Clinicopathological characteristics and prognosis of uterine sarcoma: a 10-year retrospective single-center study in China

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Abstract

Background Uterine sarcoma is a rare and heterogeneous gynecological malignancy characterized by aggressive progression and poor prognosis. The current study aimed to investigate the relationship between clinicopathological characteristics and the prognosis of uterine sarcoma in Chinese patients.

Methods In this single-center retrospective study, we reviewed the medical records of 75 patients with histologically verified uterine sarcoma treated at the First Affiliated Hospital of Xi'an Jiaotong University between 2011 and 2020. Information on clinical characteristics, treatments, pathology and survival was collected. Progression-free survival (PFS) and overall survival (OS) were visualized in Kaplan-Meier curves. Prognostic factors were identified using the log-rank test for univariate analysis and Cox-proportional hazards regression models for multivariate analysis.

Results The histopathological types included 36 endometrial stromal sarcomas (ESS,48%), 33 leiomyosarcomas (LMS,44%) and 6 adenosarcomas (8%). The mean age at diagnosis was 50.2 ± 10.7 years. Stage I and low-grade accounted for the majority. There were 26 recurrences and 25 deaths at the last follow-up. The mean PFS and OS were 89.41 (95% CI: 76.07-102.75) and 94.03 (95% CI: 81.67-106.38) months, respectively. Univariate analysis showed that > 50 years, post-menopause, advanced stage, ≥ 1/2 myometrial invasion, lymphovascular space invasion and high grade were associated with shorter survival ($P < 0.05$). Color Doppler flow imaging positive signals were associated with shorter PFS in the LMS group ($P = 0.046$). The ESS group had longer PFS than that of the LMS group (99.56 vs. 76.05 months, $P = 0.043$). The multivariate analysis showed that post-menopause and advanced stage were independent risk factors of both PFS and OS in the total cohort and LMS group. In the ESS group, diagnosis age > 50 years and high-grade were independent risk factors of PFS, while high-grade and lymphovascular space invasion were independent risk factors of OS.

Conclusion In Chinese patients with uterine sarcoma, post-menopause and advanced stage were associated with a significantly poorer prognosis. The prognosis of ESS was better than that of LMS. Color Doppler flow imaging positive signals of the tumor helped to identify LMS, which needs to be further tested in a larger sample in the future.

Keywords Uterine sarcoma, Clinicopathological characteristics, Prognosis, Survival, Chinese patients

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Introduction

Uterine sarcoma is a rare and aggressive heterogeneous malignant tumor originating from the mesodermal tissues (muscle and supportive tissues) [1]. It is characterized by nonspecific clinical presentations, high recurrence rates and poor prognosis, accounting for about 1% of female genital tract malignancies and 3–7% of uterine cancers [2]. The incidence of uterine sarcoma increases with age and is reported to be about 6.4 per 100,000 in women aged above 50 years in America [3].

According to the traditional histological classification, uterine sarcoma mainly included carcinosarcoma (CS), leiomyosarcoma (LMS), endometrial stromal sarcoma (ESS), undifferentiated sarcoma (UUS) and other less frequent histological subtypes, such as adenosarcoma. In 2009, the International Federation of Gynecology and Obstetrics (FIGO) revised the staging system and reclassified CS as endometrial cancer due to its similar dedifferentiated or metaplastic form to endometrial cancer [2]. The new uterine sarcoma classification mainly contains three pathological subtypes: LMS, ESS, adenosarcoma and undifferentiated endometrial sarcoma, of which LMS is the most common [4].

Diagnosis of uterine sarcoma is generally difficult before surgery because of nonspecific symptoms, such as irregular vaginal bleeding, abdominal or pelvic mass and pain, or even no symptom [4, 5]. Ultrasonography, magnetic resonance imaging, computed tomography and cancer antigen 125 (CA125) level are useful preoperative diagnostic methods. However, distinguishing uterine sarcoma from benign uterine lesions such as fibroids is difficult due to the lacking specific symptoms or diagnostic techniques, resulting in high misdiagnosis rates, which may lead to serious consequences [6, 7].

There is no standardized treatment for uterine sarcoma due to its rarity and heterogeneity. Early-stage uterine sarcoma is mainly treated by surgery according to different pathological types, including total hysterectomy with bilateral salpingo-oophorectomy (TH-BSO) [8]. For advanced-stage uterine sarcoma, complete cytoreduction is embraced as the most effective therapy [8]. The effects of lymphadenectomy and adjuvant treatments remain inconclusive, contributing to the dilemma in managing the disease. The reported 5-year survival rate was 45–50% for stage I-II and decreased to 0–15% for advanced stages [9]. Importantly, there are suggestions that the efficiency of treatments can be different among racial populations, indicating the need for therapeutic-tailored strategies [10].

The present study aimed to evaluate the relationship between the prognostic factors, such as clinico-pathological characteristics, surgical practices, adjuvant therapies and survival with uterine sarcoma at our institution. The objectives of our evaluation were to increase understanding and individualize the treatment of the disease, to review the data for potential guidelines for therapeutic decisions, and to compare survival outcomes with the different prognostic factors in this rare group of heterogeneous malignancies.

Materials and methods

Case inclusion

This study utilized a retrospective design to evaluate patients with histologically verified uterine sarcoma, who were diagnosed and treated at the Department of Gynecology and Obstetrics of the First Affiliated Hospital of Xi'an Jiaotong University from January 2011 to December 2020. The inclusion criteria included: (1) pathologically confirmed uterine sarcoma; (2) complete clinical, pathological and follow-up information. The exclusion criteria included: (1) other cancers excluding breast cancer; (2) metastatic or other sites' sarcomas; (3) endometrial carcinosarcoma; (4) currently pregnant; (5) histories of preoperative chemotherapy or radiotherapy; (6) lost to follow-up. Finally, a total of 75 cases were included in this study. The requirement for written informed consent from participants was waived due to the retrospective nature of the study. Verbal informed consent was obtained from surviving patients and the family members of deceased patients during phone call follow-up. They were approved by the ethics committee of the First Affiliated Hospital of Xi'an Jiaotong University (No. XJTU1AF2023LSK-275).

Data extraction

The following clinical data were extracted from medical records: age at diagnosis, menopausal status, FIGO stage, tumor size, color Doppler flow imaging (CDFI), surgery type and time, lymph node metastasis, adjuvant therapy, histological type, histological grade (low grade indicates high differentiation, while high grade indicates low differentiation), myometrial invasion (< 1/2, ≥ 1/2), and lymphovascular space invasion (LVSI). The surgical staging was defined by the FIGO 2009 staging system.

Outcome measures

Survival information was acquired by telephone and medical records. Progression-free survival (PFS) was defined from the first time for surgery to that of disease progression or recurrence. Overall survival (OS) was defined as the time from initial surgery to death from all causes [11]. The analysis cut-off date was set at July 5, 2022, with survival times calculated in months.

Statistical analysis

Categorical variables were presented as frequencies (percentages), and continuous variables as means±standard deviations (SD), or medians and ranges. Prognostic

factors for PFS and OS were examined by the log-rank tests for univariate analysis. Significant factors in univariate analysis and clinically significant indicators were included in the Cox regression model for further multivariate analysis.

Survival curves were plotted using the Kaplan-Meier method. Differences among curves were analyzed by the log-rank tests. $P<0.05$ was considered as statistically significant. All statistical analyses were performed using SPSS version 22.0 (IBM Corp., Armonk, NY, USA).

Results general information of patients

Over the 10-year study period, a total of 335 uterine sarcoma cases were confirmed and retrieved from the Department of Gynecology and Obstetrics of the First Affiliated Hospital of Xi'an Jiaotong University. Following stringent adherence to our inclusion and exclusion criteria, 75 cases were enrolled ultimately, including ESS ($n=36$), LMS ($n=33$) and adenosarcoma ($n=6$). Detailed process of case inclusion was shown in Fig. 1. The median follow-up period was 50 months (range: 4.7-132.3 months).

Table 1 showed the general information of patients. The mean age at diagnosis was 50.2 ± 10.7 years old (range: 31–81 years), which served as the threshold to categorize patients into two groups. Forty-nine (65.3%) patients were premenopausal and 26 (34.7%) were postmenopausal. A tumor size of over 5 cm was a prerequisite for surgery and was used as a critical point in this study. Among 62 cases with complete data on CDFI, 39 (62.90%) had positive signals. Surgical treatment was administered to 73 patients, with 68 (93.2%) patients, having total hysterectomy with TH-BSO, and 5 (6.8%) patients having total hysterectomy alone. Lymphadenectomy was performed in 24 patients, and only one LMS patient had lymph node metastasis with 9 months' survival. Based on FIGO staging, most patients (81.33%) were diagnosed as stage I. Most patients had adjuvant chemotherapy with 4–6 cycles after surgery (76.71%, 56/73) according to postoperative pathology including FIGO stage, histological grade, myometrial invasion, lymph node metastasis, LVSI and so on. The most common chemotherapy combination was paclitaxel and platinum (PT) (64.29%, 36/56), followed by ifosfamide+epirubicin+cisplatin (IAP) (26.79%, 15/56). A patient diagnosed with ESS
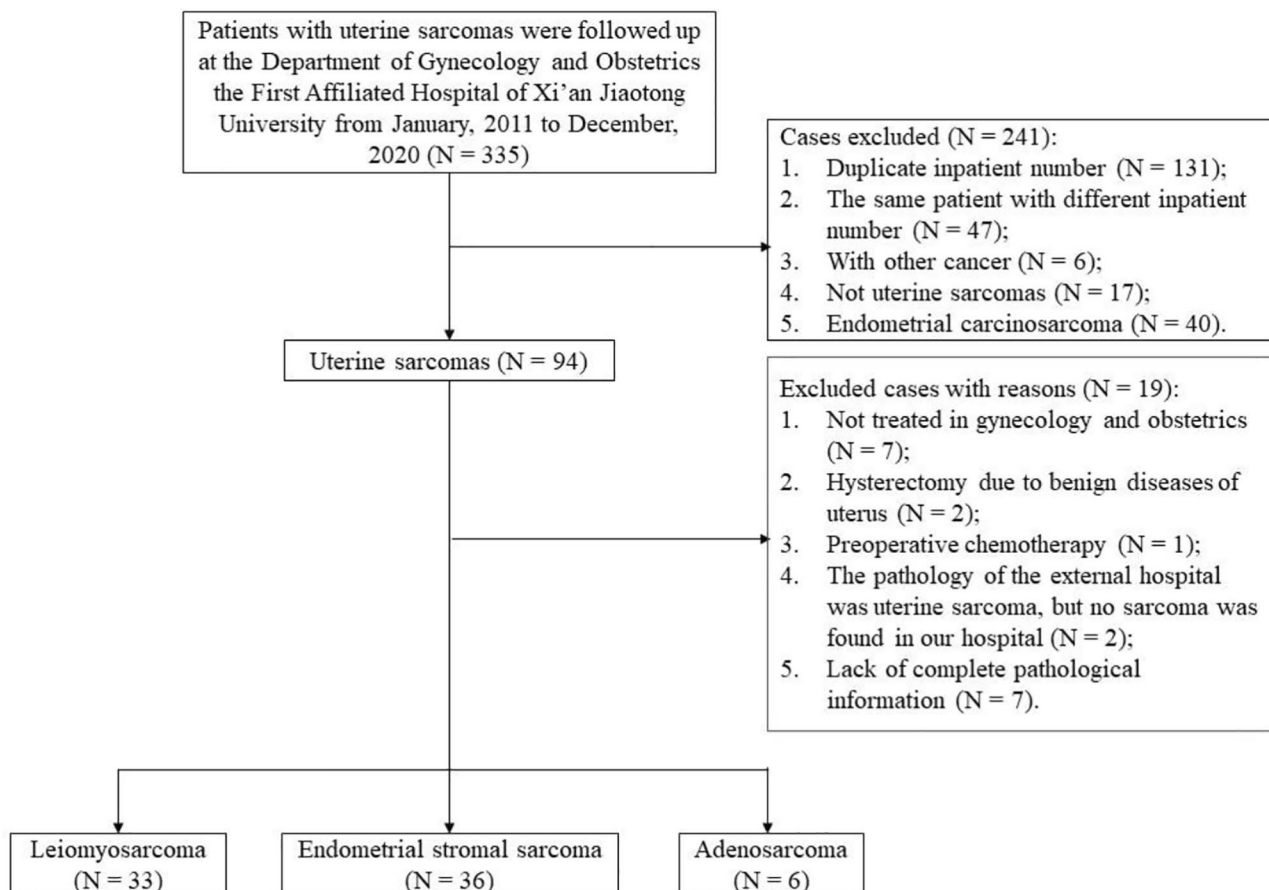

Fig. 1 Flow chart of the patient selection process

Table 1 General information about patients

	total (*n* = 75)	ESS (*n* = 36)	LMS (*n* = 33)	Adenosarcoma (*n* = 6)
Age at diagnosis (years)				
≤ 50	42	21	18	3
> 50	33	15	15	3
Mean ± standard deviation	50.2 ± 10.7	49.9 ± 11.9	51.2 ± 9.8	46.8 ± 8.9
Median (range)	48 (31–81)	48 (31–81)	48 (35–73)	47 (34–57)
Menopausal state				
premenopausal	49	23	23	3
postmenopausal	26	13	10	3
CDFI				
no	23	11	11	1
yes	39	17	17	5
miss	13	8	5	0
Tumor size (cm)				
< 5	14	9	1	4
≥ 5	48	21	25	2
miss	13	6	7	0
FIGO Stage				
I	61	31	24	6
II-IV	11	5	6	0
miss	3	0	3	0
Histological grade				
low	35	21	13	1
high	23	12	8	3
miss	17	3	12	2
Myometrial invasion				
< 1/2	28	15	9	4
≥ 1/2	33	14	17	2
miss	14	7	7	0
LVSI				
no	66	32	28	6
yes	6	3	3	0
miss	3	1	2	0
Treatment plan				
no treatment	1	0	1	0
surgery	17	9	6	2
surgery + adjuvant therapy	56	27	25	4
adjuvant therapy	1	0	1	0
Lymphadenectomy				
no	49	25	21	3
yes	24	11	10	3
Lymph node metastasis				
no	23	11	9	3
yes	1	0	1	0
Chemotherapy regimen				
Paclitaxel + platinum	36	16	17	3
Ifosfamide + epirubicin + Cisplatin	15	7	7	1
other	5	3	2	0
Disease recurrence	26	8	16	2
Died	25	7	16	2
PFS (months)				
median	46.25	46.5	44.75	55.25
range	6-132.3	6-125	7-132.3	6–96

Table 1 (continued)

	total (*n*=75)	ESS (*n*=36)	LMS (*n*=33)	Adenosarcoma (*n*=6)
OS (months)				
median	50	49	50	55.25
range	4.7-132.3	13–125	4.7-132.3	14–96

Note: LMS: leiomyosarcoma; ESS: endometrial stromal sarcoma; CA125: carbohydrate antigen 125; CDFI: color Doppler flow imaging; FIGO: International Federation of Gynecology and Obstetrics; LVSI: lymphovascular space invasion; PFS: Progression-free survival; OS: Overall survival

received progesterone therapy without chemotherapy after surgery, with an OS of 47.5 months. For the remaining two patients, one patient refused any treatment because of old age and advanced stage, with an OS of 4.7 months. Another patient received radio-chemotherapy, with an OS of 15 months.

Univariate analysis of the total cohort

Among the total 75 patients, 26 (34.67%) patients recurred at the end of follow-up, with 25 dying from recurrence. Recurrence characterized as pelvic mass mostly occurred in pelvic cavity.

The mean PFS and OS were 89.41 (95% confidence interval (CI): 76.07-102.75) and 94.03 (95% CI: 81.67-106.38) months, respectively. The corresponding 5-year PFS and OS rates were 66.5% and 71%, respectively. Compared to patients in advanced stage (FIGO II-IV), patients in stage I had a significantly better prognosis, with longer PFS (98.6 vs. 38.2 months, P=0.001) and a higher 5-year PFS rate (74.7% vs. 27.3%, P=0.001). Similarly, stage I patients had significantly longer OS (103.8 vs. 49 months, P<0.001) and a higher 5-year OS rate (80% vs. 34.1%, P<0.001) compared to their advanced-stage counterparts.

Table 2 showed the comparisons of survival outcomes among various clinicopathological parameters and treatments of the total patients using the log-rank tests. The results revealed that diagnosis age>50 years, post-menopause, advanced stage and ≥1/2 myometrial invasion were associated with shorter PFS and OS (all P<0.05). In addition, LVSI was significantly linked with shorter OS (P<0.001) and marginally significantly shorter PFS (P=0.071).

Univariate analysis of subgroups

The subgroup analysis of our study differentiated between 36 cases of ESS, 33 LMS and 6 adenosarcomata. Univariate analysis was only performed for the ESS and LMS groups due to the small sample sizes of the adenosarcoma group, and the results were shown in Table 2.

In the ESS group, 31 patients were classified with stage I and 5 with stage II-IV. 8 (22.22%) patients underwent disease recurrence and 7 (19.44%) deaths reported at the last follow-up. The mean PFS and OS were 99.56 (95% CI: 84.48-114.63) and 103.69 (95% CI: 88.73-118.64) months,

respectively. The corresponding 5-year PFS and OS rates were 80.4% and 84.9%, respectively. Univariate analysis showed that diagnosis age≤50 years, pre-menopause, low-grade, <1/2 myometrial invasion, and absence of LVSI were associated with significantly longer PFS, and high-grade and LVSI were related to significantly shorter OS (all P<0.05). Age at diagnosis, menopausal state and myometrial invasion were not significantly associated with OS (P>0.05).

ESS included low-grade ESS (LG-ESS), high-grade ESS (HG-ESS) and undifferentiated uterine sarcoma (UUS) [1]. In our study, there were 21 cases of LG-ESS, 12 cases of HG-ESS, 3 cases of unknown grade and 0 case of undifferentiated sarcoma. PFS was significantly higher in LG-ESS cohort (110.5months) than that in HG-ESS (52 months) and unknown grade (21.2 months) (P=0.003). The OS was also significantly better in LG-ESS patients (118.03 months) than that for HG-ESS (56.4 months) and unknown group (26.2 months) (P=0.001). Meanwhile, patients with unknown grade uterine sarcoma showed the worst prognosis than the other two subtypes.

The LMS group included 24 patients with stage I, 6 with stage II-IV, and 3 unclassified. Recurrence and mortality were reported in 16 patients (48.48%,16/33). The mean PFS and OS were 76.05 (95% CI: 55.87–96.23) and 83.46 (95% CI: 64.94-101.98) months, respectively. The 5-year PFS and OS rates were 52.2% and 58.3%, respectively. Univariate analysis identified that diagnosis age>51 years, post-menopause and advanced stage as predictors of shorter PFS and OS (P<0.05). Positive CDFI signal was significantly associated with decreased PFS (P<0.05) and marginally with reduced OS (P=0.098). Low-grade and <1/2 myometrial invasion were significantly associated with longer OS (P<0.05), while only marginally significantly associated with longer PFS.

Comparatively, the ESS subgroup exhibited more favorable outcomes than those of the LMS group, including a significantly lower recurrence rate (22.22% vs. 48.48%, P=0.022), significantly longer PFS (99.56 vs. 76.05 months, P=0.043), and a trend towards longer OS (103.69 vs. 83.46 months, P=0.077), underscoring the variable prognosis and treatment response across uterine sarcoma.

Table 2 Univariate analysis for PFS and OS using the log-rank tests in total cohort and subgroups

	Total cohort						ESS						LMS					
	PFS			OS			PFS			OS			PFS			OS		
	5-year rate (%)	mean	P	5-year rate (%)	mean	P	5-year rate (%)	mean	P	5-year rate (%)	mean	P	5-year rate (%)	mean	P	5-year rate (%)	mean	P
All	66.5	89.41		71.0	94.03		80.4	99.56		84.9	103.69		52.2	76.05		58.3	83.46	
Age at diagnosis			0.004			0.005			0.022			0.108			0.022			0.006
≤50	80.6	105.7		82.7	110.3		90.5	115.0		88.8	114.6							
>50	46.9	62.6		55.1	73.8		66.0	77.5		80.0	92.9							
≤51													72.2	94.8		77.8	103.3	
>51													15.0	37.5		24.4	47.7	
Menopausal state			0.001			0.001			0.022			0.057			0.001			<0.001
premenopausal	78.5	102.4		82.1	106.2		91.3	111.3		90.6	114.8		68.2	93.0		76.7	100.0	
postmenopausal	41.1	50.3		45.0	55.3		60.6	48.5		74.0	55.1		0	23.0		0	31.0	
CDFI			0.289			0.191			0.341			0.405			0.046			0.098
No	81.6	89.2		85.6	93.9		71.6	80.5		77.9	87.7		90.0	92.1		90.0	93.1	
yes	57.9	85.1		65.7	90.4		88.2	111.6		94.1	109.8		29.2	54.6		42.2	69.2	
unknown	66.6	76.3		65.8	83.4		75.0	87.4		72.9	96.7		53.3	62.1		53.3	66.6	
Tumor size (cm)			0.093			0.2			0.277			0.406			0.31			0.499
<5	92.9	94.7		92.9	95.3		100.0	/		100.0	/		100.0	/		100.0	/	
≥5	54.1	80.7		61.7	86.6		71.4	/		79.5	/		40.3	/		49.1	/	
miss	84.6	92.6		84.6	101.1		83.3	/		83.3	/		85.7	/		85.7	/	
FIGO Stage			0.001			<0.001			0.177			0.252			<0.001			<0.001
I	74.7	98.6		80.0	103.8		83.6	103.1		85.4	109.4		67.8	94.4		77.4	101.0	
II–IV	27.3	38.2		34.1	49.0		60.0	69.0		80.0	75.8		0	12.6		0	28.3	
miss	0	24.0		0	31.0		33.3						0	24.0		0	31.0	
Pathological type			0.131			0.202												
ESS	80.4	99.6		84.9	103.7		/	/		/	/		/	/		/	/	
LMS	52.2	76.1		58.3	83.5		/	/		/	/		/	/		/	/	
Adenosarcoma	66.7	66		66.7	69.2		/	/		/	/		/	/		/	/	
Histologic grade			0.137			0.097			0.003			0.001			0.059			0.026
low	79.6	99.1		86.2	104.7		90.2	110.5		94.1	118.3		60.6	74.4		71.6	80.1	
high	52.2	59.8		53.1	62.7		75.0	52.0		82.5	56.4		0	27.7		0	37.5	
miss	58.8	83.9		64.7	92.3		33.3	21.2		33.3	26.2		66.7	95.2		75.0	105.2	
Myometrial invasion			0.001			0.001			0.016			0.064			0.069			0.012
<1/2	92.2	116.3		96.4	122.3		100.0	120.3		100.0	124.0		88.9	114.8		100.0	127.0	
≥1/2	44.8	55.1		52.8	62.2		57.1	59.0		70.1	67.1		35.3	48.1		41.2	55.8	
unknown	74.1	82.7		69.4	80.9		85.7	92.7		85.7	93.1		53.3	32.3		40.0	34.4	
LVSI			0.071			<0.001			0.005			<0.001			0.178			0.103
no	67.3	90.6		72.2	95.4		81.0	/		85.9	/		54.1	79.0		60.8	87.0	

Table 2 (continued)

	Total cohort						ESS						LMS					
	PFS			OS			PFS			OS			PFS			OS		
	5-year rate (%)	mean	P	5-year rate (%)	mean	P	5-year rate (%)	mean	P	5-year rate (%)	mean	P	5-year rate (%)	mean	P	5-year rate (%)	mean	P
yes	66.7	73.5		66.7	75.2		100.0	/		/	/		33.3	28.2		33.3	31.5	
miss	0	11		0	14		0	/		0	/							
Treatment plan																		
surgery	50.7	/	0.615	48.2	/	0.305	81.8	59.7	0.999	81.8	60.5	0.554	25	39.8	0.32	25.0	47.2	0.212
surgery+adjuvant therapy	68.9	/		75.7	/		80.0	99.6		86.9	105.7		58.4	81.4		66.1	88.9	
Lymphadenectomy																		
no	62.6	85.6	0.478	69.7	91.4	0.636	79.8	91.9	0.899	87.2	93.3	0.992	43.9	66.4	0.203	53.6	78.3	0.435
yes	75.0	91.8		74.1	97.3		81.8	99.1		80.8	105.2		70.0	81.5		68.6	81.7	
Chemotherapy regimen																		
IAP	51.4	56.9	0.241	64.0	64.2	0.224	71.4	/	0.74	80.0	/	0.909	42.9	45.7	0.464	57.1	53.5	0.218
PT	77.0	100.0		82.1	105.9		81.3	/		87.5	/		68.2	91.6		72.7	100.5	
other	75.0	31.1		75.0	32.6		100.0	/		/	/		50.0	16.8		50.0	19.8	

Note: & age categorization was based on the mean age of each group. PFS: Progression-free survival; OS: Overall survival; CA125: carbohydrate antigen 125; CDFI: color Doppler flow imaging; FIGO: International Federation of Gynecology and Obstetrics; LMS: leiomyosarcoma; ESS: endometrial stromal sarcoma; LVSI: lymphovascular space invasion; IAP: Ifosfamide+epirubicin+Cisplatin; PT: Paclitaxel+platinum

Multivariable analysis

The results of the multivariable analysis were revealed in Table 3; Fig. 2, highlighting the independent prognostic risk factors affecting survival within our patient cohort. For the entire cohort, post-menopause (HR=3.861, 95% CI: 1.65–9.02, *P*=0.002 for PFS and HR=3.703, 95% CI: 1.54–8.91, *P*=0.003 for OS) and advanced stage (HR=3.418, 95% CI: 1.72–6.79, *P*<0.001 for PFS and HR=3.498, 95% CI: 1.68–7.27, *P*=0.001 for OS) were independent prognostic risk factors for survival.

Similarly, in the LMS subgroup analysis, post-menopause (HR=4.595, 95% CI:1.50-14.05, *P*=0.007 for PFS and HR=6.078, 95% CI:1.69–21.80, *P*=0.006 for OS) and advanced stage (HR=3.376, 95% CI:1.46–7.82, *P*=0.005 for PFS and HR=3.829, 95% CI:1.44–10.17, *P*=0.007 for OS) were independent prognostic risk factors of survival, underscoring similar patterns of risk across different sarcoma types.

For the ESS group, diagnosis age>50 years (HR=5.627, 95%CI:1.09–29.06, *P*=0.039) and high-grade (HR=4.660, 95%CI:1.32–16.48, *P*=0.017) were found to be independent risk factors of influencing PFS. Furthermore, high-grade (HR=8.349, 95%CI:1.58–44.13, *P*=0.012) and the presence of LVSI (HR=11.266, 95%CI:1.67–76.22, *P*=0.013) were identified as independent risk factors of OS.

These findings suggested that certain clinicopathological features, particularly menopausal status, disease stage, histological grade and LVSI, played a critical role in predicting the prognosis of patients with uterine sarcoma.

Discussion

Previous western studies, conducted almost entirely including carcinosarcoma, explored the relationships between risk factors, adjuvant treatments, and survival based on traditional classification systems [12–16]. However, there have been a few studies with respect to them in China and the patient grouping studied by newer classifications excluding carcinosarcoma. In addition, the incidence of uterine sarcoma varies by race and is higher in African-Americans than in other races [3, 17]. Our research presented is a comprehensive analysis of uterine sarcoma and examines 75 Chinese patients over a 10-year period using the latest classification system for more detailed results.

Our findings revealed that LMS had a poorer prognosis than that of ESS. Specifically, for the ESS group, we determined post-menopausal, high-grade and LVSI as key factors associated with reduced survival. Furthermore, the study highlighted the potential diagnostic value of CDFI, enabling it to distinguish between benign and malignant tumors and representing a new research topic.

CDFI provide a new direction for distinguishing uterine sarcoma from uterine fibroids. In our research, 62.9% of patients had CDFI during the examination. CDFI positive signals had a negative effect on survival of LMS group. This suggests the potentially important role of CDFI in the evaluation of the malignant transformation of uterus myoma, which is similar to a finding reported by Yang Hua [18]. Asim Kurjak reported that a cutoff in resistance index (RI) of 0.4 of tumoral blood vessels could distinguish uterine sarcoma from uterus myoma with a higher RI [19]. The diagnostic value of this cutoff is 90.91%, 99.82%, 71.43% and 99.96% in sensitivity, specificity, positive predictive value and negative predictive value, respectively [19]. However, the study had small sample sizes (*n*=10). Sun et al. found that increased vascularity on color Doppler ultrasound could sometimes favor malignancy, especially when combined with a large size and degenerative cystic changes [20]. Further studies are needed to figure out the clinical significance of CDFI for uterine sarcoma.

Univariate analysis demonstrated that over 50 years, post-menopause, advanced stage and ≥1/2 myometrial

Table 3 Multivariate analysis for PFS and OS using Cox-proportional hazards regression models in total cohort and subgroups

| Cohort			HR	95% CI	*P*
total	PFS	Menopause state	3.861	1.65–9.02	0.002
		FIGO stage	3.418	1.72–6.79	<0.001
	OS	Menopause state	3.703	1.54–8.91	0.003
		FIGO stage	3.498	1.68–7.27	0.001
subgroups					
ESS	PFS	Age at diagnosis	5.627	1.09–29.06	0.039
		Histologic grade	4.660	1.32–16.48	0.017
	OS	Menopause state	8.252	0.78–87.46	0.080
		Histologic grade	8.349	1.58–44.13	0.012
		Lymphovascular space invasion	11.266	1.67–76.22	0.013
LMS	PFS	Menopause state	4.595	1.50–14.05	0.007
		FIGO stage	3.376	1.46–7.82	0.005
	OS	Menopause state	6.078	1.69–21.80	0.006
		FIGO stage	3.829	1.44–10.17	0.007
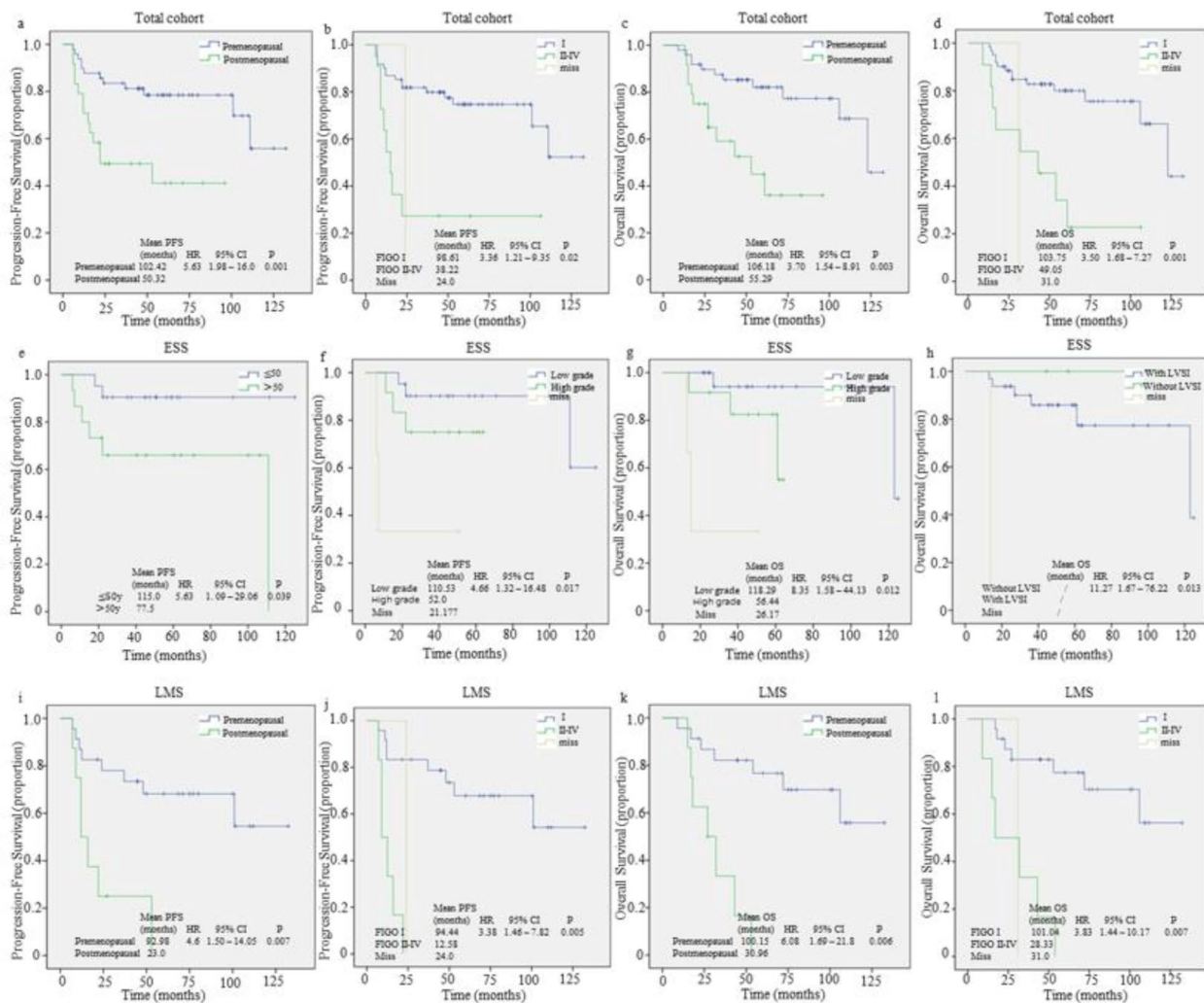
Fig. 2 Kaplan-Meier survival curves for progression-free survival (PFS) and overall survival (OS) stratified by clinical and pathological parameters in a-d: total cohort, e-h: endometrial stromal sarcoma (ESS) and i-k: leiomyosarcoma (LMS). **a-b** were stratified by menopausal status and FIGO stage for PFS in the total cohort; **c-d** were stratified by menopausal status and FIGO stage for OS in the total cohort; **e-f** were stratified by age at diagnosis and histological grade for PFS in the ESS group; **g-h** was stratified by histological grade and lymphovascular space invasion (LVSI) for OS in ESS group; **i-j** were stratified by menopausal status and FIGO stage for PFS in LMS group; **k-l** were stratified by menopausal status and FIGO stage for OS in LMS group

invasion were significantly associated with poorer survival; while multivariable analysis identified that postmenopause and advanced stage were independent prognostic factors for survival of the total cohort and the LMS group. These findings were consistent with previous studies [14, 21–23]. Thus, they were not limited by race or traditional classification systems.

Studies showed that prognoses of different pathological types of uterine sarcoma varied a lot [24–27]. Our study showed that ESS had a significantly lower recurrence and a higher 5-year survival rate than LMS, and the survival of LG-ESS is prior to those of LMS and HG-ESS, which was in agreement with previous studies [28–31]. It's reported that pathological subtype is a significant

prognostic factor for OS [30]. However, pathological type isn't a prognostic factor for survival in our study, which may be related to the merger of LG-ESS and HG-ESS into ESS because of small sample size. The proportion of FIGO I stage in the ESS group is higher than that in the LMS group (86.11% vs. 72.73%). Otherwise, misdiagnosis of LMS as uterine leiomyoma because of the same symptoms and delayed treatment due to minimally invasive therapy as well as inadvertent dissemination [32]. Alexandra Huss's study reported that three cases LMS were diagnosed at tumor recurrence [30]. LG-ESS grew slowly and had a good prognosis in initial stages than that of HG-ESS in our study. Recently several studies have shown that chromosomal rearrangments and gene

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amplifications can provide new ideas for the diagnosis and treatment of HG-ESS [33, 34], However, our study lacks exploration on relevant molecular markers because of the earlier diagnosed patients.

Compared with previous studies, our investigation is distinctive in several aspects. (1) Geographical and racial backgrounds. Our study is based on certain Chinese patients in a way. It thus considerably complements the currently available literatures that focus on the clinicopathological features and prognosis of uterine sarcomas conducted in Western population. It significantly increases the global knowledge database regarding potential ethnic and geographic differences in sarcomas. (2) Utilization of the new classification system. This study uses the new classification of uterine sarcomas from 2014 in an attempt to provide an up-to-date exploration of their clinicopathological characteristics and prognosis. (3) Detailed subtype analysis. Given the evident heterogeneity within uterine sarcomas, subgroup analysis was performed separately and most survival factors were developed for each sarcoma group, namely ESS and LMS respectively. This is a valuable supplement that should be deserving of clinical attention because different pathological types of sarcomas present their exclusive influential factors and prognoses, which agents nation planning and judgement prognosis. (4) The usage of CDFI, as a potential malignant myoma indicator, offer an innovation that it may play an important role in novel non-invasive diagnostic techniques.

Our study had some limitations. First, the small sample sizes of adenosarcoma limits the statistical power and generalizability of the findings. This constraint makes it challenging to conduct comprehensive subgroup analyses or to conclude the prognostic implications for rare sarcoma types definitively. Second, the retrospective nature of the study design made it subject to selection and recall bias. These biases could affect accuracy of the collected data and interpretation of the study's findings. Third, the study was performed in a single center. Its findings may not be broadly applicable to all populations. Forth, the study suggests CDFI as a potentially valuable tool for identifying malignant myomas, which is preliminary and requires further validation through larger, prospective studies to determine its clinical utility and accuracy.

Conclusion
According to our results, LMS is more aggressive than ESS. Post-menopause and advanced stage are independent risk factors of survival for the total patients and LMS, which were not limited to race or traditional classification system. Meanwhile, post-menopause, high-grade and LVSI are independently related to decreased survival in the ESS group. Uterine myoma with blood flow signal may be a useful indicator of malignant myoma, which

needs to further validate its diagnostic utility in large-scale, multi-center studies and refine protocols for the management of uterine sarcomas.

Abbreviations
PFS	Progression-free survival
OS	Overall survival
CS	Carcinosarcoma
ESS	Endometrial stromal sarcomas
LMS	Leiomyosarcomas
UUS	Undifferentiated sarcoma
LG-ESS	Low-grade ESS
HG-ESS	High-grade ESS
FIGO	International Federation of Gynecology and Obstetrics
CA125	Cancer antigen 125
TH-BSO	Total hysterectomy with bilateral salpingo-oophorectomy
CDFI	Color Doppler flow imaging
LVSI	Lymphovascular space invasion
SD	Standard deviations
PT	Paclitaxel and platinum
IAP	Ifosfamide + epirubicin + cisplatin
CI	Confidence interval

Author contributions
All authors contributed to the study's conception and design. Material preparation, data collection, and analysis were performed by JF W, CL and JY Y. The first draft of the manuscript was written by JF W, YL W, and JJ and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
The requirement for written informed consent from participants was waived due to the retrospective nature of the study. Verbal informed consent was obtained from surviving patients and the family members of deceased patients during phone call follow-up. They were approved by the ethics committee of the First Affiliated Hospital of Xi'an Jiaotong University (No. XJTU1AF2023LSK-275). All participants agreed to this study.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Statement
All methods were carried out in accordance with relevant guidelines and regulations in the study.

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