

ORIGINAL ARTICLE

Postoperative radiotherapy in the treatment of uterine sarcomas: long-term results and analysis of prognostic factors

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Summary

Purpose: To evaluate the role of postoperative radiotherapy (RT) in local control and survival and to identify treatment-related prognostic factors in uterine sarcomas.

Methods: Sixty patients with uterine sarcomas treated with postoperative RT were retrospectively analyzed. Median age was 49.5 years (range 24-78). The stage distribution was as follows: stage I: 60%, II: 11.7%, and III: 28.3%. All patients were treated with pelvic irradiation (dose range 45.6-54.6 Gy). Pelvic control (PC), distant metastasis-free survival (DMFS), disease-free survival (DFS), and overall survival (OS) were calculated. Age, stage, histology, tumor size, type of surgery, residual disease, time interval between surgery and RT were selected as possible prognostic factors for PC and OS. Age, total treatment time, pelvic dose, dose per fraction, and acute side effects were analyzed

as probable prognostic factors for late complications.

Results: Median follow-up was 84 months. The 10-year PC, DMFS, DFS and OS rates were 84, 67.3, 64 and 61.5%, respectively. Univariate analysis showed that age, residual disease, type of surgery and stage were significant factors for PC; residual disease, type of surgery and stage were significant factors for DMFS; stage was found as the only significant factor for DFS and OS. Total treatment time, pelvic dose, dose per fraction, and acute side effects were significant factors for late complications.

Conclusion: Although our results suggest improved PC, the role of postoperative RT should be tested in prospective randomized trials.

Key words: carcinosarcoma, leiomyosarcoma, mixed mesodermal tumor, postoperative radiotherapy, uterine sarcomas

Introduction

Uterine sarcomas are very uncommon gynecological malignancies and account for less than 5% of uterine neoplasms [1]. Currently, surgery is mandatory and the first treatment choice for these malignancies. Unfortunately, prognosis is unsatisfactory even in early stages after surgery because of high incidence of local and distant relapse. For this reason, these tumors are candidates for adjuvant treatment modalities. In various reports, results of postoperative RT and/or adjuvant chemotherapy were reported [2-11]. Nevertheless, due to the rarity of uterine sarcomas and the existence of different pathological types, the clinical studies, which evaluate the optimal management and prognostic factors, are still controversial.

A retrospective study was undertaken in our institution to evaluate the role of postoperative RT in local control and survival and to identify possible treatment-related prognostic factors in uterine sarcomas.

Methods

Patient population

During a 22-year period (1979-2001), 76 patients with uterine sarcomas were referred to our clinic. Sixteen of them were excluded, as they were lost before or during RT. Analysis was performed in the remaining 60 patients. Their median age was 49.5 years (range 24-78). Two, 6, 22, 20, 9, and 1 patient were found in

10-year age distribution increments, from 2-7 decades of life. The patients were staged according to the International Federation of Gynecology and Obstetrics (FIGO) staging criteria [12]. Most of the patients (60%) had stage I disease. The characteristics of patients according to histology are displayed in Table 1.

Surgical treatment

Although 34 patients had malignancy diagnosed before surgery, myoma uteri was found preoperatively in 25 (41.7%) patients and adenomatous hyperplasia in 1 (1.7%). Therefore, different surgical procedures were performed. Simple hysterectomy was performed in 40 patients and radical hysterectomy in 14. Due to disseminated extrauterine disease in the pelvis at exploration, optimal surgical procedures were not performed in 6 patients. As a result, those patients had macroscopic residual disease. However, microscopic residual disease was found in the pathological specimens of 3 patients who had sufficient surgery. In 41 (68.3%) cases operated at our institution, the surgical slides were reexamined by a pathologist. Except 3 patients whose tumor size was not defined, the mean value of tumor size in these series was 6 cm.

The median time from surgery to RT was 36 days (range 13-125, 95% CI: 34-45).

Radiotherapy

Pretreatment evaluation included chest X-ray, full blood count, and serum biochemistry. After 1989, computed tomography (CT) or magnetic resonance imaging (MRI) of the upper abdomen and pelvis were used in patients without detailed pathological or surgical information. Initially, all patients had received external pelvic RT. Standard whole-pelvis treatment portals were utilized. Pelvic irradiation was given by 9-18 MV photon or ⁶⁰Co teletherapy machine through 15×15 cm anterior and posterior parallel fields. Four-field box technique was preferred in obese patients. The margins of the pelvic fields were extended from L4 to L5 intervertebral space to the lower border of the obturator foramen, and lateral borders were 1-2 cm beyond the bony pelvis.

The dose was calculated at the midpoint pelvis. Fractionation size was 1.8 Gy in 14 (23.3%) patients and 2 Gy in 46 (76.7%) patients with 5 fractions per week, in 5-6 weeks. The total external pelvic dose ranged from 45.6 to 54.6 Gy (median 54, mean 52.2) and the total dose was 54 Gy (53.3%) in 32 patients. Five patients, due to macroscopic residual disease, and 1 patient for persistent pelvic lymphadenopathy had received boost doses with small pelvic field. The boost doses ranged from 7.2 to 20 Gy (7.2, 9, 12, 12.6, 16.2,

Table 1. Patient, disease and treatment characteristics by histology

	<i>All patients</i> <i>n (%)</i>	<i>ESS</i> <i>n (%)</i>	<i>LMS</i> <i>n (%)</i>	<i>MMT</i> <i>n (%)</i>
Age, years; median (range)	49.5 (24-78)	50	45	59
Stage				
I	36 (60)	13 (21.7)	16 (26.6)	7 (11.7)
II	7 (11.7)	2 (3.3)	1 (1.7)	4 (6.6)
III	17 (28.3)	4 (6.4)	7 (11.6)	6 (10)
Grade				
I	11 (18.3)	5 (8.3)	6 (10)	–
II	9 (15)		3 (5)	4 (6.6)
III	25 (41.7)	6 (10)	10 (16)	9 (15)
Unknown	15 (25)		5 (8.3)	4 (6.6)
Tumor size (cm)				
≤ 6	30 (50)	11 (18.3)	8 (13.3)	11 (18.3)
> 6	27 (45)	7 (11.6)	14 (23.3)	6 (10)
Unknown	3 (5)	1 (1.7)	2 (3.3)	–
Type of surgery				
Simple hysterectomy	40 (66.7)	13 (21.6)	19 (31.6)	8 (13.3)
Radical hysterectomy	14 (23.3)	3 (5)	2 (3.3)	9 (15)
Biopsy or debulking	6 (10)	3 (5)	3 (5)	–
Residual disease				
No	51 (85)	14 (23.3)	21 (35)	16 (26.6)
Yes	9 (15)	5 (8.3)	3 (5)	1 (1.7)
Total	60	19 (31.7)	24 (40)	17 (28.3)

ESS: endometrial stromal sarcoma, LMS: leiomyosarcoma, MMT: mixed müllerian tumor

and 20 Gy, respectively). Intracavitary brachytherapy was given to 9 patients. In this group, the intracavitary treatment was given by using a high dose rate Curietron ^{60}Co remote afterloader. The intracavitary insertion was performed using Fletcher-Suit afterloading ovoid applicators. Vaginal cuff boost dose was prescribed at 0.5 cm from the vaginal surface. Intracavitary brachytherapy was given in 3 insertions 1 week apart. The total dose was 30 Gy in one patient, 24 Gy in 4 patients, and 15 Gy in 4 patients. Only 4 patients (leiomyosarcoma/LMS 2 patients, mixed müllerian tumor/MMT 1 patient, and endometrial stromal sarcoma/ESS 1 patient) received additional adjuvant chemotherapy.

Follow-up

Patients were seen 4-6 weeks after RT and then followed every 3 months for the first 3 years, every 6 months for 5 years and annually thereafter. Physical and gynecological examinations were done at each follow-up visit. Chest X-ray and serum biochemistry were obtained every 6 months in the first 3 years and annually thereafter. Abdominopelvic CT or MRI were done annually. Cytological examination or biopsy were taken only on the grounds of clinical doubt.

Statistical analysis

All time intervals were measured from the date of surgery. In the calculation of OS, death was counted as an event and survival was censored at the time of the last follow-up visit. Treatment failures were analyzed as pelvic or distant metastasis. Pelvic failures were defined if the disease recurred centrally or in the pelvic tissues. Metastases that occurred in the para-aortic or inguinal lymph nodes or elsewhere outside the pelvis were defined as distant metastasis. PC, DMFS, DFS and OS were calculated using the Kaplan-Meier method and comparisons between curves were made using log-rank test [13,14]. Cox regression analysis was applied to significant prognostic variables found in univariate analysis [15].

Age (<50 vs. \geq 50 years), stage, histology, tumor size (\leq 6 vs. >6 cm), type of surgery (simple hysterectomy, radical hysterectomy, biopsy or debulking), residual disease (none, microscopic and macroscopic) were selected as possible prognostic factors for PC and survivals. Age and tumor size groups were chosen according to median and mean values for statistical analyses, respectively.

Treatment-related acute side effects and late complications were scored using the RTOG/EORTC tox-

icity criteria [16]. Age, pelvic treatment duration (\leq 46 vs. >46 days), pelvic dose (<54 vs. \geq 54 Gy), dose per fraction (1.8 vs. 2 Gy), and acute side effects (yes or no) were analyzed as probable prognostic factors for late complications. Median follow-up for living patients was 84 months (range 4-296).

Results

Pelvic control and survival

At the time of analysis, 19 (31.7%) patients had died of disease after a median of 20 months (range 6-69). All deaths due to uterine sarcomas occurred within 5 years except one patient. Two (3.3%) patients died because of cardiovascular disease, with no evidence of malignancy at 6th and 12th months. One (1.7%) patient was alive with disease at 36 months, and 28 (46.7%) were alive with no evidence of the disease (median 112 months, range 61-296). Ten patients were lost to follow-up (median 34 months, range 4-50).

In all patients, 10-year PC, DMFS, DFS and OS

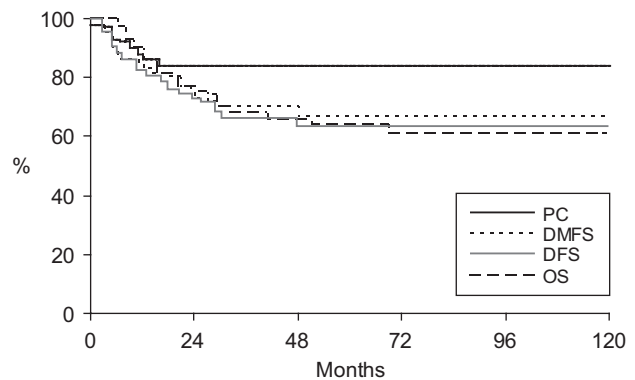


Figure 1. Ten-year pelvic control (PC), distant metastasis-free survival (DMFS), disease-free survival (DFS), and overall survival (OS) rates in all patients.

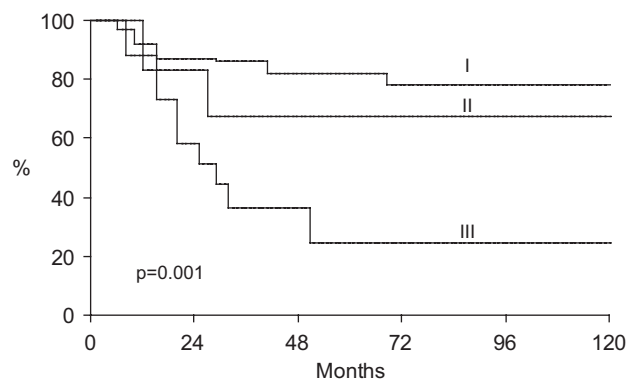


Figure 2. Ten-year overall survival rates according to stage.

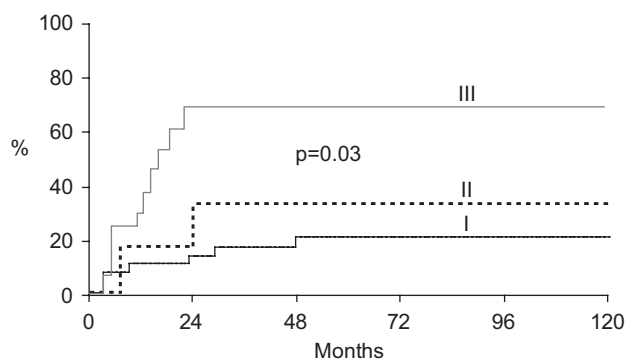


Figure 3. Ten-year treatment failure rates according to stage.

Table 2. Distribution of initial failure sites according to histological types

	<i>All patients</i>	<i>ESS</i>	<i>LMS</i>	<i>MMT</i>
Pelvic	2	—	—	2
Distant	11	—	8	3
Pelvic and distant	7	3	2	2
Total	20	3	10	7

For abbreviations see footnote of Table 1

rates were 84, 67.3, 64 and 61.5%, respectively (Figure 1). Ten-year OS according to stages I-III were 78.1, 66.7 and 24.3, respectively ($p=0.001$; Figure 2).

Treatment failure was identified in 20 (33.3%) patients. In this series, no treatment failures were seen after 48 months. Total treatment failure rates for 1-4 years were 16.5, 27.1, 33.8, and 36%, respectively. As seen in Figure 3, treatment failure distribution according to stages I-III were 20.6, 33.3 and 76.7%, respectively ($p=0.0003$).

Initial failure sites according to histology are shown in Table 2. In all patients, the rate of pelvic failure and distant metastases were 15 and 30%, respectively. Median pelvic failure time was 7 months (range 3-16). Similarly, median time to distant metastasis was 11.5 months (range 3-4). Twenty-four distant metastases were observed in 18 patients. Lung was the most frequent distant metastases site (11/18 or 18.3% of the total number of patients). Other metastatic sites were intraabdominal in 7, liver in 2, brain in 2, supraclavicular lymph node in 1, and orbital metastasis in 1 patient.

Table 3. Univariate analysis of prognostic factors for PC, DMFS, DFS and OS rate

	<i>PC (%)</i>	<i>p-value</i>	<i>DMFS (%)</i>	<i>p-value</i>	<i>DFS (%)</i>	<i>p-value</i>	<i>OS (%)</i>	<i>p-value</i>
Age (years)		0.05		NS		NS		NS
< 50	93.2		67.0		67.0		64.5	
≥ 50	74.9		68.0		61.1		63.8	
Histology		NS		NS		NS		NS
ESS	84.2		84.2		84.2		84.2	
LMS	91.0		53.3		53.3		53.4	
MMT	74.0		64.2		52.4		50.9	
Tumor size (cm)		NS		NS		NS		NS
≤ 6	83.1		73.6		67.3		62.7	
> 6	84.3		59.5		60.0		59.2	
Unknown	100.0		66.6		67.0		66.6	
Stage		0.01		0.0008		0.0003		0.001
I	94.4		82.0		79.4		78.1	
II	83.3		66.7		66.7		66.7	
III	59.9		30.9		23.2		24.3	
Type of surgery		0.03		0.05		0.08		0.03
Biopsy or debulking	44.4		22.2		22.2		20.0	
Simple hysterectomy	87.4		73.4		71.1		71.5	
Radical hysterectomy	90.9		67.1		58.7		58.3	
Residual disease		0.005		0.03		0.06		NS
No	89.7		72.0		68.2		66.4	
Yes	53.3		40.0		40.0		50.0	
Surgery-RT time (days)		NS		NS		NS		NS
≤ 36	78.8		62.1		58.6		57.7	
> 36	89.6		72.9		70.0		69.5	

PC: pelvic control, DMFS: distant metastasis-free survival, DFS: disease-free survival, OS: overall survival, ESS: endometrial stromal sarcoma, LMS: leiomyosarcoma, MMT: mixed müllerian tumor, RT: radiotherapy, NS: non-significant

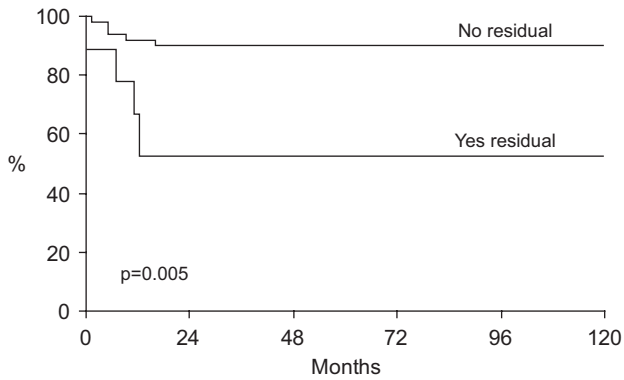


Figure 4. Relationship between residual disease and pelvic control in 10 years.

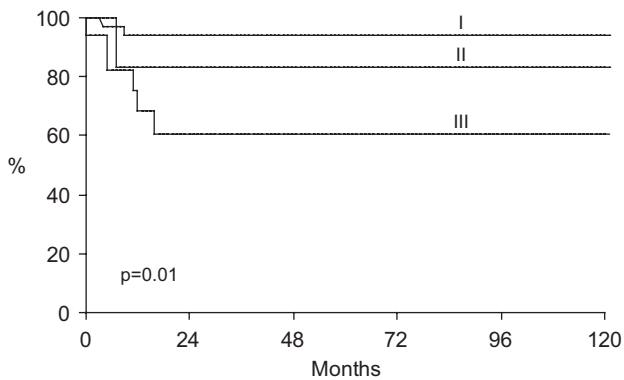


Figure 5. Ten-year pelvic control rates according to stage.

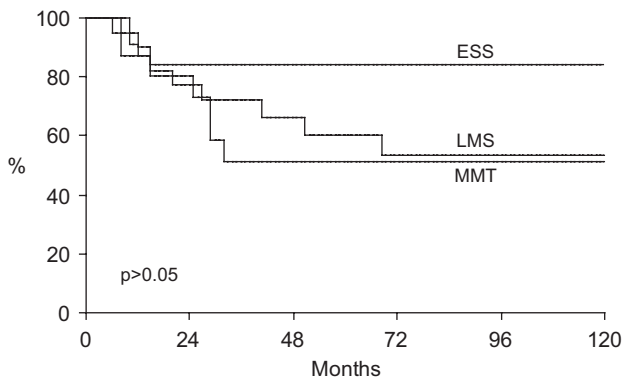


Figure 6. Ten-year overall survival rates according to histology. For abbreviations see text.

Prognostic factors analysis

Univariate analysis of each possible prognostic factor for PC is shown in Table 3. Among the factors analyzed age, residual disease, type of surgery and stage were significant factors for PC. Patients < 50 years had a better PC than those \geq 50 years (93.2 vs. 74.9%, $p < 0.05$). Presence of residual disease, insufficient surgery and ad-

Table 4. Treatment-related acute side effects and late complications

	Grade			
	I n (%)	II n (%)	III n (%)	IV n (%)
Acute side effects				
Hematological	1 (1.7)	1 (1.7)	–	–
Gastrointestinal	17 (28.3)	9 (15)	2 (3.3)	–
Urinary	13 (21.6)	1 (1.7)	–	–
Skin	4 (6.7)	6 (10)	4 (6.7)	–
Late complications				
Rectitis	2 (3.3)	3 (5)	–	1 (1.7)
Cystitis	2 (3.3)	3 (5)	–	–
Skin fibrosis	4 (6.7)	3 (5)	–	–

vanced stage were associated with low PC rate (Figure 4). Ten-year PC according to stages is shown in Figure 5.

Univariate analysis for DMFS demonstrated statistical significance for stage ($p=0.0008$), residual disease ($p=0.03$) and type of surgery ($p=0.05$; Table 3). Stage was the only significant factor for DFS. There was a trend for significance concerning the type of surgery and residual disease for DFS. Both DFS and OS decreased with insufficient surgery, but significance was identified only for OS ($p=0.03$).

With regard to histology, ESS predicted the best prognosis, followed by LMS and MMT with a 10-year OS of 84.2, 53.4 and 50.9%, respectively (Figure 6). However, no significant difference in OS in relation to different histological types was detected. Stage and type of surgery were significant prognostic factors for OS. Cox regression analysis revealed stage as the only significant factor for PC, DMFS, DFS and OS.

Acute side effects and late complications

Twenty-three grade 2-3 acute side effects were seen in 19 (31%) patients. The most common of them concerned gastrointestinal system and skin. All of the side effects were treated with symptomatic medication. None of the patients developed grade 4 acute side effects (Table 4).

All late complications occurred within a median of 19 months (range 5-33) and are shown in Table 4. Seventeen grade 1-2 late complications were seen in 10 patients, 8 of them were grade 1. Grade 3 late complications were not observed in our series. Only one patient had grade 4 proctitis requiring surgery 21 months after RT. This patient had received 1200 cGy external boost due to residual disease and followed up to 93 months without evidence of disease.

Total treatment time and total pelvic dose were significant prognostic factors for late complications.

Table 5. Univariate analysis of prognostic factors for late toxicity

	<i>N</i>	%	<i>p-value</i>
Age (years)			NS
< 50	30	26.7	
≥ 50	30	15.8	
Treatment duration (days)			0.006
≤ 46	31	5.9	
> 46	29	36.4	
Pelvic dose (Gy)			0.009
< 54	27	4.6	
≥ 54	33	37.0	
Fractionation dose			0.07
1.8 Gy	46	27.9	
2 Gy	14	0	
Acute side effects			0.06
Yes	39	29.4	
No	21	7.7	

NS: non-significant

Table 5 shows summarizes of the results of univariate analysis of prognostic factors that might influence late complication rate. There was no statistically significance in multivariate analysis.

Discussion

Although radical surgery is the treatment of choice for uterine sarcomas, different surgical procedures may be used. Initial diagnosis before surgery is the main factor responsible for the diversity of surgical procedures. The clinical symptoms of uterine sarcomas are nonspecific like abnormal vaginal bleeding [17]. This situation may be confused with myoma uteri especially in young women. In our study, 25 (41.7%) patients were initially diagnosed by ultrasonography as having myoma uteri. Therefore, some of the patients may have diagnosis of malignancy with pathological specimens after surgery. Consequently, this had caused the use of different types of surgical procedures [18-20].

One of the other major problems is the presence of occult metastatic pelvic disease and distant metastasis, even in early stages. Yamada et al. [18] found that most of the recurrences were extrapelvic. Presence of occult metastatic disease was reported as 61% (38/62 patients). In the study by Soumarova et al. [21] local recurrence rate was 24.5%, and haematogenous metastasis rate 14.3%. Extrapelvic metastatic rate was reported as over 40% in the Chi et al. study [2].

The role of adjuvant RT has not been clearly defined in a prospective randomized trial. However, several retrospective studies have demonstrated that adjuvant

pelvic RT favorably affects tumor control in the pelvis for uterine sarcomas except leiomyosarcoma [3-7, 21-24]. This favorable effect is greater in high grade sarcomas [6]. In a review of 24 previously published series with uterine sarcomas by Rovirosa et al. [24], RT was administered to 44% of 2528 patients. Irrespective of the impact of RT on survival, increased local control was reported as similar in both of these groups. Two reports by Livi and colleagues [4,23] investigated the prognostic factors and treatment outcome of patients with uterine sarcoma. Both of these studies showed statistically significant reduction in local recurrence with postoperative RT ($p=0.001$), but without prolongation of survival [4,23]. After 3 years, local recurrence rates were 23, 40, and 70% for patients who had received external pelvic RT plus intracavitary irradiation, external pelvic RT only, and no RT, respectively [23]. An epidemiological study has determined that women with disease beyond the uterus who had received RT had significantly improved survival compared with those treated with surgery alone [22]. In our study, the number of patients with disease confined to the corpus was higher than those with advanced disease, as in the Gerstzen et al. study [8]. This situation may lead to higher survival and local control rates. Some authors suggest using RT only for extensive disease beyond the uterus [22,24]. Despite this view, addition of adjuvant RT after surgery is recommended for uterine sarcomas, even in stage I disease, in order to reduce local recurrence rate [4,8]. In the study by Soumarova et al. RT had a favorable impact on local control, DFS and OS [21]. Five-year OS was 88.9 and 51.6% with and without RT ($p=0.0066$). Our results coincide with the literature: 10-year PC and OS rates were 84 and 61.5%, respectively. Some of the results of the studies discussed above are summarized in Table 6.

Another controversial problem for sarcomas is whether to add intracavitary RT (ICRT) to external beam RT (EBRT) or not. A study by Chi et al. [2] reported that the addition of ICRT to EBRT did not succeed in reducing pelvic recurrences. In this group of patients there was no vaginal recurrence; meanwhile there was only one vaginal recurrence in the surgery-alone group; therefore the necessity of additional treatment may need to be reconsidered [2].

The Gynecologic Oncology group performed the only published prospective randomized trial on adjuvant chemotherapy with stage I-II patients; there was no statistically significant difference in local control, PFS or OS. In those patients RT was optional and did not influence the outcome either [9]. In a study at Churchill hospital in Oxford, the authors mentioned that only a small group of patients (11 of 47) with stage I and II disease, good performance status and stage III

Table 6. Summary of the results of past studies

<i>First author</i>	<i>Type of surgery</i>	<i>Histology</i>	<i>Adjuvant therapy</i>	<i>Pelvic control (PC) or local recurrence (LR)</i>	<i>Disease free survival</i>	<i>Overall survival</i>
Riddle [3]	Mixed	LMS, MMT	RT ± CT			30-55%, only surgery vs. adjuvant (2 yr)
Livi [23]	Mixed	All	RT ± CT	LR (3 yr): 23% - RT and IC 40% - IC 70% - Surgery alone		39% (3 yr) 20% (10 yr)
Dinh [19]	TAHBSO	LMS	RT ± CT			65% (2 yr)
Chi [2]	Mixed	MMT	RT	LR: 50% - no RT 21% - RT		Stage I-II 62% Stage III 50% No difference between groups
Livi [4]	Mixed	All	RT ± CT	LR (5 yr): CT - 85% Surgery - 57% RT - 30%		41.8 - 27.7% (3 vs. 5 yr)
Knocke [5]	Mixed	All	RT	PC: 77.9% (5 yr)		52.3% (5 yr)
Soumarova [21]	Mixed	All	RT ± CT	LR: 24.5%	57.9% (2 yr)	51.6-88.9%, no RT vs. RT (5 yr)
Our study	Mixed	All	RT ± CT	PC: 84% (10 yr)	64% (10 yr)	61.5% (10 yr)

TAH: total abdominal hysterectomy, TAHBSO: total abdominal hysterectomy+bilateral salpingo-oophorectomy, Mixed: TAH, TAHBSO, radical hysterectomy, debulking surgery and other extended operations, All: ESS, MMT, LMS and other, RT: radiotherapy, CT: chemotherapy, IC: intracavitary brachytherapy, LMS: leiomyosarcoma, MMT: mixed müllerian tumor, ESS: endometrial stromal sarcoma

patients with complete disease surgical removal, had encouraging results with adjuvant chemo-radiotherapy [3]. Tore et al. [11] had published the results of their series including 41 patients. There were two treatment arms: pelvic RT group with 23 patients and pelvic RT plus chemotherapy group with 18 patients. The 3-year survival rates of the two adjuvant treatment arms were 36 and 66%, respectively. This difference was statistically significant.

Our experience with chemotherapy was very limited. In our series, only 4 patients were treated with adjuvant chemotherapy and this small number is not enough to make a conclusion on the impact of chemotherapy.

Although a lot of possible prognostic factors were studied, stage is still the most important prognostic factor for local control and or survival [1,3,4,6,8,18,21,23,25]. Even though gross residual disease, presence of extra-uterine extension, deep myometrial invasion, and vascular space invasion were found as independent prognostic factors of mortality [1,7,18,24], these factors are tightly related with stage. Similar results were found in our study; stage and gross residual disease were strongly associated with poor survival. Ten-year OS rate was 78.1% for stage I disease and 24.3% for stage III disease ($p=0.001$). Yamada et al. [18] reported that 5-year survival rates were 74 and 24.3% in patients with disease confined to the corpus and patients with more advanced disease, respectively ($p=0.0013$).

Some studies revealed that, with respect to histology, LMS has a poorer prognosis, while ESS and MMT show a slightly better prognosis [4,26,27]. Prognosis of MMT depends on whether they are of heterologous or homologous subtype [28-30]. In our series 11 of 17 MMT were of homologous subtype, 4 were heterologous and in 2 the subtype was not defined; whether homologous or heterologous, no impact on survival was noted. Some authors suggest that MMT predicts the worst prognosis, followed by LMS and ESS [23]. On the other hand, Olah et al. [27] reported that LMS had poorer prognosis than MMT when adjusted for other known prognostic factors. This data was supported by the findings of other authors afterwards [4,28]. Our results showed that ESS had the best prognosis followed by LMS and MMT. This may be explained by the higher number of stage I disease with LMS (66%) than stage I MMT (41%).

Different series had previously reported the importance of tumor size as prognostic factor; bigger tumor size is the forerunner of bad prognosis [31-33]. Tumor size >8 cm was reported as a poor prognostic factor for early-stage uterine sarcomas [24]. In our series tumor size was not correlated with survival or local control.

In our series we also analyzed the difference between the patients who were treated within 36 days vs. those treated >36 days after surgery and no major difference was noted, similarly to Livi et al. study [4]. We

noticed that the pelvic treatment duration (≤ 46 days vs. > 46 days) also did not influence the local disease control and survival. Age was shown as prognostic factor in previous studies [4], yet in our study age had significant prognostic value only for PC rate ($p=0.05$).

None of our patients suffered from permanent toxicity. All symptoms were transient and treated very well with symptomatic medication. Comparing with the literature our patients had slightly higher skin erythema ratio [4,23]. We observed mild late complications in most of our patients; unfortunately one patient developed grade 4 proctitis and was treated successfully with surgery. Analysis of late complications showed that treatment duration >46 days and pelvic dose ≥ 54 Gy had statistically significant effect on late complications. In the literature, some authors have reported a correlation between acute side effects and late complications during pelvic RT [34,35]. Similarly, in the present study presence of acute side effects, boost dose, intracavitary RT and 1.8 Gy fraction dose had an impact on late complications but without reaching statistical significance.

Conclusion

In our series, all of the patients were treated with postoperative RT and the 10-year PC and OS rates were 84 and 61.5%, respectively. For PC age, residual disease, type of surgery and stage; for DMFS residual disease, type of surgery and stage; for DFS stage; for OS stage and type of surgery were significant prognostic factors.

Although our results were similar with the literature and suggest improved PC and survival in these patients with acceptable toxicity, the role of postoperative RT should be tested in prospective multicentric trials.

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