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Clinical Characteristics, Prognostic Factors and Overall Survival of Patients with Uterine Sarcoma at King Chulalongkorn Memorial Hospital during 2002-2019

Rujira Manorompattarasarn, M.D.*,
Shina Oranratanaphan, M.D.*

** Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University and King Chulalongkorn Memorial Hospital, Bangkok, Thailand*

ABSTRACT

Objectives: The primary objective aimed to evaluate overall survival (OS) of patients with leiomyosarcoma (LMS), endometrial stromal sarcoma (ESS) and carcinosarcoma (CS) at King Chulalongkorn Memorial Hospital (KCMH) from 1st January 2002 to 31st December 2019. The secondary objectives were to identify disease-free survival (DFS), clinical characteristics, prognostic factors, and treatment modalities of LMS, ESS and CS treatments.

Materials and Methods: A retrospective study was conducted. Patients who were diagnosed with LMS, ESS or CS, received primary treatment at KCMH and had pathology specimens for review were recruited. Patients who had insufficient data were excluded. General characteristics, surgical treatment, prognostic factors, DFS and OS of patients were collected. Statistical analysis was performed by STATA version 14.1.

Results: One hundred and fourteen cases were reviewed. Thirteen cases were excluded due to incomplete data. OS at 2, 5, and 10 years of LMS group were 74.0%, 59.8%, and 41.9%; of ESS group were 80.8%, 80.8%, and 64.7%; and of CS group were 59.6%, 49.8%, and 49.8% respectively. Uterine weight of 400 grams or more had a significant effect on OS in CS group (hazard ratio (HR) 5.65, 95% confidence interval (CI) 1.34-23.82, p = 0.018). Pelvic lymph node status had a significant effect on DFS in LMS group (HR 8.92, 95% CI 1.09-72.97, p = 0.041).

Conclusion: Only half of the LMS and CS patients survived up to 5 years but 80% of ESS survived more than 5 years. Uterine weight of 400 grams or more was the significant prognostic factor for OS in CS, while pelvic lymph node status was the significant prognostic factor for DFS in LMS.

Keywords: uterine sarcoma, prognostic factors, overall survival, disease-free survival.

Correspondence to: *Shina Oranratanaphan, M.D., Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University and King Chulalongkorn Memorial Hospital, Bangkok, 10330, Thailand. E-mail: dr_shina@hotmail.com*

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การศึกษาลักษณะทางคลินิก ปัจจัยพยากรณ์โรค และอัตราการรอดชีวิตของผู้ป่วยมะเร็งมดลูกชนิดซาร์โคมา ในโรงพยาบาลจุฬาลงกรณ์ ในช่วงเวลาปี 2545-2562

รุจิรา มโนรมย์ภัทรสาร, ชินา โอฬารรัตนพันธ์

บทคัดย่อ

วัตถุประสงค์: *วัตถุประสงค์หลักของการศึกษานี้เพื่อประเมิน อัตราการรอดชีวิตของผู้ป่วยมะเร็งมดลูกชนิด Leiomyosarcoma (LMS) มะเร็งมดลูกชนิด Endometrial stromal sarcoma (ESS) และ มะเร็งมดลูกชนิด Carcinosarcoma (CS) ที่รับการรักษาในโรงพยาบาลจุฬาลงกรณ์ ในช่วงเวลาปี พ.ศ. 2545-2562 วัตถุประสงค์รอง เพื่อประเมิน ระยะเวลาปลอดโรค ลักษณะทางคลินิก ปัจจัยพยากรณ์โรค และการรักษาที่ได้รับ ในผู้ป่วยกลุ่มดังกล่าว*

วัสดุและวิธีการ: *เป็นการศึกษาแบบย้อนหลัง ในกลุ่มผู้ป่วยที่ได้รับการวินิจฉัยว่าเป็น LMS, ESS และ CS ที่เข้ารับการรักษาในโรงพยาบาลจุฬาลงกรณ์ และมีชิ้นเนื้อทางพยาธิวิทยาที่สามารถตรวจสอบย้อนหลังได้ ผู้ป่วยที่มีข้อมูลไม่เพียงพอในการวิเคราะห์จะถูกตัดอออกจากการศึกษา ลักษณะทางคลินิกของผู้ป่วย การผ่าตัดรักษา ปัจจัยพยากรณ์โรค การรักษา ระยะเวลาปลอดโรค และ อัตราการรอดชีวิตของผู้ป่วยจะถูกเก็บรวบรวม และ นำมาวิเคราะห์ด้วยโปรแกรม STATA version 14.1*

ผลการศึกษา: *ประวัติของผู้ป่วย 114 ราย ได้ถูกนำมาประเมิน มีผู้ป่วย 13 ราย ถูกตัดออกจากการศึกษา เนื่องจากมีข้อมูลไม่เพียงพอในการวิเคราะห์ ดังนั้น มีผู้เข้าร่วมวิจัยทั้งหมด 101 รายที่นำมาวิเคราะห์ อัตราการรอดชีวิตของผู้ป่วย LMS ในช่วง 2, 5 และ 10 ปี คือ ร้อยละ 74.0, 59.8, 41.9 ตามลำดับ อัตราการรอดชีวิตของผู้ป่วย ESS ในช่วง 2, 5 และ 10 ปี คือร้อยละ 80.8, 80.8, 64.7 ตามลำดับ อัตราการรอดชีวิตของผู้ป่วย CS ในช่วง 2, 5 และ 10 ปี คือร้อยละ 59.6, 49.8, 49.8 ตามลำดับ ปัจจัยที่มีผลต่ออัตราการรอดชีวิตของผู้ป่วย CS คือ น้ำหนักมดลูกตั้งแต่ 400 กรัม ขึ้นไป (hazard ratio (HR) 5.65, 95% confidence interval (CI) 1.34-23.82, p = 0.018) และปัจจัยที่มีผลต่อระยะเวลาปลอดโรคในผู้ป่วย LMS คือ การกระจายไปยังต่อมน้ำเหลือง (HR 8.92, 95% CI 1.09-72.97, p = 0.041)*

สรุป: *ในผู้ป่วย LMS และ CS ที่สามารถอยู่รอดได้ถึง 5 ปี เพียงร้อยละ 50 ในขณะที่ร้อยละ 80 ของผู้ป่วย ESS อยู่ได้นานเกิน 5 ปี ปัจจัยที่มีผลต่ออัตราการรอดชีวิตในผู้ป่วย CS คือ น้ำหนักของมดลูก และ การกระจายไปยังต่อมน้ำเหลืองในแง่ของระยะเวลาปลอดโรคในผู้ป่วย LMS*

คำสำคัญ: *มะเร็งมดลูกชนิดซาร์โคมา, ปัจจัยพยากรณ์โรค, ระยะเวลาปลอดโรค, อัตราการรอดชีวิตของผู้ป่วย*

Introduction

Uterine sarcoma is a rare cancer which accounts for approximately 1-3% of gynecological cancer[1] and 3-8% of uterine cancer[2,3]. The majority of uterine sarcoma consists of leiomyosarcoma (LMS) and endometrial stromal sarcoma (ESS). Previously, carcinosarcoma (CS) or malignant mixed mullerian tumor (MMMT) was classified as uterine sarcoma. Recently, it has been reclassified as dedifferentiated or metaplastic form of endometrial carcinoma[4]. However, in most retrospective studies of uterine sarcoma, CS is still included in the review[4].

LMS is an aggressive tumor with poor prognosis. The most common presenting symptom is palpable mass, which is similar to that of leiomyoma. Pre-operative diagnosis is difficult; therefore, definite diagnosis is usually obtained after surgery. The factors affecting prognosis are conflicting among previous studies[5]. ESS is also a rare tumor which abnormal uterine bleeding is the most common presenting symptom in both premenopausal and postmenopausal age[6]. CS usually occurs in older age groups with similar risk factors to endometrial carcinoma, such as obesity and exposure of exogenous estrogen. CS often presents with postmenopausal bleeding[7].

The primary treatment of uterine sarcoma includes hysterectomy and tumor removal. Oophorectomy and lymphadenectomy are standard surgical treatments in ESS and CS. Nevertheless, benefits of oophorectomy and lymphadenectomy in LMS are still unclear[8, 9]. For adjuvant treatment, chemotherapy is used in advanced or recurrent disease[8,10-12]. Radiotherapy may be useful in reducing local recurrence without significant impact on overall survival[13].

The data of uterine sarcoma is limited and controversial especially in Asia[5, 14]. Therefore, we decided to conduct a study to identify the disease-free survival (DFS), overall survival (OS), and prognostic factors of LMS, ESS and CS[15,16].

The main objective of this study aimed to identify OS of LMS, ESS and CS. The secondary objective were to study the clinical characteristics, DFS and prognostic factors associated with disease outcome and modalities of treatment in these patients.

Materials and Methods

Study population

This retrospective study was conducted after receiving approval from the Institutional Review Board of the Faculty of Medicine, Chulalongkorn University (IRB number 220/63). Data were collected from the medical records of patients who were treated at King Chulalongkorn Memorial Hospital (KCMH) from 1st January 2002 to 31st December 2019. Inclusion criteria were patients diagnosed as LMS, CS, or ESS and received primary treatment at KCMH. To confirm the diagnosis, the pathological specimens were reviewed. Exclusion criteria were patients who had insufficient medical records or those whose specimens were not available for pathology review.

Data was retrieved by searching the ICD10 (C541, C542, and C549) which concluded the diagnosis of LMS, CS, and ESS. The collected data consisted of personal data, clinical characteristics, operative data, and pathology data. Staging data before 2009 was restaged using FIGO 2009 criteria. Pathology specimens were reviewed and confirmed the diagnosis by our gynecological pathologists. Data including adjuvant treatment after surgery, location of recurrence, DFS, and OS were retrieved. This study collected every case of LMS, ESS and CS over an 18-years period. All the patients who met the inclusion criteria and did not have exclusion criteria were enrolled in this study. Patients who were lost to follow-up were contacted via telephone. If the patients could not be contacted directly, calls were made to their families to inquire about the patients' status. If both patients and their family members could not be contacted, their survival status was confirmed with the database from The National Health Security Office.

Definitions and statistical analysis

OS was defined as the length of time from the date of diagnosis to either the date of death or the date of the last follow-up[17]. DFS was defined as the duration

from the date of complete treatment to the date when recurrence occurred. Criteria for evaluating of the treatment response was based on the revised response evaluation criteria in solid tumors (RECIST) criteria (version 1.1)[18].

Statistical analyses were performed using STATA version 14.1. Numerical data were presented as mean ± standard deviation (SD) and median ± interquartile range (IQR). Qualitative data were presented as frequency and percentage. Survival analysis was analyzed using the Kaplan-Meier method. A log-rank test was used to compare each survival curve. Univariate and multivariate analyses were performed by using the Cox-regression method. A p value of less than 0.05 was considered statistically significant.

Results

From January 2002 to December 2019, there were 114 cases of LMS, ESS and CS treated at King Chulalongkorn Memorial Hospital. Thirteen cases were excluded due to insufficient data; therefore, 101 cases were analyzed. Thirty-four cases (33.6%) were LMS, 11 cases (10.9%) were ESS, and 57 cases (55.5%) were CS.

Patients' characteristics are shown in Table 1. According to the FIGO staging system, there were 53 (52.5%), 9 (8.9%), 26 (25.7%), and 13 (12.9%) patients in FIGO stages I, II, III and IV, respectively. Twenty-eight (27.7%) patients did not receive adjuvant treatment, and 51 patients (50.5%) had recurrence of the disease.

Table 1. General characteristics of LMS, ESS and CS patients.

	LMS (n = 34)	ESS (n = 11)	CS (n = 56)
Age (mean ± SD) (years)	51.8 ±11.5	49.6±12.2	61.2±12.0
Age			
< 50 years	16 (47.1%)	7 (63.6%)	8 (14.3)
> 50 years	18 (52.9%)	4 (36.4%)	48 (85.7%)
Parity			
Nulliparous	19 (55.9%)	6 (54.5%)	15 (26.8%)
Multiparous	15 (44.1%)	5 (45.5%)	41 (73.2%)
Underlying disease	7 (20.6%)	2 (18.1%)	35 (62.5%)
Previous history of Leiomyoma	3 (8.8%)	1 (9.1%)	0
Previous cancer			
No	34 (100%)	11(100%)	46 (82.1%)
Breast cancer	0	0	8 (14.3%)
* Other	0	0	2 (3.6%)
Presenting symptoms			
No symptom	0	0	1 (1.8%)
Pain	6 (17.6%)	1 (9.1%)	3 (5.4%)
AUB	6 (17.6%)	4 (36.4%)	6 (10.7%)
PMB	5 (14.7%)	3 (27.3%)	37 (66.1%)
Palpable mass	15 (44.1%)	2 (18.2%)	6 (10.7%)
** Other	2 (5.9%)	1 (9.1%)	3 (5.4%)
Pre-op diagnosis			
Benign	14 (41.2%)	6 (54.5%)	4 (7.1%)
Malignancy	9 (26.5%)	4 (36.4%)	50 (89.3%)
Pelvic mass	11 (32.4%)	1 (9.1%)	2 (3.6%)

LMS: leiomyosarcoma, ESS: endometrial stromal sarcoma, CS: carcinosarcoma, AUB: abnormal uterine bleeding, PMB: postmenopausal bleeding

* Other includes gynecological cancer and rectal cancer

** Other includes abdominal distension, pressure effect and pleural effusion

In LMS group, the mean age was 51.8 ± 11.6 years. The most common presenting symptom was palpable mass (44.1%). Twenty-four patients (70.6%) had recurrences. The most common locations of recurrence were the pelvis and lung. In ESS group, the mean age was 49.6 ± 12.2 years. Common presentations

were abnormal uterine bleeding (36.4%) and postmenopausal bleeding (27.3%). Four patients (36.4%) had recurrent disease. The most common location of recurrence was the lung. In CS group, the mean age was 61.2 ± 12.0 years, which was higher than LMS and ESS groups. The most common presenting symptom was postmenopausal bleeding (66.1%). There were 23 patients (41.1%) who had recurrent disease. The most common locations of recurrence were the pelvis and lung. Details of stage, treatment, response of treatment and disease recurrence are shown in Table 2.

Table 2. Surgical treatment, pathologic data, and treatment outcomes of LMS, ESS and CS.

	LMS (n = 34)	ESS (n = 11)	CS (n = 56)
Operation			
Myomectomy	2 (5.9%)	0	1 (1.8%)
TAH	30 (88.2%)	10(90.9%)	50 (89.3%)
TLH	2 (5.9%)	1 (9.1%)	5 (8.9%)
Surgical staging	25 (73.5%)	9 (81.8%)	53 (93%)
Omentectomy	9 (26.5%)	1 (9.1%)	25 (44.6%)
PLND	7 (20.6%)	2 (18.2%)	39 (69.6%)
PAN	3 (8.8%)	1 (9.1%)	15 (26.8%)
Tumor debulking			
Primary surgery	6 (17.6%)	1 (9.1%)	2 (3.6%)
Secondary CRS	4 (11.8%)	0	2 (3.6%)
FIGO			
I	23 (67.6%)	9 (81.8%)	21 (37.5%)
II	2 (5.9%)	1 (9.1%)	6 (10.7%)
III	8 (23.5%)	0	18 (32.1%)
IV	1 (2.9%)	1 (9.1%)	11 (19.6%)
Tumor Size	(n=28)	(n=10)	(n=43)
< 10 cm	18 (64.3%)	3 (30.0%)	9 (20.9%)
≥ 10 cm	10 (25.7%)	7 (70.0%)	34 (79.1%)
Myometrial invasion			
< 50%	N/A	2 (18.2%)	4 (7.1%)
≥ 50%		5 (45.5%)	48 (85.7%)
Unknown		4 (36.4%)	4 (7.1%)
Residual tumor	1 (2.9%)	0	7 (12.5%)
Pelvic LN positive	1 (2.9%)	0	12 (21.4%)
LVSI	1 (2.9%)	2 (18.2%)	20 (35.7%)
Omental metastasis	4 (11.8%)	1 (9.1%)	6 (10.7%)
Omental metastasis/ Omentectomy specimen	4/9 (44.4%)	1/1 (100%)	6/25 (24%)
Surgical margin positive	1 (2.9%)	1 (9.1%)	0
Adjuvant treatment			
No	13(38.2%)	5(45.5%)	10(17.9%)
CMT	16 (47.1%)	1 (9.1%)	22 (39.3%)
RT	4 (11.8%)	3 (27.3%)	11 (19.6%)
CCRT/ CMT+RT	1 (2.9%)	1(9.1%)	13 (23.2%)
Hormone	0	1(9.1%)	0
Response			
Complete	26 (76.5%)	9 (81.8%)	35 (62.5%)
Partial	1 (2.9%)	0	0
Progression	7(20.6%)	2 (18.2%)	21 (37.5%)
Recurrent of disease	24 (70.6%)	4 (36.4%)	23 (41.1%)
Local recurrence	11/24	1/4	10/23
Distant metastasis	13/24	3/4	13/23

LMS: leiomyosarcoma, ESS: endometrial stromal sarcoma, CS: carcinosarcoma, TAH: total abdominal hysterectomy, TLH: total laparoscopic hysterectomy, Surgical staging: TAH with BSO, BSO: bilateral salpingo-oophorectomy, CRS:cytoreductive surgery, PLND: pelvic lymph node dissection, PAN: paraaortic lymph node dissection, LN: lymph node, LVSI: lymphovascular space invasion, CMT: chemotherapy, RT: radiotherapy, CCRT: concurrent chemoradiotherapy, N/A: not applicable.

The 2-year, 5-year, and 10-year DFS and OS are shown in Table 3. DFS curve and OS curve are shown in Fig. 1 and Fig. 2.

Stage, pelvic lymph node status, and lymphovascular space invasion (LVSI) status had significant impact on DFS of LMS in univariate analysis. However, in multivariate analysis, only pelvic lymph node status was an independent prognostic factor (Table 4). No factors had significant effect on DFS of ESS and CS. Therefore, multivariate analysis was not performed for DFS in ESS and CS.

Table 3. General characteristics of LMS, ESS and CS patients.

	LMS (n=34)	ESS (n=11)	CS (N=56)
	% (95%CI)	% (95%CI)	% (95%CI)
Time to recurrent mean (95%CI)	17.4 mo (5.3, 29.5)	107.3 mo (61.7, 153)	6.03 mo (0, 15.4)
2-year DFS	42.5 (25.6, 58.4)	71.6 (35.0, 89.9)	37.2 (24.2, 50.2)
5-year DFS	36.4 (20.6, 52.4)	71.6 (35.0, 89.9)	35.0 (22.2, 48.0)
10-year DFS	15.6 (4.4, 33.2)	57.3 (20.6, 82.2)	19.4 (7.4, 35.7)
Survival mean (95%CI)	105.7 mo (27.5, 183.8)	119.3 mo (76.1, 162.5)	40.16 mo (0, 96.0)
2-year OS	74 (52.9, 86.8)	80.8 (42.4, 94.9)	59.6 (42.8, 73.0)
5-year OS	59.8 (37.5, 76.4)	80.8 (42.4, 94.9)	49.8 (32.8, 64.7)
10-year OS	41.9 (17.3, 64.9)	64.7 (23.0, 87.8)	49.8 (32.8, 64.7)

LMS: leiomyosarcoma, ESS: endometrial stromal sarcoma, CS: carcinosarcoma, DFS: Disease-free survival, OS: overall survival.

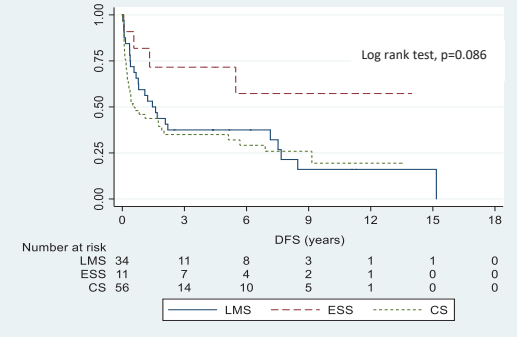

Fig. 1. Kaplan- Meier curves of disease-free survival curves for LMS, ESS and CS.

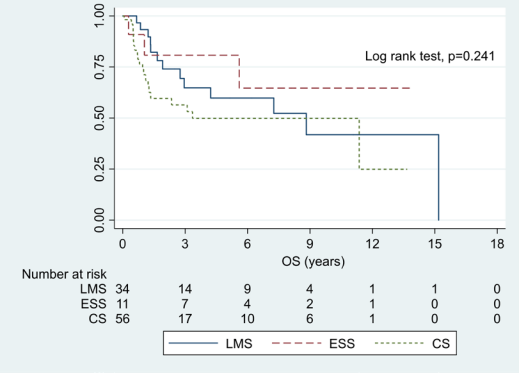

Fig. 2. Kaplan- Meier curves of overall survival curves for LMS, ESS and CS.

Table 4. Univariate and multivariate analysis of DFS in patients with LMS, ESS, CS.

Disease-free survival	Univariate analysis		Multivariate analysis	
	HR (95% CI)	p value[a]	HR (95% CI)	p value[a]
LMS				
Age (years)				
< 50	1		N/A*	N/A*
≥ 50	1.80 (0.69-4.66)	0.228		
Stage				
I-II	1		1	
III-IV	3.99 (1.50-10.58)	0.006	0.39 (0.08-1.80)	0.226
Pelvic LN positive				
No	1		1	
Yes	33.00 (2.06-527.59)	0.013	8.92 (1.09-72.97)	0.041
LVSI				
No	1		1	
Yes	33.00 (2.06-527.59)	0.013	0.39 (0.09-1.60)	0.387
ESS*				
Age (years)				
< 50	1		N/A*	N/A*
≥ 50	1.41 (0.20-10.11)	0.733		
Stage				
I-II	1		N/A*	N/A*
III-IV	>100 (0.00-106)	0.951		
LVSI				
No	1		N/A*	N/A*
Yes	2.48 (0.22-27.77)	0.461		
CS*				
Age (years)				
< 50	1		N/A*	N/A*
≥ 50	1.22 (0.28-5.33)	0.788		
Stage				
I-II	1		N/A*	N/A*
III-IV	1.31 (0.51-3.37)	0.575		
Pelvic LN positive				
No	1		N/A*	N/A*
Yes	2.11 (0.74-6.02)	0.163		
LVSI				
No	1		N/A*	N/A*
Yes	0.73 (0.24-2.26)	0.590		

[a]: Proportional hazards regression, LMS: Leiomyosarcoma, ESS: Endometrial stromal sarcoma, CS: Carcinosarcoma, LN: Lymph node, LVSI: Lymphovascular space invasion, HR: Hazard Ratio

N/A* : Not applicable (Multivariate analysis was not performed due to insignificance in univariate analysis).

*Multivariate analysis was not performed in ESS and CS because there were no significant factors detected from univariate analysis.

Age and abdominal distension were significant for OS of LMS in univariate analysis but not in multivariate analysis. Uterine weight of 400 grams or more, residual tumor and pelvic lymph node status had significant impact on OS of CS in univariate analysis. However, only uterine weight was statistically significant in multivariate analysis. No factor was significant in univariate analysis for OS of ESS. Therefore, multivariate analysis was not performed in this group of patients (Table 5).

Table 5. Univariate analysis and multivariate analysis of OS in patients with LMS, ESS, CS.

Overall Survival	Univariate analysis		Multivariate analysis	
	HR (95% CI)	p value[a]	HR (95% CI)	p value[a]
LMS				
Age (years)				
< 50	1		1	
≥ 50	2.92 (1.14-7.47)	0.025	3.33(0.37-29.61)	0.281
Abdominal distension				
No	1		1	
Yes	32.00 (2.00-511.60)	0.014	3.88(0.11-133.35)	0.455
Uterine Weight (g)				
< 400	1		N/A*	N/A*
≥ 400	1.13 (0.21-6.2)	0.885		
Residual tumor				
No	1		N/A*	N/A*
Yes	4.83 (0.58-40.18)	0.145		
Pelvic LN positive				
No	1		N/A*	N/A*
Yes	4.06 (0.50-33.05)	0.190		
ESS				
Age (years)				
< 50	1		N/A*	N/A*
≥ 50	1.35 (0.19-9.67)	0.768		
Abdominal distension				
No	1		N/A*	N/A*
Yes	0.04 (0.00-12788.4)	0.617		
Uterine Weight (g)				
< 400	1		N/A*	N/A*
≥ 400	105.97 (0.00-106)	0.584		
CS				
Age (years)				
< 50	1		N/A*	N/A*
≥ 50	0.90 (0.35-2.33)	0.824		
Abdominal distension				
No	1.88 (0.25-13.97)	0.537	N/A*	N/A*
Yes				
Uterine Weight (g)				
< 400	1		1	
≥ 400	2.56 (1.05-6.23)	0.038	5.65(1.34-23.82)	0.018
Residual tumor				
No	1		1	
Yes	4.74 (1.94-11.55)	0.001	28.19(0.93-856.28)	0.055
Pelvic LN positive				
No	1		1	
Yes	2.08 (1.02-4.26)	0.045	1.33(0.25-7.03)	0.740

[a]: Proportional hazards regression, LMS: Leiomyosarcoma, ESS: Endometrial stromal sarcoma, CS: Carcinosarcoma, LN: Lymph node, LVSI: Lymphovascular space invasion, HR: Hazard Ratio

N/A*: Not applicable (Multivariate analysis was not performed due to insignificance in univariate analysis).

Discussion

Several retrospective studies have reported that LMS is the most common type of uterine sarcoma. However, some studies have shown that CS is more common than LMS[19-21]. In the present study, 56 of 101 patients (55.4%) were diagnosed with CS, while 34 patients (33.6%) had LMS. The average age of CS (61.2 years) in our study was highest among all groups. Our findings were consistent with those previously reported[13,19,22,23]. Moreover, Park et al demonstrated that the mean age of MMMT or CS, LMS and ESS were 57.1, 47.5, 43.9 years, respectively[22]. The mean age in their series was slightly younger than that of our study. However, patients with CS still had higher mean age than the other groups.

Abnormal vaginal bleeding in both premenopausal and postmenopausal age group was the most common presenting symptoms in CS and ESS in our study (76.8% and 63.7%, respectively). This finding was in line with the results of Park et al. They reported that 68.2% of their patients with CS and 73% of those with ESS presented with abnormal bleeding. However, 44.1% of the patients with LMS in our study had palpable mass as the presenting symptom, while only 21.7% of those in the series of Park et al presented with palpable mass. This may result from the difference in the size of the uterine mass in different studies. Most of the patients in the series of Park et al (82.7%) had uterine masses of less than 10 cm in diameter, while only 37.0% of our participants had less than 10-cm uterine masses[22].

Pre-operative diagnosis of LMS is quite difficult. Nearly half of the patients with LMS in our study were diagnosed as benign and the other 32.4% were diagnosed pre-operatively as pelvic mass of uncertain nature. Half of ESS also had preoperative diagnoses as benign condition. However, surgical staging in the initial operation was performed in 73.5% of LMS and 81.8% of ESS (Table 2). Intraoperative specimen opening may be crucial for proper management. However, preoperative diagnosis is important in situations where a gynecologic oncologist is not available. Ultrasonogram is commonly used in gynecologic patients. However, the diagnostic accuracy of this technique for differentiating benign uterine mass from uterine sarcoma is lower than that of magnetic resonance imaging (MRI)[24]. Sensitivity, specificity, negative predictive value, positive predictive value and accuracy of ultrasonogram are inferior to those of MRI (35.1% vs 94.6%, 88.4% vs 92.3%, 48.9% vs 92.3%, 81.2% vs 94.6% and 57.1% vs 93.7%, respectively)[24, 25]. Therefore, MRI may be helpful in suspicious cases[24].

Vanichtantikul et al[26] reported 40.5% of 5-year DFS and 56% of 5-year OS in all uterine sarcoma. They found that factors such as age, histology, tumor size, lymph node dissection, or adjuvant treatment did not have a significant effect on OS. In the present study, the 5-year DFS and the 5-year OS of all participants were 39.3% and 57.6%, respectively. Our findings were quite similar to those previously reported. However, the 5-year DFS and the 5-year OS in our study were somewhat higher than those reported by Park et al, which had 5-year DFS and 5-year OS of 30% and 48%, respectively[22]. These differences may result from different proportions of the initial disease staging at diagnosis. Fifteen percent of the patients in Park et al were in stage IV, while 12.9% of our patients had stage IV[22].

In our study, ESS group had the most favorable prognosis with 5-year OS of 80% and median survival time of 119.3 months, followed by LMS group with 5-year OS of 59.8% and median survival time of 105.7 months. Patients with CS had the worst prognosis with 5-year OS of 49.8% and median survival time of 40.2 months. 5-year OS of ESS group in our study was worse than that reported by Munoz et al, which had 5-year OS of 100%. This difference may result from subgroup analysis. Munoz et al analyzed patients with undifferentiated endometrial stromal sarcoma (UES) separately from patients with ESS[27],while we analyzed both UES and ESS as one group. However, 5-year OS of patients with LMS in their study was consistent with that of our study (61.6% VS 59.8%).

Park et al found that the significant factors affecting DFS were FIGO stage, depth of myometrial

invasion, and complete cytoreduction[22]. Furthermore, some studies also found that prognostic factors associated with the OS of patients with LMS were age, clinical stage, and tumor size. The results of those previous studies were quite different from our study. We found pelvic lymph node status to be the significant prognostic factor for PFS in patients with LMS, while uterine weight of 400 grams or more was an independent prognostic factor for OS in CS group.

The strength of this study was the long data collection period of up to 18 years (from 2002 to 2019) with a 10-year OS report. However, this study still had some limitations due to the retrospective nature of the study. Therefore, some information could not be obtained from the medical record. Moreover, the sample size in ESS group was too small (11 cases) to perform subgroup analysis of high-grade and low-grade ESS. Further prospective study with larger sample size in these certain groups may be warranted. Furthermore, some data such as uterine weight and cervical invasion could not be completely obtained. For example, uterine weight records were only available in 18 of 34 cases with LMS, 6 of 11 cases of ESS and 40 of 56 cases of CS. However, the significance of having uterine weight more than 400 grams was found in CS group. Therefore, the association uterine weight and prognostic significance in CS group can be used for patient counselling and we may need further study to determine the significance of uterine weight on the prognosis of patients with LMS and ESS.

Regarding omental metastasis, 4 patients with LMS, 1 with ESS and 6 with CS had omental metastasis. Due to the limitation of this retrospective study, omentectomy may be performed only in suspicious cases based on the surgeon's decision. Therefore, the percentage of omental metastasis could not reflect the true incidence of omental metastasis as shown in Table 2.

Conclusion

In conclusion, two-thirds of patients with LMS and CS had disease recurrence within 5 years, while most of those with ESS had late recurrence. Only half of LMS and CS could survive to 5 years, while 80% of ESS survived longer. Significant prognostic factors for PFS in LMS group and OS in CS group were pelvic lymph node status and uterine weight of 400 grams or more, respectively. The information from our study would be useful for general gynecologists and gynecologic oncologists to counsel the patients about the course of the disease and prognosis of uterine sarcoma.

Potential conflicts of interest

The authors declare no conflicts of interest.

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