55.1%), followed by low-/high-grade endometrial stromal sarcoma (LG/HG-ESS, 20/78, 25.6%) and adenosarcoma (AS, 11/78, 14.1%). Undifferentiated uterine sarcoma (UUS) was the rarest subtype, accounting for 5.1% (4/78) of all cases.

The mean age of patients was 48.94 years, with UUS patients tending to be older. There were 45 premenopausal women (57.7%) and 33 postmenopausal women (42.3%). Fifty patients (64.1%) had more than two pregnancies, and 52 patients (66.7%) had more than one delivery. Irregular vaginal bleeding was reported in 39 patients (50%).

Most patients were diagnosed at FIGO stage I (48/78, 61.5%), followed by stage II (13/78, 16.7%), stage III (3/78, 3.8%), and stage IV (14/78, 18.0%). The mean tumor size was 91.09 ± 43.59 mm. Among them, 43 patients (55.1%) had submucosal tumors, 28 patients (35.9%) had intramural tumors, and 7 patients (9.0%) had subserosal tumors.

Comparisons among the four histopathological subtypes revealed statistically significant differences in age, menstrual status, parity, irregular vaginal bleeding, tumor location, and surgical procedure ($P < 0.05$), as shown in Table 1.

Table 1. Clinical Characteristics of 78 Patients with Uterine Sarcoma

Clinical Characteristics	u-LMS	LG/HGESS	UUS	AS	<i>P</i> value
n (%)	43 (55.1%)	20 (25.6%)	4 (5.1%)	11 (14.1%)	
Age, median (IQR)	53 (47.5, 58.5)	43 (37.75, 47.25)	55.5 (52.5, 62)	44 (36, 49)	< 0.001
Menstrual status, n (%)					0.007
Postmenopausal	24 (30.8%)	3 (3.8%)	3 (3.8%)	3 (3.8%)	
Premenopausal	19 (24.4%)	17 (21.8%)	1 (1.3%)	8 (10.3%)	
Gravidity, median (IQR)	3 (2, 4)	3 (2, 4)	3.5 (2.75, 4)	2 (1, 2.5)	0.039
Parity, median (IQR)	2 (1.5, 2)	2 (1, 2)	2 (1.75, 2.25)	1 (1, 2)	0.062
Irregular vaginal bleeding, n (%)					0.387
Yes	25 (32.1%)	7 (9%)	2 (2.6%)	5 (6.4%)	
No	18 (23.1%)	13 (16.7%)	2 (2.6%)	6 (7.7%)	

Clinical Characteristics	u-LMS	LG/HGESS	UUS	AS	<i>P</i> value
Abdominal pain, n (%)					0.822
Yes	14 (17.9%)	6 (7.7%)	1 (1.3%)	2 (2.6%)	
No	29 (37.2%)	14 (17.9%)	3 (3.8%)	9 (11.5%)	
Abdominal distension, n (%)					0.723
Yes	7 (9%)	2 (2.6%)	0 (0%)	1 (1.3%)	
No	36 (46.2%)	18 (23.1%)	4 (5.1%)	10 (12.8%)	
FIGO stage (2009), n (%)					0.872
Stage I	26 (33.3%)	10 (12.8%)	3 (3.8%)	9 (11.5%)	
Stage II	2 (2.6%)	1 (1.3%)	0 (0%)	0 (0%)	
Stage III	7 (9%)	5 (6.4%)	0 (0%)	1 (1.3%)	
Stage IV	8 (10.3%)	4 (5.1%)	1 (1.3%)	1 (1.3%)	
Tumor size (mm), median (IQR)	80 (60, 130)	70.5 (51.25, 107)	105 (97.5, 125)	58 (55, 102.5)	0.244
Tumor location, n (%)					< 0.001
Intramural	21 (26.9%)	4 (5.1%)	3 (3.8%)	0 (0%)	
Subserosal	6 (7.7%)	0 (0%)	1 (1.3%)	0 (0%)	
Submucosal	16 (20.5%)	16 (20.5%)	0 (0%)	11 (14.1%)	
Progression-free survival (PFS, months), median (IQR)	38 (15, 49)	47.5 (17.75, 70)	20 (15, 22.75)	28 (24.5, 35)	0.196
Overall survival (OS, months), mean \pm SD	54.651 \pm 25.146	63.7 \pm 28.173	37.5 \pm 19.227	62.545 \pm 21.116	0.206
Survival status, n (%)					0.022
Alive	31 (39.7%)	9 (11.5%)	3 (3.8%)	3 (3.8%)	
Deceased	12 (15.4%)	11 (14.1%)	1 (1.3%)	8 (10.3%)	
Incidental discovery, n (%)					0.265
Yes	29 (37.2%)	15 (19.2%)	1 (1.3%)	8 (10.3%)	
No	14 (17.9%)	5 (6.4%)	3 (3.8%)	3 (3.8%)	
Ultrasound findings, n (%)					0.219

Clinical Characteristics	u-LMS	LG/HGESS	UUS	AS	<i>P</i> value
Benign	20 (25.6%)	12 (15.4%)	0 (0%)	8 (10.3%)	
Indeterminate	8 (10.3%)	4 (5.1%)	1 (1.3%)	1 (1.3%)	
Malignant	15 (19.2%)	4 (5.1%)	3 (3.8%)	2 (2.6%)	
Surgical procedure, n (%)					< 0.001
Total hysterectomy with bilateral salpingo-oophorectomy	29 (37.2%)	3 (3.8%)	4 (5.1%)	4 (5.1%)	
Myomectomy	5 (6.4%)	10 (12.8%)	0 (0%)	6 (7.7%)	
Total hysterectomy	9 (11.5%)	7 (9%)	0 (0%)	1 (1.3%)	

* $P < 0.05$

2.2 Relationship Between Pathological Subtypes, Clinical Characteristics, and Survival Outcomes

A total of 78 patients diagnosed with uterine sarcoma at the Affiliated Hospital of North Sichuan Medical College between January 2014 and January 2024, with a follow-up duration exceeding five years, were included in the survival analysis. The median progression-free survival (PFS) and overall survival (OS) were 49.5 months and 59 months, respectively.

Univariate analysis revealed that histological subtype, age, menstrual status, irregular vaginal bleeding, FIGO stage, tumor location, and incidental tumor detection were significantly associated with OS (Table 2). Moreover, histological subtype, menstrual status, FIGO stage, and tumor location were significantly correlated with PFS (Table 3).

Variables that showed significant associations in the univariate analysis were included in the multivariate Cox regression analysis. The results of the multivariate analysis demonstrated that histological subtype and tumor location were independent prognostic factors for OS ($P < 0.05$) (Table 2). FIGO stage was also significantly associated with PFS ($P < 0.05$) (Table 3).

Among all histological types, undifferentiated uterine sarcoma (UUS) and uterine leiomyosarcoma (ULMS) showed the poorest survival outcomes, whereas adenosarcoma (AS) exhibited a more favorable prognosis, followed by endometrial stromal sarcoma (ESS).

Table 2. Univariate and Multivariate Cox Proportional Hazards Regression Analysis of Overall Survival (OS) in Patients with Uterine Sarcoma (n = 78)

Clinical Characteristics	Total(N)	Univariate analysis		Multivariate analysis	
		Hazard ratio (95% CI)	<i>P</i> value	Hazard ratio (95% CI)	<i>P</i> value

Histological subtype	78				
Uterine leiomyosarcoma (u-LMS)	43	Reference		Reference	
Low-/high-grade endometrial stromal sarcoma (LG/HG-ESS)	20	0.531 (0.252 - 1.117)	0.095	1.680 (0.648 - 4.359)	0.286
Undifferentiated uterine sarcoma (UUS)	4	1.611 (0.487 - 5.329)	0.435	0.297 (0.058 - 1.527)	0.146
Adenosarcoma (AS)	11	0.309 (0.094 - 1.014)	0.053	0.075 (0.016 - 0.364)	0.001
Age (years)	78	1.039 (1.006 - 1.074)	0.021	1.046 (0.990 - 1.106)	0.111
Menstrual status	78				
Yes	33	Reference		Reference	
No	45	0.527 (0.294 - 0.944)	0.031	0.929 (0.341 - 2.528)	0.885
Gravidity	78	1.122 (0.900 - 1.398)	0.307		
Parity	78	1.383 (0.884 - 2.164)	0.156		
Vaginal bleeding	78				
Yes	39	Reference			
No	39	0.591 (0.328 - 1.064)	0.080		
Abdominal pain	78				
Yes	23	Reference			
No	55	0.926 (0.500 - 1.717)	0.808		

Abdominal distension	78				
Yes	10	Reference			
No	68	0.519 (0.241 - 1.116)	0.093		
FIGO stage (2009)	78				
Stage I	48	Reference		Reference	
Stage III	3	18.351 (4.658 - 72.300)	< 0.001	0.707 (0.117 - 4.280)	0.706
Stage II	13	2.934 (1.317 - 6.536)	0.008	0.421 (0.132 - 1.342)	0.143
Stage IV	14	40.180 (15.553 - 103.802)	< 0.001	0.893 (0.149 - 5.334)	0.901
Tumor size (mm)	78	1.018 (1.012 - 1.024)	< 0.001	1.001 (0.988 - 1.015)	0.831
Tumor location	78				
Intramural	28	Reference		Reference	
Subserosal	7	10.817 (3.735 - 31.330)	< 0.001	3.347 (1.051 - 10.652)	0.041
Submucosal	43	0.412 (0.219 - 0.776)	0.006	1.937 (0.806 - 4.656)	0.139
Incidental discovery	78				
Yes	53	Reference		Reference	
No	25	2.749 (1.526 - 4.953)	< 0.001	1.144 (0.464 - 2.822)	0.770
Ultrasound findings	78				
Benign	40	Reference		Reference	
Indeterminate	14	1.966 (0.873 - 4.427)	0.103	0.835 (0.285 - 2.441)	0.741
Malignant	24	3.681 (1.918 - 7.065)	< 0.001	1.595 (0.500 - 5.081)	0.430
Surgical procedure	78				

Myomectomy	40	Reference	
Total hysterectomy	21	0.489 (0.223 - 1.075)	0.075
Total hysterectomy with bilateral salpingo-oophorectomy	17	0.931 (0.452 - 1.918)	0.846

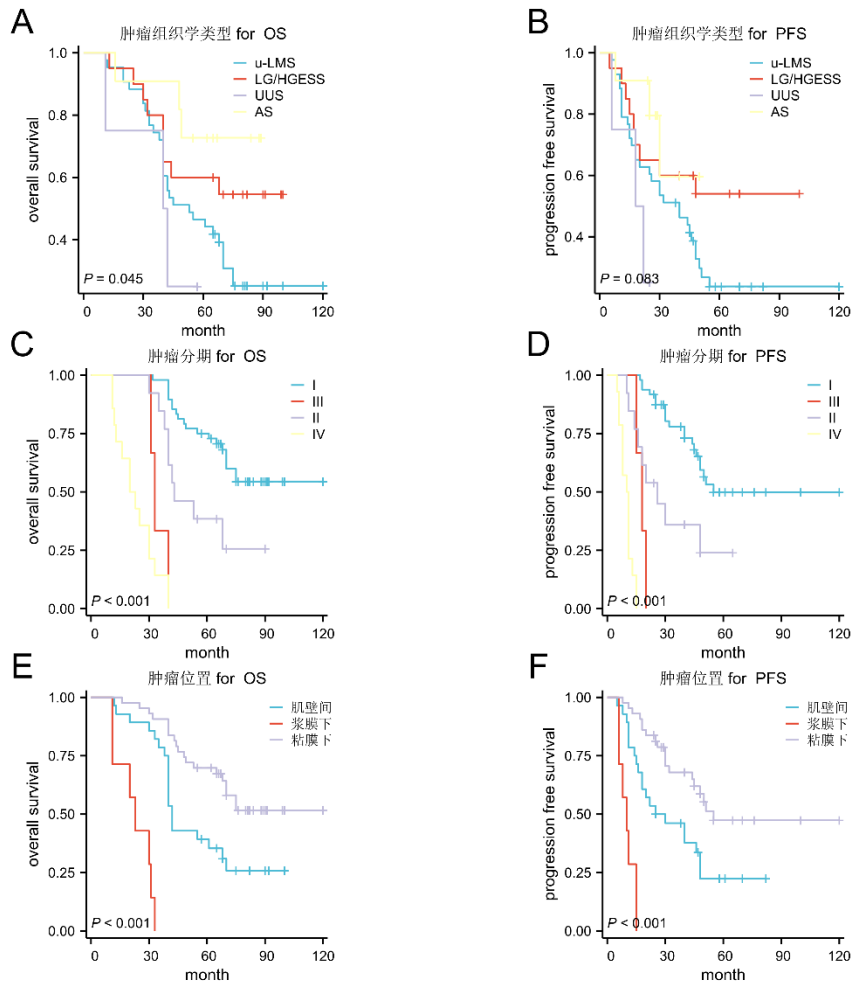
Table 3. Univariate and Multivariate Cox Proportional Hazards Regression Analysis of Progression-Free Survival (PFS) in Patients with Uterine Sarcoma (n = 78)

Clinical Characteristics	Total(N)	Univariate analysis		Multivariate analysis	
		Hazard ratio (95% CI)	P value	Hazard ratio (95% CI)	P value
Histological subtype	78				
Uterine leiomyosarcoma (u-LMS)	43	Reference			
Low-/high-grade endometrial stromal sarcoma (LG/HG-ESS)	20	0.527 (0.250 - 1.109)	0.091		
Undifferentiated uterine sarcoma (UUS)	4	1.975 (0.588 - 6.633)	0.271		
Adenosarcoma (AS)	11	0.416 (0.126 - 1.367)	0.148		
Age (years)	78	1.038 (1.004 - 1.074)	0.028	1.043 (0.990 - 1.099)	0.114
Menstrual status	78				

Yes	33	Reference		Reference	
No	45	0.540 (0.302 - 0.969)	0.039	0.645 (0.267 - 1.558)	0.330
Gravidity	78	1.094 (0.874 - 1.370)	0.431		
Parity	78	1.266 (0.808 - 1.983)	0.303		
Vaginal bleeding	78				
Yes	39	Reference			
No	39	0.576 (0.319 - 1.037)	0.066		
Abdominal pain	78				
Yes	23	Reference			
No	55	0.914 (0.493 - 1.694)	0.775		
Abdominal distension	78				
Yes	10	Reference			
No	68	0.572 (0.266 - 1.228)	0.152		
FIGO stage (2009)	78				
Stage I	48	Reference		Reference	
Stage III	3	14.032 (3.596 - 54.752)	< 0.001	8.393 (1.920 - 36.692)	0.005
Stage II	13	3.256 (1.468 - 7.220)	0.004	4.581 (1.771 - 11.845)	0.002
Stage IV	14	102.504 (27.775 - 378.296)	< 0.001	84.508 (16.270 - 438.941)	< 0.001
Tumor size (mm)	78	1.018 (1.012 - 1.025)	< 0.001	1.009 (0.999 - 1.020)	0.084
Tumor location	78				
Intramural	28	Reference		Reference	

Subserosal	7	8.670 (3.159 - 23.798)	< 0.001	1.053 (0.349 - 3.173)	0.927
Submucosal	43	0.425 (0.226 - 0.801)	0.008	0.578 (0.283 - 1.181)	0.133
Incidental discovery	78				
Yes	53	Reference		Reference	
No	25	2.666 (1.482 - 4.796)	0.001	1.089 (0.496 - 2.394)	0.831
Ultrasound findings	78				
Benign	40	Reference		Reference	
Indeterminate	14	2.024 (0.898 - 4.559)	0.089	0.838 (0.325 - 2.162)	0.715
Malignant	24	3.685 (1.920 - 7.071)	< 0.001	1.061 (0.416 - 2.701)	0.902
Surgical procedure	78				
Myomectomy	40	Reference			
Total hysterectomy	21	0.498 (0.227 - 1.095)	0.083		
Total hysterectomy with bilateral salpingo-oophorectomy	17	0.918 (0.445 - 1.896)	0.818		

* $P < 0.05$



As shown in Figure 1, histological subtype was significantly associated with OS ($P < 0.05$), with patients diagnosed with undifferentiated uterine sarcoma (UUS) exhibiting the poorest PFS and OS. Tumor location and FIGO stage were significantly correlated with both PFS ($P < 0.001$) and OS ($P < 0.001$), with subserosal tumors demonstrating the worst survival outcomes.

3. Discussion

3.1 Clinical Examination and Diagnosis

Uterine sarcoma is a rare but highly aggressive malignancy originating from smooth muscle or stromal cells of the uterus, accounting for approximately 3%–9% of all uterine tumors. Due to non-specific clinical manifestations, most cases are incidentally diagnosed after hysterectomy or morcellation of presumed leiomyomas. In our cohort of 78 patients, 40 cases were initially suggested as benign uterine leiomyomas by ultrasound, 24 cases were suspected malignant, and 14 cases were indeterminate. Therefore, in postmenopausal women, rapid growth of uterine

leiomyomas should raise high suspicion for malignant transformation. Early diagnosis remains the primary challenge in the management of uterine sarcomas.

Previous studies have shown that serum CA-125 and lactate dehydrogenase levels are elevated in patients with uterine sarcomas and may serve as adjunctive diagnostic markers, though they are not definitive. With advances in molecular biology, circulating microRNAs may represent potential diagnostic biomarkers ^[3, 4]. The incidence of uterine sarcoma is associated with age, hormonal status, and personal medical history, commonly occurring in women over 50 years old. Imaging modalities such as MRI and CT play an important role in the initial tumor assessment; however, definitive diagnosis still requires pathological confirmation ^[5]. Histological biopsy remains the gold standard. Retrospective studies indicate that endometrial sampling, whether by hysteroscopic biopsy or diagnostic curettage, provides accurate pathological diagnosis in only 35%–64% of cases ^[6]. Rapidly enlarging leiomyomas in postmenopausal women require further evaluation, often via hysterectomy rather than intra-abdominal morcellation. Currently, transvaginal and Doppler ultrasound are the most important initial evaluations. Nevertheless, no imaging modality—including ultrasound, CT, MRI, or PET-CT—can reliably differentiate uterine sarcoma from benign lesions; thus, histopathological examination remains the only definitive method of diagnosis.

3.2 Treatment of Uterine Sarcoma

Surgery is the mainstay of treatment for uterine sarcoma, typically involving total hysterectomy with or without bilateral salpingo-oophorectomy. Regardless of whether minimally invasive or open surgery is performed, maintaining specimen integrity is crucial. Previous studies have shown that 15% of uterine sarcomas are discovered postoperatively following hysterectomy or myomectomy, and morcellation of presumed leiomyomas is not recommended ^[7].

The role of pelvic lymphadenectomy remains controversial. For u-LMS and ESS, reported lymph node metastasis rates are 3% and less than 10%, respectively; routine lymphadenectomy is generally not required in early-stage disease ^[8]. Recent retrospective studies have confirmed that systematic lymphadenectomy in early-stage low-grade ESS does not improve survival ^[9]. High-quality evidence guiding ovarian preservation or fertility-sparing approaches in uterine sarcoma is limited. In u-LMS, retaining macroscopically normal ovaries does not appear to increase recurrence risk. Fertility preservation may be considered in premenopausal women without extensive metastatic disease ^[10, 11]. For estrogen receptor- and progesterone receptor-positive tumors, oophorectomy is recommended. Regardless of menopausal status, bilateral salpingo-oophorectomy in ESS has been shown to confer survival benefits ^[12]. Due to the rarity and complexity of uterine sarcomas, specific risk factors for identifying candidates for conservative management remain

unclear. Management of patients desiring fertility preservation should therefore involve a multidisciplinary expert team and individualized treatment planning.

Radiotherapy may achieve local control, but most evidence does not demonstrate a survival benefit due to small sample sizes and heterogeneity of sarcoma subtypes. Cox models for LMS have shown that radiotherapy does not impact survival, regardless of lymphadenectomy status, particularly in early-stage LMS ^[13].

3.3 Prognostic Factors

Nordal et al. reported that tumor stage, menopausal status, and positive surgical margins were independent prognostic factors for endometrial stromal tumors ^[14]. Other studies indicate that residual tumor burden is closely associated with overall survival ^[15]. In our study, histological subtype was significantly associated with OS ($P < 0.05$), with UUS exhibiting the poorest PFS and OS. Tumor location and FIGO stage were significantly correlated with both PFS ($P < 0.001$) and OS ($P < 0.001$), and subserosal tumors had the worst survival outcomes. For aggressive subtypes such as LMS, maximal cytoreduction and absence of lymphovascular invasion are critical prognostic factors for both OS and PFS.

In summary, this single-center retrospective study found that histological subtype is significantly associated with OS in uterine sarcoma patients. Adenosarcoma exhibits relatively favorable prognosis, whereas UUS and LMS have the lowest survival rates, followed by ESS. Additionally, tumor location, FIGO stage, tumor size, and incidental tumor detection are relevant prognostic factors for OS. However, due to limited sample size and follow-up duration, the impact of evolving treatment strategies over the past decade—particularly for recurrent or metastatic disease—remains unclear. Larger, multicenter prospective studies are warranted to validate these findings in contemporary patient populations.

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