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Clinical outcomes and prognostic factors in 55 patients with uterine sarcoma at a single institution

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Summary

Objective: Uterine sarcomas are rare gynecological malignancies with poor prognosis. This study evaluated clinical outcomes and prognostic factors of patients with uterine sarcoma. *Materials and Methods:* A retrospective analysis was performed on 55 patients with uterine sarcoma, who had been treated and followed from 2004 to 2015 at Chonnam National University Hospital. *Results:* The median age of patients was 53 (range: 27-80) years, with 60.0% having postmenopausal status. Seventeen patients (30.9%) were diagnosed with endometrial stromal sarcoma (ESS), four (7.3%) with undifferentiated endometrial sarcoma (UES), three (5.4%) with leiomyosarcoma (LMS), and 31 (56.4%) with carcinosarcoma (CS). Surgery was the first line of treatment, including complete surgery for 54 patients and only myomectomy for one. FIGO Stage was I in 38 patients (69.1%), II in six (10.9%), III in seven (12.7%), and IV in four (7.3%). After a surgery, 37 patients (67.3%) received the adjuvant therapy, including 13 of chemotherapy, 11 of radiation, and 13 of chemoradiation. Complete and partial response presented in 78.2% and 1.8%, respectively. Progressive and stable disease presented in 16.4% and 3.6%, respectively. After a mean follow-up period of 43.5 (range: 1-136) months, relapses were detected in 20 patients (36.4%). The two- and five-year overall survival (OS) rates were 80.4% and 70.6%, respectively. The two- and five-year disease free survival (DFS) rates were 69.3% and 49.7%, respectively. Multivariate analysis revealed that menopause ($p < 0.05$), preoperative serum CA-125 elevation ($p < 0.05$), histological subtypes ($p < 0.05$), lymphovascular space invasion (LVSI) ($p < 0.05$), and LN involvement ($p < 0.05$) were associated with DFS, while no factor affected OS. *Conclusions:* In this study, the survival rates were higher than in many previous studies. The complete surgery and proper adjuvant therapies might lead to better outcomes. However, menopause, preoperative serum CA-125 elevation, more aggressive subtypes, LVSI, and LN involvement adversely affected prognosis.

Key words: Uterine sarcoma; Treatment; Outcome; Prognostic factor.

Introduction

Uterine sarcomas are rare tumors that account for 1–3% of all malignancies of the female genital tract and 3–9% of malignancies of the uterus [1, 2]. Traditionally, the main histological categories of uterine sarcomas have been leiomyosarcoma (about 40% of all sarcomas), carcinosarcoma (about 30-40%), and endometrial stromal sarcoma (about 15%), with the remaining about 5% consisting of a heterogeneous group of vascular, lymphatic, and heterologous sarcomas [3]. Each group was reported to have different spread patterns, prognostic factors, and various responses to treatments [3, 4].

Unlike epithelial malignant tumors of the uterus, uterine sarcomas are commonly more aggressive and have poor outcomes [5]. The prognosis of uterine sarcomas has not markedly changed in recent decades. The overall five-year survival has been between 17.5% to 64.5%, as reported in different studies [1-4, 6-13]. Because these tumors are so rare and pathologically diverse, there is still the problem of inaccurate preoperative diagnosis [14]. Uterine sarcomas are frequently discovered after myomectomy or hysterectomy for different reasons (uterine myoma, endometrial polyp, vaginal bleeding, etc.). Furthermore, optimal management strategies and prognostic factors have not been well established [5, 8, 15]. Therefore, this study evaluated the treatment outcomes of patients with uterine sarcoma and analyzed the prognostic factors.

Materials and Methods

Patients who had been diagnosed with uterine sarcoma from 2004 to 2015 at Chonnam National University Hospital (CNUH; Gwangju, Korea) were identified from a computerized database. Patients who had refused treatments or had been transferred to another hospital or had insufficient data associated with their cases were excluded in this study. Patients who had been treated and followed in the same period at the present institution were included in the final analysis. Uterine sarcomas were categorized into histological subtypes, such as "uterine carcinosarcoma (CS)", "endometrial stromal sarcoma (ESS)", "undifferentiated endometrial sarcoma (UES)", and "leiomyosarcoma (LMS)", following the 2003 World Health Organization (WHO) classification.

Demographic data from each patient's medical record included age, menopausal status, parity, body mass index (BMI), symptoms at the time of diagnosis, and patient histories of medical dis-

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Table 1. — *Patients' characteristics with respect to different subtypes of uterine sarcomas.*

Characteristics	Total (n=55) No. (%)	CS (n=31) No. (%)	ESS (n=17) No. (%)	UES (n=4) No. (%)	LMS (n=3) No. (%)
Age, years median (range)	53 (27-80)	60 (27-80)	45 (34-62)	55 (47-68)	49 (40-59)
Menopause					
No	22 (40.0)	4 (12.9)	14 (82.4)	2 (50.0)	2 (66.7)
Yes	33 (60.0)	27 (87.1)	3 (17.6)	2 (50.0)	1 (33.3)
Delivery status					
No	3	2	1	-	-
One	4	3	1	-	-
Two	18	7	7	1	3
≥ three	30	19	8	3	-
BMI, mean (kg/m^2) (range)	24.0 (16.0-32.0)	24.2 (16.0-32.0)	23.4 (16.7-31.1)	24.3 (21.1-28.4)	27.5 (24.5-30.5)
Main symptoms					
Bleeding	30 (54.5)	24 (77.4)	2 (11.8)	2 (50.0)	2 (66.7)
Uterine mass	20 (36.4)	4 (12.9)	13 (76.4)	2 (50.0)	1 (33.3)
Abdominal pain	5 (9.1)	3 (9.7)	2 (11.8)	-	-
Medical disease					
Hypertension	12 (21.8)	10 (32.3)	2 (11.8)	-	-
Diabetes mellitus	9 (16.4)	9 (29.0)	-	-	-
Others	5 (9.1)	4 (12.8)	1 (5.9)	-	-
Previous cancer					
No	46 (83.6)	26 (83.9)	13 (76.5)	4 (100)	3 (100)
Yes	9 (16.4)	5 (16.1)	4 (23.5)	-	-
Prior pelvic radiation					
No	53 (96.4)	29 (93.5)	17 (100)	4 (100)	3 (100)
Yes	2 (3.6)	2 (6.5)	-	-	-
Prior chemotherapy					
No	51 (92.7)	28 (90.3)	16 (94.1)	4 (100)	3 (100)
Yes	4 (7.3)	3 (9.7)	1 (5.9)	-	-
Preoperative CA-125					
Not elevated	31 (56.4)	22 (71.0)	7 (41.2)	2 (50.0)	-
Elevated	8 (14.5)	5 (16.1)	2 (11.7)	1 (25.0)	-
Not checked	16 (29.1)	4 (12.9)	8 (47.1)	1 (25.0)	3 (100)
Operation					
AH	28 (50.9)	17 (54.8)	8 (47.1)	1 (25.0)	2 (66.7)
LH	21 (38.2)	12 (38.7)	6 (35.3)	2 (50.0)	1 (33.3)
VH	5 (9.1)	2 (6.5)	2 (11.7)	1 (25.0)	-
Myomectomy	1 (1.8)	-	1 (5.9)	-	-
BSO					
No	8 (14.5)	4 (12.9)	2 (11.8)	1 (25.0)	1 (33.3)
Yes	47 (85.5)	27 (87.1)	15 (88.2)	3 (75.0)	2 (66.7)
LN evaluation					
No	32 (58.1)	13 (41.9)	13 (76.5)	3 (75.0)	3 (100)
Yes	23 (41.9)	18 (58.1)	4 (23.5)	1 (25.0)	-

CS=carcinosarcoma, ESS=endometrial stromal sarcoma, UES=undifferentiated endometrial sarcoma, LMS=leiomyosarcoma, BMI=body mass index, AH=abdominal hysterectomy, LH=laparoscopic hysterectomy, VH=vaginal hysterectomy, BSO=bilateral salpingooophorectomy, LN=lymph node.

eases, previous cancers, prior chemotherapy and prior pelvic radiation. The authors also obtained tumor clinical data on histological subtype, size, depth of myometrial invasion, presence of lymphovascular space invasion (LVSI), presence of lymph node (LN) involvement, surgical stage by the International Federation of Obstetrics and Gynecology (FIGO) system, adjuvant therapies, and outcomes of treatments. Experienced pathologists from the present institution assessed the histological findings. The response to treatment was determined from radiologic images(CT, MRI, or PET-CT after treatments. This study design was approved by the institutional review board (IRB) of the present institution for retrospective chart reviews.

The overall survival (OS) time was calculated as the number of months from the date of primary management to the date of death. The disease-free survival (DFS) time was calculated as the number of months from the date of primary management to the date of recurrence. Frequency distributions were compared by the Chi-squared and Fisher's exact tests and the mean or median values in groups of uterine sarcoma were compared by the Student's *T*-test and Mann–Whitney *U*-test. The survival curves and rates were generated using the Kaplan–Meier method. The comparison of survival curves in groups was made by using the log-rank test. Multivariate analysis was performed to determine the survival benefit when the model was adjusted for favorable prognostic variables, using the Cox's proportional hazards model. A *p*-value of less than 0.05 in the two-sided test was considered statistically

Table 2. — *Tumor characteristics with respect to different subtypes of uterine sarcomas.*

Characteristics	Total (n=55) No. (%)	CS (n=31) No. (%)	ESS (n=17) No. (%)	UES (n=4) No. (%)	LMS (n=3) No. (%)
Tumor size					
≤ 5cm	21 (38.2)	16 (51.6)	4 (23.5)	1 (25.0)	-
> 5cm	34 (61.8)	15 (48.4)	13 (76.5)	3 (75.0)	3 (100)
Myometrial invasion					
≤ 50%	19 (34.5)	15 (48.4)	3 (17.6)	1 (25.0)	-
> 50%	19 (34.5)	13 (41.9)	2 (11.8)	3 (75.0)	1 (33.3)
Unknown	17 (31.0	3 (9.7)	12 (70.6)	-	2 (66.7)
LVSI					
No	17 (30.9)	15 (48.4)	2 (11.8)	-	-
Yes	11 (20.0)	5 (16.1)	4 (23.5)	1 (25.0)	1 (33.3)
Unknown	27 (49.1)	11 (35.5)	11 (64.7)	3 (75.0)	2 (66.7)
LN involvement					
No	20 (36.4)	16 (51.6)	3 (17.6)	1 (25.0)	-
Yes	3 (5.5)	2 (6.5)	1 (5.9)	-	-
Unknown	32 (58.1)	13 (41.9)	13 (76.5)	3 (75.0)	3 (100)
FIGO Stage					
I	38 (69.1)	23 (74.2)	12 (70.6)	2 (50.0)	1 (33.3)
II	6 (10.9)	1 (3.2)	3 (17.6)	1 (25.0)	1 (33.3)
III	7 (12.7)	6 (19.4)	1 (5.9)	-	-
IV	4 (7.3)	1 (3.2)	1 (5.9)	1 (25.0)	1 (33.3)
Only adjuvant chemotherapy	13 (23.6)	11 (35.5)	-	1 (25.0)	1 (33.3)
Only adjuvant radiotherapy	11 (20.0)	5 (16.1)	3 (17.6)	1 (25.0)	2 (66.7)
Adjuvant CCRT	13 (23.6)	9 (29.0)	3 (17.6)	1 (25.0)	-
Response to therapies					
CR	43 (78.2)	22 (71.0)	17 (100)	2 (50.0)	2 (66.7)
PR	1 (1.8)	1 (3.2)	-	-	-
SD	2 (3.6)	2 (6.4)	-	-	-
PD	9 (16.4)	6 (19.4)	-	2 (50.0)	1 (33.3)
Recurrence of disease					
No. (%)	20 (36.4)	15 (48.4)	2 (11.8)	2 (50.0)	1 (33.3)

CS=carcinosarcoma, ESS=endometrial stromal sarcoma, UES=undifferentiated endometrial sarcoma, LMS=leiomyosarcoma, LVSI=lymphovascular space invasion, LN=lymph node, FIGO=the International Federation of Obstetrics and Gynecology, CCRT= concurrent chemoradiation therapy, CR=complete response, PR=partial response, SD=stable disease, PD=progressive disease.

significant. The data were analyzed using the SPSS software version 21.0.

Results

The authors identified 72 patients who had been histologically diagnosed with uterine sarcoma from 2004 to 2015 at CNUH. Among them, 17 were excluded because of refusal of treatment, transfer to another hospital, or insufficient data. A total of 55 patients were included in the final analysis, namely those who had been treated and followed in the same period.

Patients' characteristics are summarized in Table 1. The median age of all was 53 years (ranging from 27 to 80 years) and the median age of patients in the CS group was relatively higher than in the other groups. Sixty percent of all patients were postmenopausal. Conversely, the ESS group had a high proportion of premenopausal women (82.4%). Forty-eight women (87.3%) had delivered two babies or more and each group also had similar results. The mean BMI was 24.0 kg/m^2 (ranging from 16.0 to 32.0 kg/m^2). At the time of the first visit, patients had presented with several main symptoms, such as vaginal bleeding (54.5%), uterine mass (36.4%), or abdominal pain (9.1%). Most of the patients with CS had complained of vaginal bleeding (77.4%), while most of the patients with ESS had been discovered with a uterine mass (76.4%). The common medical diseases of patients included hypertension and diabetes mellitus. Nine patients had a previous history of different cancers. Of these patients, two had received prior pelvic radiation and four had received prior chemotherapy. Thirty-nine patients had a measurement of serum CA-125 level before treatment, and eight of them had an elevated serum CA-125 level.

In the first operation, all patients underwent hysterectomy or myomectomy for various reasons (the diagnosis of uterine sarcoma, the diagnosis of uterine myoma, severe vaginal bleeding, *etc.*). Forty-two patients were initially operated on at CNUH, with the remaining 13 patients transferred to the present institution after the diagnosis of uterine sarcomas and receiving additional surgeries. Finally, 54 patients underwent complete surgery with or without staging procedures. However, one patient, who had been diagnosed with ESS after myomectomy, received only concurrent chemora-

Table 3. — *Prognostic factors for uterine sarcomas (multivariate analysis).*

Variables	No.	Disease free survival			Overall survival		
		O.R.	95% C.I.	*p*-value	O.R.	95% C.I.	*p*-value
Menopause							
No	22	1			1		
Yes	33	20.6	1.4-296.8	<0.05	25.4	2.1-351.7	0.90
Elevated CA-125							
No	31	1			1		
Yes	8	12.4	1.3-121.1	<0.05	31.7	3.8-185.3	0.86
FIGO Stage							
I	38	1			1		
II	6	0.0	0.0-0.2	0.07	0.0	0.0-3.9	0.87
III	7	0.5	0.1-4.0	0.49	0.8	0.2-3.7	0.78
IV	4	19.9	0.8-279.4	0.06	16.1	0.6-163.3	0.84
Tumor size							
≤ 5cm	21	1			1		
> 5cm	34	0.6	0.1-2.7	0.46	0.6	0.1-4.1	0.58
Histologic type							
ESS	17	1			1		
CS	31	8.5	1.0-70.9	<0.05	21.6	7.4-121.3	0.77
UES	4	69.3	1.7-282.5	<0.05	35.8	1.3-171.5	0.80
LMS	3	49.6	2.2-417.2	<0.05	41.1	0.7-375.1	0.86
Myometrial invasion							
≤ 50%	19	1			1		
> 50%	19	1.7	0.3-9.1	0.51	3.4	0.6-21.7	0.77
LVSI							
No	17	1			1		
Yes	11	12.7	1.1-149.6	<0.05	10.8	0.2-160.3	0.24
LN involvement							
No	20	1			1		
Yes	3	86.0	8.3-785.1	<0.05	22.7	0.0-269.8	0.88

O.R.=Odds ratio, C.I.=confidence interval, FIGO=the International Federation of Obstetrics and Gynecology, ESS=endometrial stromal sarcoma, CS=carcinosarcoma, UES=undifferentiated endometrial sarcoma, LMS=leiomyosarcoma, LVSI=lymphovascular space invasion, LN=lymph node.

diation therapy (CCRT) without added surgery because of patient demand. The final surgical procedures are listed in Table 1. Fifty-four patients (98.2%) underwent different types of hysterectomy. Bilateral salpingo-oophorectomy (BSO) was carried out in 47 patients (85.5%). Lymph node (LN) status was surgically clarified in 23 patients (41.9%).

Table 2 shows the postoperative histological results. Histological subtypes were as follows: 31 cases had been diagnosed with CS, 17 with ESS, four with UES, and three with LMS. Tumor size of greater than 5 cm was found in 34 cases (61.8%). These cases were more common in the ESS (76.5%), UES (75.0%), and LMS group (100%), excepted CS group (48.4%). Myometrial invasion exceeding half of the depth was observed in 19 cases (34.5%), and these were half of the cases revealing myometrial invasion. LVSI was found in 11 cases (20.0%), but LVSI was determined with certainty in only about half of all cases. LN metastasis was uncommon. Only three cases were confirmed to be LN metastasis out of 23 lymphadenectomy cases. It was difficult to compare the frequency of LVSI and LN involvement in subtype groups. The present study included 38, 6, 7, and 4 diseases with FIGO Stage I, II, III and IV, respectively. Most CS or ESS were found as early-staged, while LMS or UES demonstrated a variety of stages. It is however difficult to accept these results as presented, because of the small number of LMS or UES.

After the surgical treatments, additional therapies were administered to 37 patients (67.3%) (Table 2). Thirteen patients received only chemotherapy, while 11 underwent only radiation and/or vaginal brachytherapy. Adjuvant CCRT was given to 13 patients. The criteria for administering adjuvant therapy for uterine sarcomas were determined at the discretion of the gynecologic oncologists. The selection of chemotherapeutic regimens also depended on the discretion of the gynecologic oncologists. Chemotherapeutic regimens included a combination of ifosfamide, paclitaxel, doxorubicin, or platinum (cisplatin or carboplatin).

A complete response (CR) was achieved in 78.2% of all patients and a partial response (PR) in 1.8%. The diseases were progressive in 16.4% and remained unchanged in 3.6% (Table 2). The surgical treatments and adjuvant therapies worked well in most of the patients. Notably, all patients with ESS achieved a CR.

After a mean follow-up time of 43.5 months (ranging from 1 to 136 months), 20 patients (36.4%) were observed to have recurrent diseases (Table 2). The CS group had a high incidence of relapse (48.4%), whereas the ESS group had the least incidence (11.8%). The UES and LMS group included two (50.0%) and one (33.3%) recurrence cases,

respectively. Among 20 patients with relapse, five were diagnosed with local pelvic recurrences, seven with peritoneal sarcomatosis, five with distant metastases to lung or brain, and three with both local pelvic recurrences and distant metastases to lung or bone. Recurrent diseases were managed with the following treatments: resection of recurrent tumors, systemic chemotherapy, radiation to recurrent tumors, or gamma-knife for metastatic brain tumors. However, three patients refused treatments at the time of recurrence and subsequently died from the worsened disease.

Kaplan–Meier survival curves were used to evaluate the OS and DFS with respect to all uterine sarcomas and the disease-specific OS and DFS with respect to the subtypes of uterine sarcoma (Figure 1). The two- and five-year OS rate were 80.4% and 70.6%, respectively. Additionally, the two- and five-year DFS rate were 69.3% and 49.7%, respectively. The OS rate in the ESS group was excellent and better than in the UES, LMS, or CS group. Likewise, the DFS rate in the ESS group was also better than in the LMS, UES, or CS group.

Multivariate analysis was performed to assess individual variables that were statistically significant in the univariate analysis. The results are summarized in Table 3. Postmenopausal status, elevated preoperative serum CA-125 level, more aggressive histological subtypes than ESS, positive LVSI, and LN involvement were significantly associated with poor DFS. However, postmenopausal status, elevated preoperative serum CA-125 level, advanced FIGO stage, histological subtypes, tumors larger than 5 cm, myometrial invasion > 50%, LVSI, and LN involvement did not affect OS. The factors having a adverse influence on DFS are shown in Figure 2.

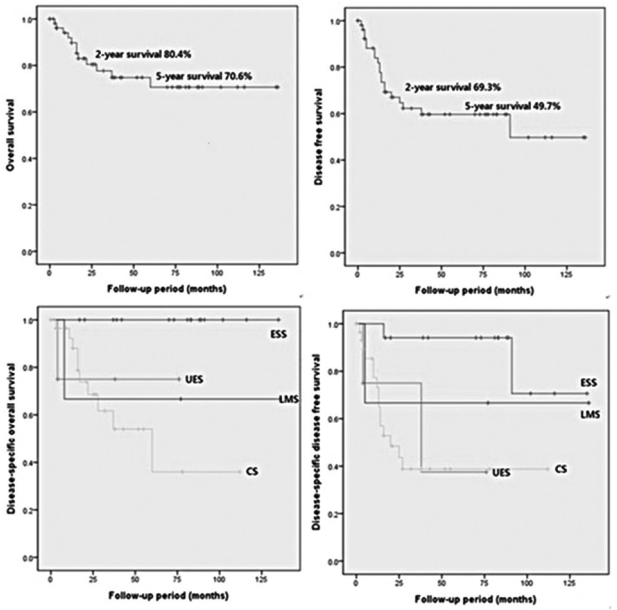

Figure 1. — Kaplan–Meier analysis of the overall survival and disease free survival with respect to all uterine sarcomas (A, B) and the disease-specific overall survival and disease free survival with respect to the uterine sarcoma subtypes. Carcinosarcoma (CS), endometrial stromal sarcoma (ESS), undifferentiated endometrial sarcoma (UES), and leiomyosarcoma (LMS)] (C, D).

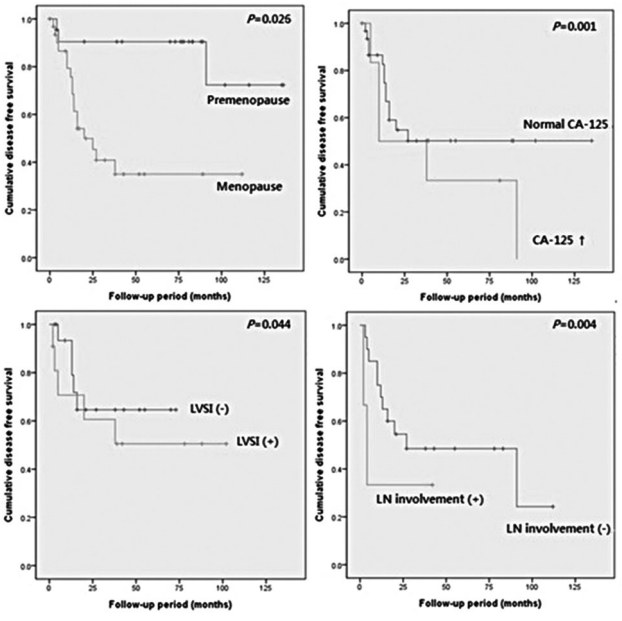

Figure 2. — Disease free survival by menopausal status (A), preoperative serum CA-125 level (B), lymphovascular space invasion (LVSI), and lymph node (LN) involvement (D). Multivariate analysis was adjusted for postmenopausal status, elevated preoperative serum CA-125 level, positive LVSI, and LN involvement (Cox proportional hazards model).

Discussion

Uterine sarcomas are known to be aggressive gynecological malignancies. Various studies to date evaluated the outcome of uterine sarcomas, reporting the five-year OS rates to range from 17.5 to 64.5% (Table 4) [1-4, 6-13]. However, the five-year OS rate was 70.6% in the present study, and this was higher than results of previous studies. This study also revealed that the five-year DFS rate was 49.7%. This is similar to results of previous reports and also slightly higher, ranging from 34 to 53% [1, 4, 7, 8]. The present results could be interpreted as the beneficial effect of surgical treatment and subsequent adjuvant therapy for uterine sarcomas. However, the present results could also result from the fact that the distribution of subtypes of uterine sarcomas in this study is not in accordance with the description in the literature (Table 4). In many studies, LMS was the most common histological subtype, followed by CS and ESS. However, in the present study, CS tumors were predominant (56.4%) and LMS tumors only occurred in three cases (5.5%). Furthermore, ESS tumors occurred in about one-third of all cases in the present study, while general tumors occurred in about one-sixth. Because of this

Table 4. — *The distribution and five-year overall survival rate of uterine sarcomas in different studies.*

Study	No. of patients	No. of CS (%)	No. of ESS (%)	No. of LMS (%)	No. of others (%)	Study period	5-year overall survival, %
Nordal *et al.* 1997 [2]	1042	284 (27)	124 (12)	476 (46)	158 (15)	1956–1992	48 (1983–1987) 50.2 (1971–1975) (relative)
Gonzalez *et al.* 1997 [6]	88	18 (20)	26 (30)	44 (50)	0 (0)	1967-1995	64.5
Chauveinc *et al.* 1999 [1]	73	23 (32)	14 (19)	32 (44)	4 (5)	1975–1995	45
Pautier *et al.* 2000 [7]	157	52 (33)	27 (17)	78 (59)	0 (0)	1976–1995	40
El Husseiny *et al.* 2002 [8]	59	20 (34)	14 (24)	25 (42)	0 (0)	1980–1997	48
Brooks *et al.* 2004 [9]	2677	-	-	-	-	1989–1999	42 (Black women) 53 (White women) (relative)
Kelly *et al.* 2005 [13]	87	36 (41)	14 (16)	33 (38)	4 (5)	1988-1997	48
Livi *et al.* 2005 [10]	40	12 (30)	3 (8)	24 (60)	1 (2)	1980–2001	25
Benoit *et al.* 2005 [11]	72	25 (35)	12 (17)	34 (47)	1 (1)	1966–2001	36.1
Kokawa *et al.* 2006 [12]	97	46 (47)	15 (16)	36 (37)	0 (0)	1990–2003	17.5
Koivisto *et al.* 2008 [3]	100	40 (40)	21 (21)	39 (39)	0 (0)	1990-2001	51
Park *et al.* 2008 [4]	127	44 (35)	37 (29)	46 (36)	0 (0)	1989-2007	59

CS=carcinosarcoma, ESS=endometrial stromal sarcoma, LMS=leiomyosarcoma.

distribution of subtypes of uterine sarcomas, the present study might have shown better outcomes than previous studies. In other words, this finding could mean that each subtype of uterine sarcoma has different prognoses. In this study, the disease-specific OS rate and DFS rate were the highest in the ESS group, followed by the LMS and UES group, and were the lowest in the CS group (Figure 1). Similarly, it has been reported that ESS showed better outcomes in comparison to other subtypes [1, 3, 7, 10, 14, 16].

Total hysterectomy (TH) with or without BSO is known as the standard surgical treatment for uterine sarcomas. The value of lymphadenectomy is still ongoing [15, 17, 18]. In this study, 54 patients (98.2%) underwent TH and 47 patients (85.5%) underwent BSO. Lymphadenectomy was performed in 38.2% of cases. After surgical treatments 37 patients (67.3%) received adjuvant therapies as follows: CCRT 23.6%, only chemotherapy 23.6%, or only radiotherapy 20.0%. The present study showed that surgery and additional treatment were important for more favorable outcomes for the management of uterine sarcomas. The fact is that adjuvant therapy has not yet been clearly shown to increase the survival of patients with uterine sarcoma. There is a general agreement on the role of radiotherapy with regards to being a control of local diseases. However, survival benefits are controversial with different conclusions [1, 3, 7, 10, 16]. Adjuvant chemotherapy did not decrease the risk of metastatic spread and improve survival in several reports [11, 14, 16]. Nonetheless, several studies have reported that complete surgical resection and adjuvant therapy (chemotherapy and/or radiotherapy) in patients with advanced stage disease had significantly longer OS times when compared with patients who did not receive adjuvant therapy [4, 9, 10, 12, 19]. Although the present study does not address the effects of hormone therapy for uterine sarcomas, this has been assessed in some studies. In a recent study [20], LMS with estrogen and progesterone receptors was associated with a better prognosis after hormone therapy. In a review [21] of hormone therapy in gynecological cancers, authors stated that the ESS was the only uterine sarcoma that responded to hormone therapy.

It is unclear whether the histological subtypes of uterine sarcomas affect prognosis. Several studies have reported that the histological subtype is an independent prognostic factor in multivariate analyses [1, 3, 7, 10, 14, 16]. In these studies, the outcome of ESS was significantly better than LMS and CS, because ESS tends to present as a low-grade tumor and an early-stage disease with uncommon metastasis. Similarly, in the present study, patients with ESS showed the best survival rate. However, other multivariate analyses found that the histological subtypes did not affect survival and ESS did not have a better outcome [4, 12]. This result might be because the ESS group included low-grade ESS and high-grade ESS by a categorization based on past classification. The prognosis of high-grade ESS was worse than low-grade ESS and was similar to other high-grade uterine sarcomas. In this study, uterine sarcomas were categorized into CS, ESS, UES, and LMS according to the 2003 WHO classification. Additionally, ESS had a better outcome than UES, LMS, or CS.

The literature contains conflicting data regarding the significance of age in survival. Some studies have found no relationship between age and survival [1, 4, 7, 8, 16]. On the contrary, others have reported that patients younger than 50 years of age have significantly longer DFS and OS times [3, 10, 12]. The present multivariate analysis revealed that postmenopausal women had a significantly shorter DFS time. This study shows that the elevated preoperative serum CA-125 level may be another significant prognostic factor. LVSI generally indicates an aggressive neoplasm with a marked tendency of local recurrences and distant metastases. The literature [4, 22] has documented independent prognostic impacts on survival for LVSI, particularly in early-stage diseases. A similar result was observed in the present study. Additionally, the authors found that LN in-

volvement was also a significant prognostic factor, similar to results from previous studies [4, 8].

The present authors relied on the FIGO system to stage uterine sarcomas, using pathological data obtained by surgical procedures. Many reports have found that the FIGO stage is one of the most important prognostic factors [1, 3-5, 7, 10, 19]. However, this study found no relationship between the FIGO stage and survival. The same result was shown in tumor size associated with FIGO stage. Tumor size is known to be a significant prognostic factor. However, the present analysis did not find that tumor size was a significant predictor. The present study also did not suggest that a tumor invasion of more than half of the myometrium was a prognostic factor, contrary to previous studies [4, 14, 22].

Conclusions

In this study, the OS and DFS rates were better than in nearly all previous retrospective studies of uterine sarcomas. The use of adjuvant therapies was common in this series. Furthermore, although there was no statistical evaluation of the effect on survival, the survival rates were observed to be increased. To improve the prognosis of patients with uterine sarcoma, there is a need for a new and proper management strategy of adjuvant therapies. Menopause, elevated preoperative serum CA-125 level, lymphovascular space invasion, lymph node involvement, and more aggressive histological subtypes were found to be prognostic factors with respect to DFS. Interestingly, stage or tumor size (> 5 cm) did not have an influence on survival. Because of the difficulty of preoperative diagnosis and the aggressive nature of uterine sarcomas, it is important to concentrate on appropriate primary surgery and better adjuvant therapies with thorough monitoring.

References

[1] Chauveinc L., Deniaud E., Plancher C., Sastre X., Amsani F., de la Rochefordiere A., *et al.*: "Uterine sarcomas: the Curie Institut experience. Prognosis factors and adjuvant treatments". *Gynecol. Oncol.*, 1999, *72*, 232.

[2] Nordal R.R., Thoresen S.O.: "Uterine sarcomas in Norway 1956–1992: incidence, survival and mortality". *Eur. J. Cancer.*, 1997, *33*, 907.

[3] Koivisto-Korander R., Butzow R., Koivisto A.M., Leminen A.: "Clinical outcome and prognostic factors in 100 cases of uterine sarcoma: Experience in Helsinki University Central Hospital 1990–2001". *Gynecol. Oncol.*, 2008, *111*, 74.

[4] Park J.Y., Kim D.Y., Suh D.S., Kim J.H., Kim Y.M., Kim Y.T., et al.: "Prognostic factors and treatment outcomes of patients with uterine sarcoma: analysis of 127 patients at a single institution, 1989–2007". *J. Cancer Res. Clin. Oncol.*, 2008, *134*, 1277.

[5] Akahira J., Tokunaga H., Toyoshima M., Takano T., Nagase S., Yoshinaga K., *et al.*: "Prognoses and prognostic factors of carcinosarcoma, endometrial stromal sarcoma and uterine leiomyosarcoma; a comparison with endometrial adenocarcinoma". *Oncology*, 2006, *71*, 333-340.

[6] González-Bosquet E., Martínez-Palones J.M., González-Bosquet J., García Jiménez A., Xercavins J.: "Uterine sarcoma: a clinicopathological study of 93 cases". *Eur. J. Gynaecol. Oncol.*, 1997, *18*, 192.

[7] Pautier P., Genestie C., Rey A., Morice P., Roche B., Lhommé C., *et al.*: "Analysis of clinicopathologic prognostic factors for 157 uterine sarcomas and evaluation of a grading score validated for soft tissue sarcoma". *Cancer*, 2000, *88*, 1425.

[8] El Husseiny G., Al Bareedy N., Mourad W.A., Mohamed G., Shoukri M., Subhi J., *et al.*: "Prognostic factors and treatment modalities in uterine sarcoma". *Am. J. Clin. Oncol.*, 2002, *25*, 256.

[9] Brooks S.E., Zhan M., Cote T., Baquet C.R.: "Surveillance, epidemiology, and end results analysis of 2677 cases of uterine sarcoma 1989–1999". *Gynecol. Oncol.*, 2004, *93*, 204.

[10] Livi L., Paiar F., Meldolesi E., Simontacchi G., Amunni G., Barca R., *et al.*: "Treatment of uterine sarcoma at the University of Florence from 1980–2001". *Tumori*, 2005, *91*, 139.

[11] Benoit L., Arnould L., Cheynel N., Goui S., Collin F., Fraisse J., *et al.*: "The role of surgery and treatment trends in uterine sarcoma". *Eur. J. Surg. Oncol.*, 2005, *31*, 434.

[12] Kokawa K., Nishiyama K., Ikeuchi M., Ihara Y., Akamatsu N., Enomoto T., *et al.*: "Clinical outcomes of uterine sarcomas: results from 14 years worth of experience in the Kinki district in Japan (1990–2003)". *Int. J. Gynecol. Cancer.*, 2006, *16*, 1358.

[13] Kelly K.L., Craighead P.S.: "Characteristics and management of uterine sarcoma patients treated at the Tom Baker Cancer Centre". *Int. J. Gynecol. Cancer.,* 2005, *15*, 132.

[14] Sagae S., Yamashita K., Ishioka S., Nishioka Y., Terasawa K., Mori M., *et al.*: "Preoperative diagnosis and treatment results in 106 patients with uterine sarcoma in Hokkaido, Japan". *Oncology*, 2004, 67, 33.

[15] Gadducci A., Cosio S., Romanini A., Genazzani A.R.: "The management of patients with uterine sarcoma: a debated clinical challenge". *Crit. Rev. Oncol. Hematol.*, 2008, 65, 129-142.

[16] Denschlag D., Masoud I., Stanimir G., Gilbert L.: "Prognostic factors and outcome in women with uterine sarcoma". *Eur. J. Surg. Oncol.*, 2007, *33*, 91.

[17] Leitao M.M., Sonoda Y., Brennan M.F., Barakat R.R., Chi D.S.: "Incidence of lymph node and ovarian metastases in leiomyosarcoma of the uterus". *Gynecol. Oncol.*, 2003, *91*, 209.

[18] Temkin S.M., Hellmann M., Lee Y.C., Abulafia O.: "Early stage carcinosarcoma of the uterus: The significance of lymph node count". *Int. J. Gynecol. Cancer*, 2007, *17*, 215.

[19] Wu T.I., Chang T.C., Hsueh S., Hsu K.H., Chou H.H., Huang H.J., *et al.*: "Prognostic factors and impact of adjuvant chemotherapy for uterine leiomyosarcoma". *Gynecol. Oncol.*, 2006, *100*, 166.

[20] Akhan S.E., Yavuz E., Tecer A., Iyibozkurt C.A., Topuz S., Tuzlali S., *et al.*: "The expression of Ki-67, p53, estrogen and progesterone receptors affecting survival in uterine leiomyosarcomas. A clinicopathologic study". *Gynecol. Oncol.*, 2005, *99*, 36.

[21] Garrett A., Quinn M.A.: "Hormonal therapies and gynaecological cancers". *Best Pract. Res. Clin. Obstet. Gynaecol.*, 2008, *22*, 407.

[22] Rovirosa A., Ascaso C., Ordi J., Abellana R., Arenas M., Lejarcegui J.A., *et al.*: "Is vascular and lymphatic space invasion a main prognostic factor in uterine neoplasms with a sarcomatous component? A retrospective study of prognostic factors of 60 patients stratified by stages". *Int. J. Radiat. Oncol. Biol. Phys.*, 2002, *1*, 1320.

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