Uterine sarcoma

Clinico-pathological characteristics and outcome

Hesham K. Sait, *MS,* ***Nisrin M. Anfinan,*** *MBChB, SBOG,* ***Mohamed E. El Sayed,*** *MBBCh, PhD,* ***Shadi S. Alkhayyat,*** *MBBS, FRCPC,* ***Ahmed T. Ghanem,*** *MD, PhD,* ***Reem M. Abayazid,*** *MBBS, SBOG,* ***Khalid H. Sait,*** *MBChB, FRCS(C).*

ABSTRACT

الأهداف: أجريت هذه الدراسة الاستعادية للتحقيق في الخصائص السريرية والتشريحية المرضية، جنب إلى جنب مع العوامل المؤثرة، نتائج العلاج، ونمط الانتكاس وتحليل وبقاء مرض ساركوما الرحم.

الطريقة: تم تحديد جميع المرضى اللذين يعانون من ساركوما الرحم واستخدم قاعدة بيانات لمستشفى جامعة الملك عبدالعزيز، جدة، المملكة العربية السعودية خلال الفترة ما بين2000م وديسمبر 2012م.

النتائج: تم استعراض 36 مريضا يعانون من ساركوما الرحم. وقد أفادت التقارير أن متوسط العمر للمجموعة 57 عاماً، وقد وجد أن 21 (58%) من الحالات carcinosarcoma و 7(19%) leiomyosarcoma (LMS)، بطانة الرحم اللحمية ساركوما (undifferentiated endometrial sarcom) شخصت في 6 مرضى 17% وحالتين 6% (RMS) Rhabdomyosarcoma. وقد وجد أن ما يقارب نصف الحالات شخصت في المرحلة الثالثة والرابعة(25%و 28%) على التوالي. في حين كانت (15 حالة أي 41%) من المرحلة الأولى، وحالتين فقط (6%) من المرحلة الثانية. كان العلاج الجراحي باستئصال كامل للرحم والمبايض وقنوات فالوب بالإضافة إلى استئصال الغدد اللمفاوية لدى 18 مريضة 50%، أما استئصال كامل الرحم والمبايض وقنوات فالوب وكامل الورم debulking اجريت على 4 مريضات (19%). العلاج الكيميائي والعلاج الإشعاعي المصاحب اعطي ل 24 مريضة (69%) و 5 مريضات (14%) على التوالي. وفي متوسط فترة المتابعة 13.5 شهراً. أصيبت 8 مريضات (22%) بانتكاسه. وفي الدارسة وجدنا أن 2-5 DFS للمرضى هو 14% و 22% على التوالي و ارتبطت المراحل المتقدمة أن الأوعية الدموية اللمفاوية وغزو DFS (p=0.0001 and p=0.015) في حين استخدم العلاج الكيماوي في تحسن DFS (p=0.027).

الخاتمة: في هذه السلسلة الصغيرة من المرضى تم تحديد العوامل التي تزيد من سوء مرض ساركوما الرحم فقط 30% من المرضى على قيد الحياة لمدة سنتين. و يدعو ذلك للضرورة الملحة إلى أدوات أكثر عدوانية للقضاء على هذا المرض.

Objectives: To investigate the clinical and histopathological characteristics, with the prognostic factors, treatment outcome, pattern of relapse, and survival analysis of uterine sarcoma patients.

Methods: All patients with histologically proven uterine sarcoma were identified using the database at King Abdulaziz University Hospital, Jeddah, Saudi Arabia between January 2000 and December 2012.

Results: A total of 36 patients with uterine sarcoma were reviewed. The median age of all patients was 57 years, and the mean age was 57.72±13.17 years. Carcinosarcoma was reported in 21 patients (58%), leiomyosarcoma in 7 (19%), undifferentiated endometrial sarcoma in 6 (17%), and rhabdomyosarcoma in 2 (6%). Approximately half of the patients were stages III and IV (28% and 25%), while 15 patients (41%) were stage I; only 2 patients (6%) were stage II. The surgical treatment was hysterectomy and bilateral salpingoophorectomy (H+BSO) plus staging in 18 patients (50%), while in 4 patients (19%), H+BSO plus debulking was performed. Adjuvant chemotherapy was given in 24 (69%) and adjuvant radiotherapy in 5 (14%) cases, At a median follow-up period of 13.5 months, 8 patients (22%) relapsed. The 2-year disease-free survival (DFS) rate was 22% and the 5-year was 14%. In the multivariate analysis, the advanced stages (p=0.015) and lymph vascular invasion (p=0.0001) were associated with poor DFS, while the use of chemotherapy significantly improved the DFS (p=0.027).

Conclusions: The poor outcome of high-grade uterine sarcoma patients was identified, and only one third of patients (30%) survived for 2 years. This finding necessitates the need for more aggressive tools to fight this disease.

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From the Scientific Chair of Prof. Abdullah Hussein Basalamah for Gynecological Cancer (Sait H, Abayazid, Sait K), Gynecology Oncology Unit (Anfinan), Department of Medicine (Alkhayyat), Department of Pathology (Ghanem), Faculty of Medicine, King Abdulaziz University, Jeddah, Kingdom of Saudi Arabia, and the National Cancer Institute, Radiotherapy and Nuclear Medicine Department (El Sayed), Cairo University, Cairo, Egypt.

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Address correspondence and reprint request to: Dr. Khalid H. Sait, Gynecology Oncology Unit, Faculty of Medicine, King Abdulaziz University, Jeddah, Kingdom of Saudi Arabia. E-mail: khalidsait@yahoo.com

Uterine sarcomas are rare tumors that account for 1-3% of all female genital tract malignancies and 3-8% of all uterine malignancies.[1-3] This heterogeneous group of tumors originates from uterine mesodermal tissue. The major uterine sarcomas consist of leiomyosarcoma (LMS) and endometrial stromal tumors (EST), the latter of which are sub-classified into 3 categories by the World Health Organization (WHO): endometrial stromal nodules (ESNs), endometrial stromal sarcoma (ESS, historically referred to as low-grade sarcoma), and undifferentiated endometrial sarcoma (UES, historically called high-grade sarcoma). Carcinosarcoma, previously called malignant mixed mullerian tumor, is considered a deviant of carcinoma, and its behavior, and treatment resembles those of high-grade carcinoma. However, there are still some centers that treat this as sarcoma.[4] Uterine sarcomas occur primarily in women who are 40-60 years old.[5,6] A history of pelvic irradiation was also considered a risk factor in 5-10% of cases.[7] Compared with the more common types of endometrial cancer, women with uterine sarcoma have a poor prognosis due to the aggressiveness of the disease.[5-7] The most frequent prognostic factors include the stage, histological subtype, grade, lymph vascular invasion, and menopausal status.[8-10] Standard treatment of early stage patients are hysterectomy and surgical staging, and approximately half of these patients develop recurrent disease.[10] Post-operative radiotherapy reduces local recurrence and improves local disease but does not affect the overall survival.[11,12] Adjuvant chemotherapy with a single agent, isofosamide or doxorubicin, has been used,[11] and combination chemotherapy (which did not show any superiority) has non-proven value over a single agent.[13] Due to its rarity, heterogeneity, and aggressiveness, there is no consensus regarding the optional therapeutic approaches with considerable variation in the type of surgery and choice of adjuvant treatment. The purpose of this study is to investigate the clinical and histopathological characteristics, with the prognostic factors, treatment outcome, and pattern of relapse and survival analysis of uterine sarcoma patients.

Methods. All patients with histologically proven uterine sarcoma were identified using the database at King Abdulaziz University Hospital, Jeddah, Saudi Arabia between January 2000 and December 2012. The study inclusion criteria required the pathological diagnosis of uterine sarcoma at the time of the study. The patients' medical records were reviewed, and information regarding the patients' characteristics, medical history, tumor characteristics, treatment modalities, follow-up, and survival data was reviewed and recorded. A single pathologist reviewed all the cases, and the stages of the disease were determined and adjusted retrospectively according to the FIGO staging 2009.[14] The surgical procedures included one of the following procedures: hysterectomy and bilateral salpingoophorectomy (H+BSO), H+BSO+staging (pelvic and para-aortic lymphadenectomy ± omentectomy), or H+BSO+debulking (cytoreductive surgery). Patients were offered adjuvant therapy chemotherapy, radiotherapy, or hormonal therapy based on the patients' performance status, histological type, and tumor board decision. Study approval was obtained from the Unit of Biomedical Ethics, Faculty of Medicine, King Abdulaziz University.

Statistical analysis. The Statistical Science for Social Package Version 20 (IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY, USA) was used for data analysis. Data were expressed as median (minimum-maximum) or number (percentage) as appropriate. The overall survival (OS) time was calculated as the number of months from the date of surgery to either the date of death or the date of last follow up. The disease-free survival (DFS) time was calculated as the number of months from the date of surgery to either the date of recurrence or the date of last follow up. The endpoints were 2 and 5 years OS and DFS. Survival curves were calculated with the Kaplan-Meir estimator. The statistical significance of each variable was first tested by the log rank test (univariate analysis). A Cox regression model was used for multivariate analysis. For all tests, $p<0.05$ was considered significant.

Results. A total of 36 patients with uterine sarcoma were reviewed. The median age of all patients was 57 years, and the mean age was 57.72±13.17 years. The median parity was 4 (minimum-maximum, 0.00-15.00). Carcinosarcoma was the most common presenting histopathological type (58%), followed by LMS (20%). No patients with endometrial stromal sarcoma (previously called a low-grade stromal sarcoma) were found during the study period. The stage of the tumors was mostly stage I (41%), followed by stage III (28%), stage IV (25%) and stage II (6%). Cervical involvement was found in 8 (38.1%) in carcinosarcoma and 2 (33%) in undifferentiated endometrial sarcoma. Adnexal involvement was present in 3 (50%) and 7 (33.3%) in undifferentiated endometrial sarcoma and carcinosarcoma (**Table 1**).

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Table 2 shows the lines of treatment and adjuvant therapy of the uterine sarcoma patients. In all patients, the surgical procedure was mostly H+BSO+staging (50% of patients), followed by H+BSO (39%), and H+BSO+debulking (11%). Thirty-three (91.7%) underwent surgery using an open approach. Two patients had subtotal abdominal hysterectomy for clinical diagnosis of uterine fibroids; the final pathology showed LMS, and the cases were referred to us and had complete surgery with removal of the cervix and pelvic and para-aortic lymphadenectomy using the Robot DeVinci method. Both patients received adjuvant chemotherapy. One patient had initial laparoscopic total hysterectomy and BSO for uterine fibroids. The uterus was delivered vaginally and was found in the final pathology to have LMS; the patient was given adjuvant chemotherapy and is alive and well. Approximately two-thirds (24/36, 69%) of the patients received adjuvant chemotherapy. Adjuvant chemotherapy was given in 81% of patients with carcinosarcoma and 72% of LMS patients (72%). The type of adjuvant chemotherapy in all carcinosarcoma

Table 1 - Demographic, clinical characteristics, and tumor characteristics of the patients with uterine sarcoma.

Parameters	Carcinosarcoma (n=21)	Leiomyo sarcoma (n=7)	Undifferentiated endometrial sarcoma (n=6)	Rhabdomyo sarcoma (n=2)	Total (n=36)
Age (years) (mean±SD)	65.05±10.40	45.43±10.00	46.00±7.67	59.00±0.00	57.72±13.17
Body mass index (kg/m^2)	26.24±6.09	31.07±9.79	27.53±6.97	21.05±2.19	27.11±7.10
Parity: median (range)	4 (0.00-12.00)	1 (0.00-6.00)	5.50 (3.00-15.00)	0.50 (0.00-1.00)	4 (0.00-15.00)
Medical illness					
Diabetes mellitus	2 (9.5)	1 (14.3)	1 (16.7)	- -	**4 (11.1)**
Hypertension	2 (9.5)	1 (14.3)	- -	- -	**3 (8.3)**
Preoperative biopsy					
Yes	11 (52.4)	3 (42.9)	2 (33.3)	1 (50)	**17 (47.2)**
No	10 (47.6)	4 (57.1)	4 (66.7)	1 (50)	**19 (52.9)**
Staging					
I	7 (33.3)	5 (71.4)	3 (50.0)	- -	**15 (41.7)**
II	2 (9.5)	- -	- -	- -	**2 (5.6)**
III	7 (33.3)	1 (14.3)	1 (16.7)	1 (50)	**10 (27.8)**
IV	5 (23.8)	1 (14.3)	2 (33.3)	1 (50)	**9 (25.0)**
Myometrium invasion					
None	5 (23.8)	7 (100.0)	3 (50.0)	1 (50)	**16 (44.4)**
<50	5 (23.8)	- -	1 (16.7)	- -	**6 (16.7)**
≥50	11 (52.4)	- -	2 (33.3)	1 (50)	**14 (38.9)**
Cervical involvement					
Yes	8 (38.1)	- -	2 (33.3)	- -	**10 (27.8)**
No	13 (61.9)	7 (100.0)	4 (66.7)	2 (100)	**26 (72.2)**
Lymph nodes					
Negative	9 (42.9)	2 (28.6)	1 (16.7)	- -	**12 (33.3)**
Positive	5 (23.8)	- -	- -	2 (100)	**7 (19.4)**
Not done	7 (33.3)	5 (71.4)	5 (83.3)	- -	**17 (47.2)**
Lymph vascular involvement					
Negative	10 (47.6)	7 (100.0)	3 (50.0)	1 (50)	**21 (58.3)**
Positive	11 (52.4)	- -	3 (50.0)	1 (50)	**15 (41.7)**
Adnexa involvement					
Negative	14 (66.6)	6 (85.7)	3 (50.0)	2 (100)	**25 (69.4)**
Positive	7 (33.3)	1 (14.3)	3 (50.0)	- -	**11 (30.6)**
Pelvic washing					
Negative	12 (57.1)	3 (42.9)	1 (16.7)	1 (50)	**17 (47.2)**
Positive	7 (33.3)	1 (14.3)	2 (33.3)	- -	**10 (27.8)**
Not done	2 (9.5)	3 (42.9)	3 (50.0)	1 (50)	**9 (25.0)**
Omentum involvement					
Negative	12 (57.1)	- -	- -	- -	**12 (33.0)**
Positive	6 (28.6)	1 (14.3)	3 (50.0)	1 (50)	**11 (30.6)**
Not done	3 (14.3)	6 (85.7)	3 (50.0)	1 (50)	**13 (36.1)**

Data are expressed as the median (minimum-maximum) and number and percentage (%) as appropriate

cases was carboplatin (AUC 5) + docetaxel at 75 mg/m^2. The LMS patients were treated with doxorubicin at a dose of 65 mg/m^2 + cisplatian at dose of 65 mg/m^2. For rhabdomyosarcoma, we administered VAC (vincristine, 65 mg/m^2, actinomycin 1.5 mg/m^2, and 500 mg/m^2 of cyclophosphamide). Adjuvant radiotherapy was given to only 5 out of the 36 patients (14%), including 3 patients with carcinosarcoma, one with LMS and one with undifferentiated endometrial sarcoma. The adjuvant radiotherapy consisted of pelvis radiotherapy with a dose of 45-50 Gy/25-28 fractions/5 weeks. Vaginal brachytherapy was added if there was a cervical invasion, a positive vaginal margin or parametrial infiltration, and was performed with high dose-rate brachytherapy using a vaginal cylinder applicator with dose 12 Gy/3F and a dose calculated at a depth of 0.50 CM.

At a mean follow-up period of 24.00±0.00 months, 8 patients (22%) relapsed (**Table 3**). The median time of relapse was 7.50 months. The initial clinical stages of the relapsed patients were stages III, IV, and I. Most relapses occurred in patients who did not receive adjuvant chemotherapy (62.5% versus 37.5%) or adjuvant radiotherapy (75% versus 25%). Relapse was reported in the peritoneum, vaginal vault, abdominal wall, inguinal region, omentum and lung. Six out of 8 (75%) with recurrence were in advanced stages III and IV. The treatment of recurrence was mostly palliative, surgery, radiotherapy, and surgery or chemotherapy and radiotherapy (**Table 3**). Thirteen patients (36.1%) died during follow-up; 10 cases had carcinosarcoma, 2 cases had undifferentiated endometrial sarcoma, and one case had rhabdomyosarcoma.

The 2-year DFS rates were 22% and 5-year was 14% (**Figure 1**). The advanced stage (p=0.015) and lymph vascular invasion (p=0.0001) were significantly associated with poor DFS in the multivariate analysis. The use of chemotherapy significantly improved the DFS (p=0.027). The 2-year OS rate was 30%, and the 5-year was 18% (**Figure 2**). Older age (>71 years of age) and lymph node involvement were significantly associated with poor OS (p=0.005, p=0.029). Adjuvant chemotherapy (p=0.033) and radiotherapy were significantly associated with a better OS (p=0.015).

Table 2 - Treatment characteristics and outcomes of the patients with uterine sarcoma.

Parameters	Carcinosarcoma (n=21)	Leiomyosarcoma (n=7)	Undifferentiated endometrial sarcoma (n=6)	Rhabdomyo sarcoma (n=2)	Total (n=36)
Surgical procedure (%)					
H+BSO	5 (23.8)	4 (57.1)	4 (66.7)	1 (50)	**14 (39)**
H+BSO+staging	12 (57.1)	3 (42.9)	2 (33.3)	1 (50)	**18 (50)**
H+BSO+debulking	4 (19.0)	0 (0)	0 (0)	0 (0)	**4 (11)**
Adjuvant chemotherapy (%)					
Yes	17 (80.9)	5 (71.4)	0 (0)	2 (100)	**24 (69)**
No	4 (19.0)	2 (28.6)	6 (100)	0 (0)	**12 (31)**
Carboplatin + taxoter	17 (80.9)	- -	- -	1 (50)	**18 (75)**
Doxorubicin + cisplatian	- -	5 (71.4)	- -	- -	**5 (20)**
Vincristine + actinomycin + cyclophosphamide	- -	- -	- -	1 (50)	**1 (5)**
Adjuvant radiotherapy (%)					
Yes	3 (14.3)	1 (14.3)	1 (16.7)	(0) (0)	**5 (14)**
No	18 (85.7)	6 (85.7)	5 (83.3)	2 (100)	**31 (86)**
Recurrence (%)					
No	18 (85.7)	6 (85.7)	2 (33.3)	2 (100)	**28 (78)**
Yes	3 (14.3)	1 (14.3)	4 (66.7)	0 (0)	**8 (22)**
Follow-up (months) (median) (Minimum-maximum)	13 (1.00-88.00)	14 (12.00-118.00)	23.5 (2.00-136.00)	9.5 (7.00-12.00)	**13.5 (1.00-136.00)**
Duration free from diseases (months) (median) (Minimum-maximum)	12.00 (1.00-88.00)	14.00 (11.00-118.00)	13.50 (1.00-108.00)	9.50 (7.00-12.00)	**13.50 (1.00-118.00)**
Duration till recurrence (months) (median) (Minimum-maximum)	8.00 (7.00-11.00)	11.00 (11.00-11.00)	3.00 (1.00-10.8.00)	-	**7.50 (1.00-108.00)**
Alive (%)					
Yes	1 (4.7)	7 (100)	4 (66.7)	1 (50)	**23 (64)**
No	10 (47.6)	0 (0)	2 (33.3)	1 (50)	**13 (36)**
Duration until death (months) (median) (Minimum-maximum)	9.50 (1.00-36.00)	-	2 (2.00-2.00)	7 (7.00-7.00)	**8 (1.00-36.00)**

H+BSO - hysterectomy + bilateral salpingo-opherectomy

Discussion. Uterine sarcomas are relatively uncommon cancers, accounting for between 3% and 8% of all uterine malignancies.[1-3] The age at presentation varies with the different histologic subtypes; LMS often occurs in women of peri-menopausal age, but carcinosarcoma and EST tend to be associated with women who are beyond menopause.[1,15] In our center, we treated only 36 cases with uterine sarcoma over a 13-year period. The mean age for LMS was 45, whereas for carcinosarcoma and EST, the ages were 65 and 46 years old, Although rabdomyosarcoma is usually present in the pediatric age group,[16] we had 2 patients who presented at the age of 59 years; they were in the advanced stages. Carcinosarcoma was the most common presenting histopathological type (58%), followed by LMS (20%), and EST in 6 (17%) patients. However, Nassar et al[15] reported in their series that LMS was the most commonly reported (42% of patients), followed by carcinosarcoma in 35.5%, and EST in 18.6%.[15] In our study, 10 (28%) of the patients were stage III and 9 (25%) were stage IV, at presentation, while 15 patients (41%) were stage I and only 2 patients (6%) were stage II. This finding is different from other series that reported that stages I and II disease comprise approximately 70% of the patients at presentation, while stages III and IV comprise 30% of the group.[15,17]

Hysterectomy and BSO are the standard treatment for uterine sarcomas.[18] Recent reports insist that patients who undergo extended or radical hysterectomy have a more favorable outcome than those who

Table 3 - Characteristics of the recurrence among patients with uterine sarcoma.

Parameters	Patients with recurrence (n=8)
Surgical procedure	
H+BSO	4 (50.0)
H+BSO+staging	3 (38.0)
H+BSO+debulking	1 (12.0)
Final histopathology	
Undifferentiated endometrial sarcoma	4 (50.0)
Carcinosarcoma	3 (38.0)
Leiomyosarcoma	1 (12.0)
Adjuvant chemotherapy	
No	5 (63.0)
Yes	3 (37.0)
Adjuvant radiotherapy	
No	6 (75.0)
Yes	2 (25.0)
Initial stage	
Stage I	2 (25.0)
Stage III	3 (37.5)
Stage IV	3 (37.5)
Site of recurrence	
Peritoneum	2 (25.0)
Vault	2 (25.0)
Abdominal	1 (12.5)
Abdominal wall + inguinal	1 (12.5)
Omental	1 (12.5)
Lung	1 (12.5)
Treatment	
Palliative care	5 (62.5)
Surgery	1 (12.5)
Radiotherapy	1 (12.5)
Surgery, chemotherapy and radiotherapy	1 (12.5)
Alive	
No	4 (50.0)
Yes	4 (50.0)

H+BSO - hysterectomy + bilateral salpingo-opherectomy
Data are expressed as number and percentage (%)

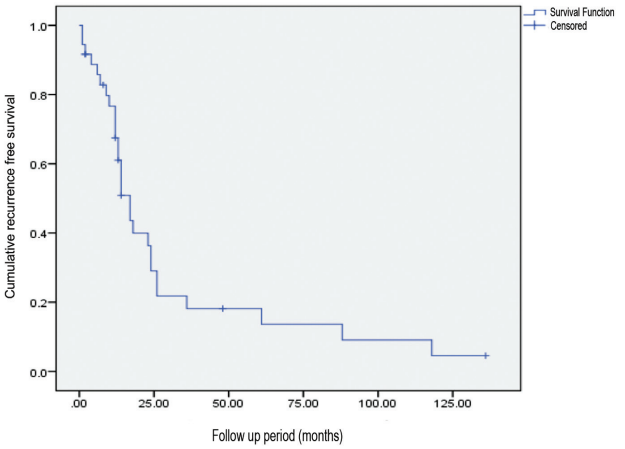

Figure 1 - Disease-free survival for patients with uterine sarcomas.

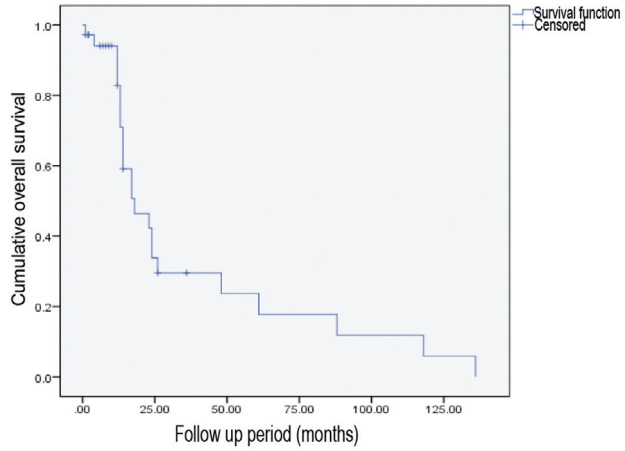

Figure 2 - Overall survival for patients with uterine sarcomas.

undergo hysterectomy.[19] The role of BSO in uterine sarcoma is controversial. Some studies have found that adnexectomy is associated with improved prognosis in patients with LMS and decreased recurrence in patients with EST.[20,21] However, others have reported contradictory results.[22,23] In our series, the surgical procedure was mostly H+BSO+staging (50%), followed by H+BSO (39%) and H+BSO+debulking (11%). The role of lymphadenectomy in uterine sarcoma is controversial;[24,25] in a cohort study performed by Hoellen et al[25] involving 52 patients diagnosed with uterine sarcoma, pelvic lymphadenectomy was performed in 48%, while 10% had both pelvic and para-aortic lymphadenectomy. These authors[25] found that patients who underwent lymphadenectomy had better survival. In our study, 50% of our patients underwent pelvic and para-aortic lymphadenectomy.

Figure 3 shows that there are no significant differences among the different surgical procedures performed for uterine sarcoma (log rank, p=0.786). Park et al[17] reported in their series that complete surgical resection is an important factor affecting patient outcome. Complete surgical resection may be the best option for uterine sarcomas because the role of effective adjuvant treatment remains undetermined. Approximately two-thirds of the patients (69%) received adjuvant chemotherapy in this series. The adjuvant chemotherapy was given in 81% and 71% of carcinosarcoma and LMS patients. Adjuvant radiotherapy was given in 5/36 (14%). Other series[15,17,21] reported a variable percentage of patients who received adjuvant chemotherapy or radiotherapy (50-60% for adjuvant chemotherapy and 5-30% for adjuvant radiotherapy).

In this study, 8 patients (22%) had confirmed relapse during the follow-up period; 75% of relapses occurred in patients who were initially stages III and IV, whereas other series reported an incidence of relapse between 30-37%.[4,14] Although relapse occurred in 63% and 75% of patients who did not receive adjuvant chemotherapy or radiotherapy versus 38% and 25% of patients who did, respectively, this difference was not statistically significant due to the small number of patients (p<0.480 and p<0.157).

Our 2-year DFS rate was 22% and the 5-year was 14% (**Figure 1**). Ghaemmaghami et al[26] reported that the median survival for their patients was 2.8 years. Moskovic et al[27] reported a median survival of 22 months. Advanced stage and lymph vascular invasion were significantly associated with poor DFS (p=0.015 and p=0.0001). The use of chemotherapy significantly improved the DFS (p=0.027). Park et al[17] reported a 10-year DFS of 30%; adjuvant chemotherapy and

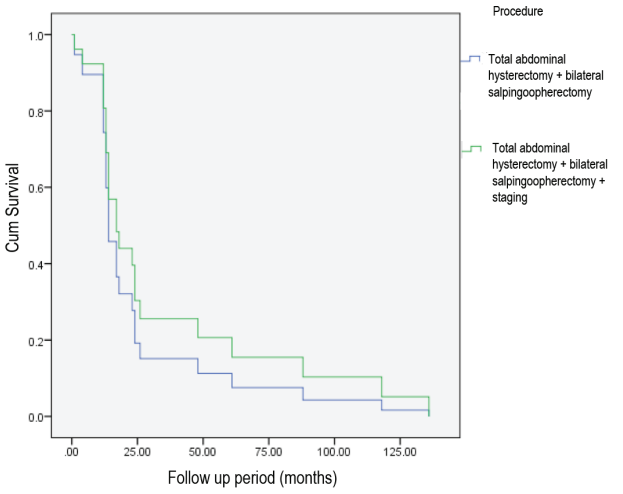

Figure 3 - Overall survival for patients with uterine sarcomas per surgical procedure. Log rank, p=0.786.

radiotherapy have limited impact on the outcome of early stage disease. However, patients with advanced disease that received adjuvant chemotherapy had significantly longer OS times. Multivariate analysis revealed that the FIGO stage (p=0.025), depth of myometrium invasion (p=0.004), and complete cytoreduction (p=0.030) significantly affected the DFS. Nassar et al[15] also reported that the DFS was significantly affected by the stage, adjuvant radiotherapy, tumor size, depth of invasion, and cervical and lymph vascular invasion, while the histological type had no significant value.[15] In their series of 127 patients, which had a median follow-up period of 38 months, Park et al[17] reported a 10-year OS of 48%; the menopausal status (p=0.044), FIGO stage (p=0.016), depth of myometrium invasion (p=0.029), and lymph vascular invasion (p=0.020) were significantly associated with the OS. In our series, the 2-year overall survival (OS) rate was 30% and in the 5-year was 18%. Older age (>71 years) and lymph node involvement were significantly associated with poor OS (p=0.005 and p=0.029). The use of adjuvant chemotherapy (p=0.033) and radiotherapy (p=0.015) was significantly associated with a better OS. Nassar et al[15] reported that patients who received adjuvant chemotherapy showed a poorer median survival time, with a 2-year survival of 40% versus 53% for those who did not receive chemotherapy; the difference was not statistically significant. The role of adjuvant chemotherapy is poorly defined, although chemotherapy has been used because of the high risk of systemic relapse for stage I uterine LMS and undifferentiated sarcoma

with complete resection of the tumor. However, for stages II and III, because of the increase risk profile for systemic relapse, it is appropriate to consider adjuvant chemotherapy.[28] Adjuvant chemotherapy is still performed with controversial results.[11-13] The value of post-operative radiotherapy, if any, was shown to reduce local recurrence and improve local disease, but it had no effect on the overall survival.[11,12] An ongoing phase III randomized trial (GOG 277) is currently assessing the role of postoperative chemotherapy versus observation in patients with uterine LMS and undifferentiated sarcoma. If chemotherapy is needed, docetaxel and gemcitabine have been the most commonly used regimen based on data evaluating their used in LMS.[29] For undifferentiated endometrial sarcoma, some data suggest that docetaxel plus gemcitabine and a doxorubicin-containing regimen exhibit activity.[30] Although radiotherapy was given in only 5 patients in our series, these patients had better outcomes than patients who did not receive radiotherapy. The role of adjuvant radiotherapy in non-metastatic disease is controversial. Most of the retrospective studies of adjuvant radiation with LMS and undifferentiated sarcoma suggest an improvement in the local pelvic control but not in the overall survival.[31] However, in a phase III randomized trial performed by Reed et al[32] on 224 patients diagnosed with uterine sarcoma that underwent radiation versus observation, the initial analysis showed a reduction in the local relapse (14 versus 24; p=0.004), but there was no effect on either the OS or PFS.

In conclusion, we report the first survival data for uterine sarcoma in Saudi Arabia. The poor outcome of high grade uterine sarcoma patients was identified and one third of patients survived for 2 years. The management of uterine sarcomas is challenging due to the lack of consensus or guidelines. Adjuvant treatment should be individualized.

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