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Uterine sarcoma – A retrospective analysis of 19 years experience from a tertiary care centre in south India

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Abstract:
Aim: *Retrospective analysis of uterine sarcomas to identify the histological type , prognostic factors, adjuvant treatment and their outcome.*
Materials and Methods*: From 1991 to 2009, 55 uterine sarcomas were treated in the Department of Medical Oncology at Institute of Obstetrics and Gynecology Chennai. This series consists of 27(49%) malignant mixed mullerian tumors (MMMT) , 16(29%) leiomyosarcoma (LMS); and 12(22%) endometrial stromal sarcoma (ESS). The median age is in 55years. In 53% of patients ,the presenting symptom was abnormal uterine bleeding .Twenty (36.4%) of patients were in stage I, 4(7.3%) in stage II, 18(32.7%) in stage III and 7 (12.7%) in stage IV according to International Federation of Gynecology and obstetrics(FIGO-1989) system. Patients were treated with hysterectomy followed by either chemotherapy or radiotherapy or both. The median follow up period was 17.5 months.*
Results: *Histological type, grade and FIGO stage were identified as the most significant independent prognostic factors in univariate analysis . The median overall survival was 20 months and median disease-free survival was 10.5 months. 5-year survival rate was 38%. Women with low grade ESS were found to have better survival than high grade ESS, MMMT and LMS .*
Conclusion: *The incidence of uterine sarcoma in our hospital was 23.5%(55/234) of uterine malignancies during the study period. The most common histology was malignant mixed mullerian tumors. In comparison to LMS and MMMT , low grade ESS tends to present as a less aggressive disease with favorable outcome. The treatment was mainly hysterectomy, post operative treatment with radiotherapy and chemotherapy had no demonstrable impact on overall survival.*
Keywords: *Malignant mixed mullerian tumors , Leiomyosarcoma ; Endometrial stromal sarcoma, Uterine sarcoma, FIGO.*

I. Introduction

Uterine sarcomas represent a heterogeneous tumor group comprising of several histologic types originating from the mesenchymal tissues of the uterus, including the endometrial stroma, uterine muscle, and supporting tissue. The most frequent types are carcinosarcoma (formerly known as malignant mixed mullerian tumor), leiomyosarcoma (LMS), and endometrial stromal sarcoma (ESS), in the order of decreasing incidence. These variants in combination account for over 90% of all uterine sarcomas. Uterine sarcoma represents 1–3% of all the female genital tract malignancies and 3–5% of uterine malignancies[1,2], however recent reports [3,4,5] suggests that the incidence of uterine sarcoma is increasing and may constitute up to 8% of all uterine malignancies. Despite its rarity uterine sarcoma is the most malignant tumor uterine tumor and is generally associated with worse outcomes than carcinomas.

Published literature on uterine sarcoma is sparse due to rarity and pathological heterogeneity, both precluding conduct of prospective studies or randomized trials to assess the effect of therapy. Therefore, no standardized treatment for any histologic type has yet been established. Recently, the International Federation of Obstetrics and Gynecology (FIGO) established a staging system unique to each histologic type [6].Two major changes recently occurred in the way in which uterine sarcoma is viewed. The first was the development of a new FIGO staging system for uterine sarcoma. Previously, uterine sarcoma had been surgically staged with reference to the FIGO staging system for endometrial adenocarcinoma, regardless of histologic type [7]. However, studies [8,9,10] seeking to validate the FIGO staging system have suggested that an independent system is required for each of the major histological sarcoma types. Therefore, new FIGO staging systems were developed for LMS and ESS in 2009 [6] (**Table 1),** despite these changes carcinosarcoma continues to be staged similar to the FIGO system for endometrial adenocarcinoma [6].

The second major change is a new interpretation of the pathogenesis and the logical classification of carcinosarcoma and ESS. Recent studies have suggested that carcinosarcoma is monoclonal in origin, with the sarcomatous component representing dedifferentiation of the carcinomatous component, with the latter element driving the tumor [11]. ESS has been traditionally divided into low and high grade ESS according to morphology, mitotic activity, cellularity, and the presence of necrosis. Recent findings have suggested, however,

that these variants are rather two separate entities. Low-grade ESS is a hormone-sensitive low-grade malignancy with an indolent course, while high-grade ESS is characterized by an aggressive clinical course that cannot be differentiated from that of other high-grade uterine sarcomas such as LMS and carcinosarcoma. High-grade ESS tumors do not demonstrate endometrial stromal differentiation or estrogen or progesterone receptor expression. Thus, it has been suggested that high-grade ESS should be classified as an undifferentiated or poorly differentiated endometrial sarcoma rather than included in the category of ESS, and that only low-grade ESS should be classified as ESS [12,13].

II. Patients and methods

In this study, we retrospectively analyzed 55 patients, who were treated at department of Medical Oncology, Government Hospital for women and children & Institute of Obstetrics and Gynecology, Chennai, between January 1991 and December 2009. This hospital is a major tertiary referral centre for the management of Gynecological malignancies in south India. Patient records, surgical reports, pathological reports and follow data from the clinical archives were examined. We used International federation of Gynecology and Obstetrics (FIGO) staging 1989 for Endometrial Adenocarcinoma . Most of the patients were scheduled for post-operative follow-up every 1 – 3months for 2 years and thereafter for every 6 months. We evaluated the general features, treatments applied and the survival of 50 patients and 5 patients (MMMT-4,LMS-1) were excluded from the study due to insufficient follow up details.

In order to evaluate prognostic factors, and assess the outcome according to treatment, study endpoints included recurrence and overall survival. Disease free survival (DFS) as well as overall survival (OS) was defined as the time from the date of diagnosis (date of surgery - histopathological confirmation) until date of recurrence or death, respectively. Initial univariate analysis associated with overall survival was performed using the Kaplan Meier method. The log rank test was used to compare survival curves. SPSS (Statistical Package for Social Sciences) for Windows 10.0 program was used for statistical analyses. P-values <0.05 were considered to be statistically significant.

III. Results

During the period of study, 55 cases of uterine sarcomas were treated. The hospital-based incidence of the disease was 23.5% (55/234) of uterine malignancy patients admitted. Patient, tumor and treatment characteristics are as given in **table 2.** The median age of the patients were 55 (range, 25-66) years. Twenty two patients (40%) were under 50 years of age and 33 (60%) were above 50. The two most frequently presenting symptoms were abnormal uterine bleeding and abdominal pain. Only nine (16.4%) patients were diagnosed pre –operatively by curettage.

Malignant Mixed Mullerian Tumors (MMMT)

The mean age of the 27 MMMT patients were 55.4 (range,45 - 66)years. They were distributed as 25 Carcinosarcoma (Heterologous- 6, Homologous-19) and 2 Adenosarcoma patients. There was one patient with a history of pelvic radiotherapy for carcinoma cervix and developed carcinosarcoma after 5 years. Only 4 patients were diagnosed pre-operatively. FIGO 1989 staging distribution were stage I -11, stage II-3, stage III-9, stage IV-3 and stage unknown in one patient. Twenty one MMMT patients underwent TAH & BSO and 6 patients had sub optimal surgery (STH&BSO -2, VH & BSO -1, VH 1, BIOPSY alone 2). Post operatively 15 patients received chemotherapy alone, 4 patients radiotherapy alone and 2 patients chemoradiotherapy. Six patients did not receive any post operative treatment. Four MMMTpatients excluded from the study due to insufficient data. The median overall survival was 26 months. Five patients developed disease progression (3 pelvic, 2 distant sites) during treatment. Eight patients developed recurrence (5 pelvic, 3 distant sites) after completion of treatment. Only 17.3 % (4/23) patients were alive. All 4 patients were in stage I, among them 2 patients treated with TAH &BSO alone , 2 patients had TAH & BSO + post op Radiotherapy.

Leiomyosarcoma (LMS)

The mean age of the 16 LMS patients were 47 (range, 28- 60)years. FIGO staging distribution was stage I -2, stage II -1, stage III -7, stage IV -2 and stage un known in 4 patients. Only 3 patients were diagnosed pre-operatively. Thirteen LMS patients underwent TAH & BSO and 3 patients had sub optimal surgery (STH&BSO -2, BIOPSY alone 1). Post operatively 10 patients received chemotherapy alone, 1 patient radiotherapy alone and 1 patient received chemoradiotherapy after development pelvic recurrence. Four patients did not receive any post operative treatment. One LMS patient excluded from the study. The median overall survival was 14 months. Three patients developed disease progression (1 pelvic, 2 distant sites) during treatment. Six patients developed recurrence (4 pelvic, 1 distant, 1 pelvic and distant sites) after completion of treatment. Only 26.7 % (4/15) patients were alive.

Endometrial Stromal Sarcomas (ESS)

The mean age of the 12 ESS patients were 45 (range, 25- 59)years. In ESS 8 patients were low grade and 4 patients had high grade histology. In low grade ESS 7 patients had FIGO stage I disease and were treated with surgery alone. All low grade ESS were alive without any recurrence at the time of analysis. One patient with undesignated stage developed local recurrence after 43 months and was subsequently salvaged with excision and radiotherapy. The same patient had a second local recurrence after 22 years and she lived for a total of 27 years after diagnosis. The median overall survival for low grade ESS was 324 months.

In the 4 undifferentiated uterine sarcoma (High grade ESS) patients, FIGO staging distribution was stage III -2 and stage IV 2 patients respectively. They were treated with surgery and chemotherapy. One patient in stage III developed pelvic recurrence after 84 months. All 4 patients died and the median overall survival for high grade ESS [UUS] was 9 months.

Treatment Outcome

Total abdominal hysterectomy and bilateral salpingo- oophorectomy [TAH & BSO] remains the standard surgical care. Lymph node dissection is indicated for carcinosarcomas given their high incidence of lymph node metastases. Eighty percent [44] patients were underwent TAH & BSO, 20%[11] were treated by suboptimal surgical procedures like biopsy alone 3, subtotal hysterectomy and bilateral salpingo- oophorectomy [STH &BSO] -6, vaginal hysterectomy -1 and vaginal hysterectomy and bilateral salpingo- oophorectomy [VH &BSO] -1. Lymph node dissection was carried out only in 3 early stage [I,II] MMMT patients. Fourty eight patients received adjuvant therapy with 29 receiving chemotherapy, 6 receiving radiotherapy and 3 receiving chemotherapy and radiotherapy. The criteria for adjuvant therapy of uterine sarcoma was on the discretion of the gynaecologic oncologist. In most cases, chemotherapeutic regimens included cisplatin, cyclophosphamide and Adriamycin or vincristine.

After a mean follow-up time of 17.5 months [range from 2 to 127 months] 25 patients had recurrent disease. Fifteen patients were diagnosed with pelvic recurrence, 8 patients with distant metastases and 2 patients with pelvic and distant metastases **[Table 3].** Recurrent disease was treated with chemotherapy in 6 patients, radiotherapy in 2 patients and chemotherapy and radiotherapy in one patient. Two patients refused treatment at the time of recurrence. At the time of our analysis, 35 patients had died from disease ,14 patients were living without disease, and one patient living with disease. The 1- ,2- and 5 year DFS rates were 58.2%, 53% and 40.9% respectively. The median DFS rate was 10.5 months [range, 2 -148 months]. The 1- ,2- and 5 year OS rates were 60%, 51.6% and 30.8% respectively. The median OS rate was 20 months [range, 4- 324 months] figures **1 & 2.**

Patients had significantly longer DFS and OS when tumor cells were completely removed during surgery, when compared with patients who still had residual tumor cells following surgery. No differences in DFS and OS were observed between patients who received adjuvant therapy and who did not receive adjuvant therapy. DFS and OS outcomes were not influenced by adjuvant therapy modality (chemotherapy, radiation therapy or chemoradiation therapy); and these results held true when each of the histologic subtypes were analyzed separately, **Figures 3& 4**.

Prognostic Factors

The results of univariate analyses of the relationships between prognostic variables and survival are summarized in **Table 4**. Histological type ESS and FIGO stage I [$p < 0.0001$] were significantly associated with good disease free survival and overall survival . Advanced FIGO stage , high grade ESS, LMS and MMMT histological types had poor DFS and OS**.[figure 5 & 6**]. Age and menopausal status had no impact on DFS and OS [p- 0.9582] . In our series mitotic index [MI] of 24 [43.6 %]patients are known among them 14 patients MI < 10/HPF , 10 patients MI >10/HPF. Even though the patients with MI < 10/ HPF had better overall survival than MI >10/HPF [$p <0.0001$] , it is difficult to consider one of the prognostic factor due to the status of the mitotic index of the 31[56.4%] patients were not known.

IV. Discussion

Uterine Sarcomas are rare tumors arising from the mesenchyme. Only little is known about the epidemiology of uterine sarcomas [2]. They account for 3-7% of all uterine malignancies [1]. In one of the major retrospective series ever published including 423 cases of uterine sarcoma between years 1967-1981 Olah et al. has reported one uterine sarcoma case for every 11 uterine adenocarcinoma [14]. In our series uterine sarcomas composed 23.5%(55/234) i.e 1 in 5 of all uterine malignancies. A decade ago, worldwide reports ranked LMS as the most common histologic subtype [15,16,17] but more recent data revealed MMMT as the most common, followed by LMS and ESS. [18-20]. In this series the most frequent histological type noted was (49.1%) MMMT which is comparable with the recent literature.

Most reports revealed a mean age of 55 - 60 years among patients with uterine sarcomas. (17,18,22) Mean age for LMS patients is usually around 45 - 55 years which is 10 - 15 years younger than MMMT patients. (16,17,20,22) . In our series the median age for MMMT, LMS and ESS were 57, 48, and 44 years respectively. A previous pelvic irradiation history is reported in 2-14% of patients with uterine sarcoma, notably with a higher ratio in those with MMMT [1]. Recently the incidence is 0 - 29%. [16,22, 23,) We had one patient with such history in our series. She developed carcinosarcoma 5 years after pelvic radiotherapy for carcinoma cervix. The two most frequently presenting symptoms are abnormal uterine bleeding and abdominal pain, a pattern noted in the present series as well. Reported percentage of preoperative diagnosis in the literature is 30 – 44%, [17,24] but it was only 16.4% (9/55) in our study.

Surgical Treatment

Surgical treatment of MMMT [Carcinosarcomas (CSs)] includes exploratory laparotomy, total abdominal hysterectomy (TAH), bilateral salpingo-oophorectomy (BSO), omentectomy, aspiration of abdominal fluid for cytologic evaluation, pelvic and para-aortic lymph node dissection and tumor debulking at the time of presentation [25- 30]. Lymph node dissection is indicated for CSs given their high incidence of lymph node metastases [20,31,32]. For LMS total abdominal hysterectomy and bilateral salpingooophorectomy is considered to be the standard surgical treatment [2,25,26,27,33]. Contrary to CS, pelvic and/or para-aortic lymphadenectomy is not indicated for LMS, unless macroscopic extra-uterine disease is present; due to the low rates of negative nodes and the fact that the dominant pattern of recurrence in LMS is outside the pelvis and the abdominal cavity [26-28, 33]. Surgical treatment of ESS typically includes an exploratory laparotomy, total abdominal hysterectomy and bilateral salpingo-oophorectomy, omental biopsy, and aspiration of abdominal fluid for cytologic evaluation [25,26, 34-37]. Lymph node sampling is not the standard of care, as nodal involvement by low-grade ESS is supposed to be rare [25]. The treatment of choice for undifferentiated uterine sarcomas(High grade ESS) is total abdominal hysterectomy and hysterectomy [25- 29]. There are no data in the literature to support or challenge lymph node dissection.

In our series 84% (42/50) of patients underwent TAH & BSO. Among them only 3 carcinosarcoma patients underwent omentectomy, aspiration of abdominal fluid for cytologic evaluation, pelvic and para-aortic lymph node dissection along with TAH & BSO. Thirty one percent (13/42) patients (Low grade ESS 1, High grade ESS 1, LMS 5, MMMT 6) developed pelvic recurrence. Eight (16%) patients (High grade ESS 2, LMS 2, MMMT 4) underwent sub optimal surgeries like subtotal hysterectomy (STH) ,vaginal hysterectomy (VH) with or without bilateral salpingo-oophorectomy (BSO). Local recurrence was high 62.5% (5/8) in patients with suboptimal surgery.

Adjuvant treatment

One of the major difficulties in assessing the value of adjuvant therapy is that the majority of the studies published do not have the statistical power to evaluate the role of adjuvant therapy on different histological subtypes individually. However, as indicated above, the subtypes seem to differ not only in terms of prognosis, but also in terms of their response to adjuvant treatment.

Radiation Therapy

Historically, treatment for uterine CSs has included adjuvant pelvic radiation therapy with or without brachytherapy [25]. Until 2007, no well-controlled, randomized studies had been published, and most reports were based on small non-randomized trials [32 38,39]. The best conclusion that could be drawn from these reports is that the routine place of adjuvant pelvic radiation was limited as it only led to a statistically significant reduction of recurrences within the radiation field, and did not confer an overall survival advantage[32,38-40]. In a retrospective analysis of 2461 women with uterine CSs within the SEER (Surveillance, Epidemiology, and End results program) database of the US National Cancer Institute, radiation therapy predicted an improved overall and disease specific survival [32/ 41]. Five-year overall survival rates were 41.5% and 33.2% ($p < 0.001$) for women receiving or not irradiation, respectively. More analytically, women with stage I-III disease experienced a benefit in overall survival (hazard ratio = 0.87, $p = 0.03$), while those with stage IV disease experienced benefit in both overall (HR = 0.63, $p < 0.001$) and uterine-specific survival (HR = 0.63, $p = 0.004$).

In the mid-1980s, the European Organization for Research and Treatment of Cancer (EORTC) Gynecological Cancer Group proposed a trial to evaluate adjuvant radiotherapy in stage I+II uterine sarcomas (protocol 55874). The study opened in 1987 taking 13 years to accrue 224 patients and its results were first published in 2008. Patients were required to have undergone as a minimum, TAH and BSO and washings, but nodal sampling was optional. There were 103 LMSs, 91 CSs and 28 ESSs. Patients were randomized to either observation or pelvic radiation, 51 Gy in 28 fractions over 5 weeks. Analysis for all patients revealed a reduction in local relapse ($p = 0.004$), but no effect on either OS or PFS. Furthermore, no difference in either

overall or disease-free survival was demonstrated among CS patients but there was an increased local control for those receiving radiation, while this benefit was not observed for women with LMSs.

Adjuvant radiation therapy is effective treatment for patients with ESS due to excellent local control in all stages and good disease-specific survival in early stages [36, 37]. Adjuvant radiation therapy clearly reduces the incidence of pelvic recurrence; however, in the majority of the studies conducted it has no effect on OS [37, 41-44]. Radiation therapy is typically recommended for stage I and II UUSs [25, 26,43]. However, concern regarding distant recurrences has led to the consideration of combining irradiation with chemotherapy.

In our series only 6 patients (Early stage MMMT 5, Late stage LMS 1) received adjuvant external beam radiotherapy (EBRT) of 50 Gy at 200cy per fraction. Two patients (Low grade ESS 1, MMMT 1) received palliative EBRT after development of pelvic recurrence. Among the 5 early stage MMMT , one patient developed pelvic recurrence even after post op adjuvant radiotherapy. We cannot conclude that radiotherapy can reduce the local recurrence rate as only a small number of the patients in this series received radiotherapy.

Chemotherapy

The high incidence of distant metastasis in uterine sarcomas makes adjuvant chemotherapy an appealing option. Although adjuvant chemotherapy has been studied in a number of trials, considerable controversy still surrounds its use. The question is whether or not adjuvant chemotherapy can achieve a significant increase in disease-free and overall survival without major treatment-related toxicity. It should be noted, that due to the rarity of uterine sarcomas, very few prospective randomized studies have been conducted. Also, the non randomized clinical-trial reports often include a broad range of histological subtypes, which restricts interpretation and application of results.

In a recently published retrospective analysis, 49 women with completely resected stage I-IV CSs received in the adjuvant setting either platinum-based chemotherapy with or without radiation therapy (pelvic or WAI), or radiation therapy alone. Three-year PFS for chemotherapy group (with or without radiation therapy) was 35% versus 9% for radiation therapy alone (HR = 1.74, p = 0.164), while the corresponding 3-year OS rates were 66% and 34%, respectively (HR = 2.02, p = 0.146) [46] interestingly, the majority of patients in the chemotherapy group were treated with paclitaxel and carboplatin [47]. In LMS - No adjuvant treatment has been shown to improve survival, although prospective data are limited. However, in a small phase II study, four cycles of adjuvant chemotherapy with gemcitabine and docetaxel in patients with completely resected stage I-IV, high-grade uterine LMSs resulted in 2-year PFS rates that appear superior to historical rates.[48]

Low-grade endometrial stromal sarcomas are estrogen and progesterone receptor positive tumors [49,50]. In the past, hormonal therapy consisted of progestins for advanced, recurrent or metastatic low-grade ESS. Medroxyprogesterone acetate (MPA) and megestrole acetate are synthetic derivatives of progesterone that exert their activity after binding to the progesterone receptor [51]. Aromatase inhibitors [52- 55] and GnRH analogues [56-58] have become new effective alternatives for first and second line treatment. The high recurrence rates after short disease free intervals in low-grade ESS patients were partly due to inadvertent growth stimulation during estrogen-containing hormone replacement therapy and tamoxifen treatment, which are contraindicated [55,59,60]. Recently, hormonal therapy has been introduced for the prevention of recurrences. However, it should be noted that well controlled randomized studies on ESSs have not been conducted and the majority of the results reported are based on small series. Undifferentiated Uterine Sarcomas (UUSs) -Hormonal therapy plays no role for UUSs due to the lack of steroid receptor expression.

In our study, only 26 patients received adjuvant chemotherapy, 6 patients received palliative chemotherapy. Eight patients developed distant recurrence during chemotherapy(MMMT 4, LMS 4) .Impact of chemotherapy in overall survival, we cannot come to any conclusions due to over the 19 years, different chemotherapy regimens combination with cisplatin, cyclophosphamide and doxorubicin/vincristine and variable number of cycles (1 – 6 cycle) were used. In addition hormone receptor status was not studied and hormonal therapy was not given to our patients.

Combination of radiation therapy and chemotherapy

Combined adjuvant therapy using radiation therapy and chemotherapy may also be effective in patients with uterine sarcoma. For example, a pilot study [61] of 38 patients with early-stage carcinosarcoma found that combined adjuvant therapy administered in a 'sandwich' technique (sequence of chemotherapy–radiation therapy–chemotherapy) was well tolerated and showed a survival benefit greater than that in patients who did not receive the combined treatment (OS rate, 97 vs. 47%, P¼0.01). In a retrospective analysis [62] of 49 patients with carcinosarcoma, the highest survival rate was observed in those who received sequential adjuvant therapy including chemotherapy followed by pelvic radiation therapy. In our series 2 MMMT patients received sequential chemotherapy and radiation therapy. One LMS patient received combination therapy after development of pelvic recurrence is still alive at the time of analysis.

Figures and Tables

Table 1 Stage for uterine sarcoma (leiomyosarcomas, endometrial stromal sarcomas, adenosarcomas, and carcinosarcomas)

Stage	Definition
Leiomyosarcomas	
I	Tumor limited to uterus
IA	<5 cm
IB	>5 cm
II	Tumor extends to the pelvis
IIA	Adnexal involvement
IIB	Tumor extends to extrauterine pelvic tissue
III	Tumor invades abdominal tissues (not just protruding into the abdomen)
IIIA	One site
IIIB	>one site
IIIC	Metastasis to pelvic, paraaortic lymph nodes, or both
IV	Tumor invades bladder, rectum, or both
IVA	
IVB	Distant metastasis
Endometrial stromal sarcomas and adenosarcomas[a]	
I	Tumor limited to uterus
IA	Tumor limited to endometrium/endocervix with no myometrial invasion
IB	Less than or equal to half myometrial invasion
IC	More than half myometrial invasion
II	Tumor extends to the pelvis
IIA	Adnexal involvement
IIB	Tumor extends to extrauterine pelvic tissue
III	Tumor invades abdominal tissues (not just protruding into the abdomen)
IIIA	One site
IIIB	>one site
IIIC	Metastasis to pelvic, paraaortic lymph nodes, or both
IV	Tumor invades bladder, rectum, or both
IVA	
IVB	Distant metastasis
Carcinosarcomas	
Carcinosarcomas should be staged as carcinomas of the endometrium	

[a] Simultaneous tumors of the uterine corpus and ovary/pelvis in association with ovarian/pelvic endometriosis should be classified as independent primary tumors.

Table 2. Patients, tumor and treatment characteristics

Characteristics	Mmmt(N=27)	Lms(N=16)	Ess(N=12)	Total(N=55)
Patients Characteristics				
Age,Years Mean(Range)	55.4(45-66)	47(28-60)	45(25-59)	51.4(25-66)
Menopause,N(%) Yes	25	8	5	38(69.1%)
No	2	8	7	17(30.9%)
Prior Pelvic Radiotherapy N,(%)	1	0	0	1(1.8%)
Previous Cancer	1	0	0	1(1.8%)
Presenting Symptoms N,(%)				
Vaginal Bleeding	17	5	7	29(52.3%)
Abdominal Pain	11	9	7	27(49.1%)
Pelvic Mass	7	5	4	16(29.1%)
Leucorrhea	7	2	1	10(18.2%)
Tumor Characteristics				
Figo Stage N,(%)				
I	11	2	7	20(36.4%)
Ii	3	1	0	4(7.3%)
Iii	9	7	2	18(32.7%)
Iv	3	2	2	7(12.7%)
Not Known	1	4	1	6(10.9%)
Mitotic Index N,(%)				
<10	1	5	8	14(25.4%)
>10	2	4	4	10(18.2%)

Not Known	24	7	0	31(56.4%)
Treatment Characteristics				
Pre Operative Diagnosis - Known	4	3	2	9(16.4%)
Not Known	23	13	10	46(83.6%)
Treatment Surgery -				
Biopsy Alone	2	1	0	3(5.4%)
Vh	1	0	0	1(1.8%)
Tah &Bso	21	13	10	44(80%)
Sth &Bso	2	2	2	6(11%)
Vh &Bso	1	0	0	1(1.8%)
Adjuvant Therapy				
Not Done	6	4	7	17(30.9%)
Chemotherapy	15	10	4	29(52.7%)
Radiotherapy	4	1	1	6(11%)
Chemoradiotherapy	2	1	0	3(5.4%)

VH-Vaginal hysteretcomy, TAH- Total abdominal hysterectomy , STH- Subtotal hysterectomy BSO – Bilateral salpingo- oophorectomy

Table 3 Disease progression and recurrence

	MMMT(n=23)	LMS(n=15)	ESS(n=12)	TOTAL(n=50)
Progression during treatment(total)	5	3	1	9(18%)
Pelvic	3	o	1	4
Distant site	2	2	0	4
Pelvic +Distant sites	0	1	0	1
Recurrence after treatment(total)	8	6	2	16(32%)
Pelvic	5	4	2	11
Distant site	3	1	0	4
Pelvic +Distant sites	0	1	0	1
Distant sites				
Lung	2	3	0	5(10%)
Liver	5	1	0	6(12%)
Left supra clavicular lymph node	0	1	0	1(2%)
Para aortic lymph nodes	2	0	0	2(4%)
Multiple sites	2	0	0	2(4%)

Table 4. Univariate log rank survival analysis(n=50)

Group	Alive(%)	Dead/Total	Median Survival (Months)	Df	P-Value	Survival Improved In
Histologial Type				2	0.0399	Ess
Mmmt	4(17.3%)	19/23	26			
Lms	4(26.7%)	11/15	14			
Ess	7(58.3%)	5/12	324			
Total	15(30%)	35/50				
Stage				4	<0.0001	Stage I
I	12(62.3%)	7/19	150			
Ii	1(25%)	3/4	11			
Iii	1(6.6%)	15/16	8			
Iv	0%	6/6	4			
Nk	1(20%)	4/5	37			
Age				1	0.9582	No Difference
<50	7(41.2%)	10/17	20			
>50	8(24.2%)	25/33	28			
Mitotic Index				1	0.0001	<10
<10	10(76.9%)	3/13	324			
>10	0%	10/10	7			
Menopausal Status				1	0.9582	No Difference
Pre	7(41.2%)	10/17	20			
Post	8(24.2%)	25/33	28			
Treatment				3	0.0018	Surgery Alone
Surgery Alone	10(76.9%)	3/13	127			
Surgery+Ct	2(7.1%)	26/28	11			

Surgery+Rt	2(33.3%)	4/6	48
Surgery+Rt+Ct	1(33.3%)	2/3	27

Fig 1 Kaplan-Meier overall survival curve.

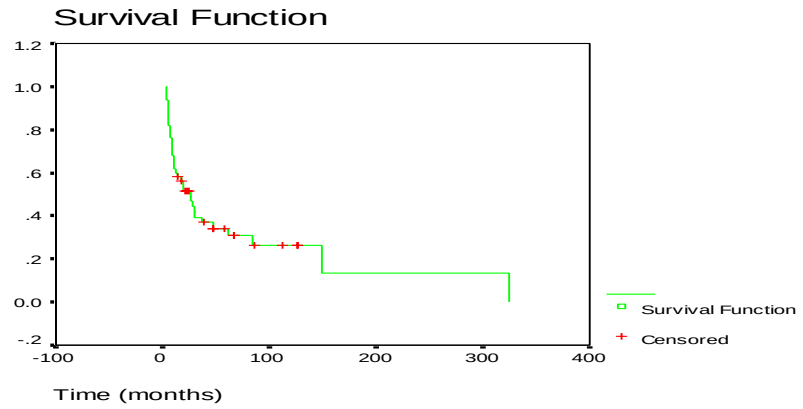


Fig 2 Kaplan-Meier disease free survival curve

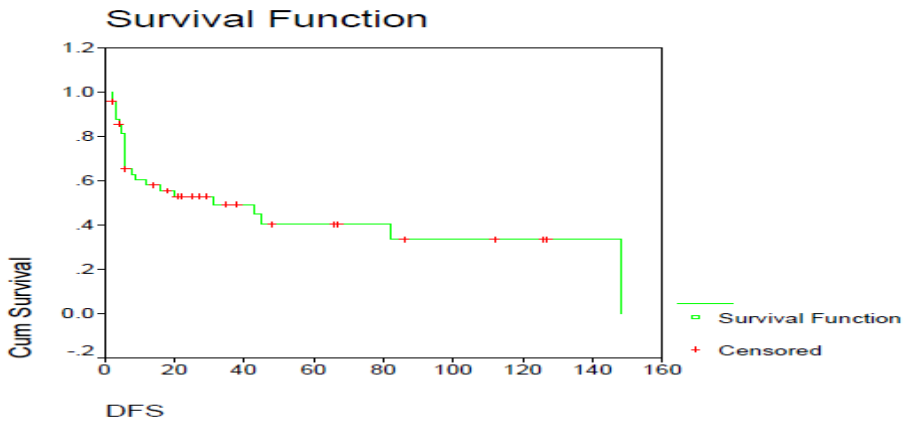


Fig 3.Kaplan-Meier OS curve (Adjuvant treatment)

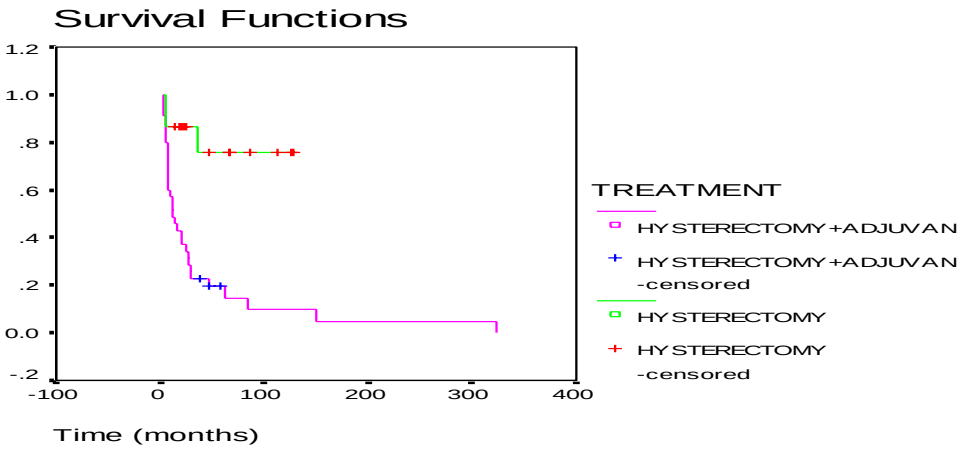


Fig 4. Kaplan-Meier DFS curve (Adjuvant treatment)

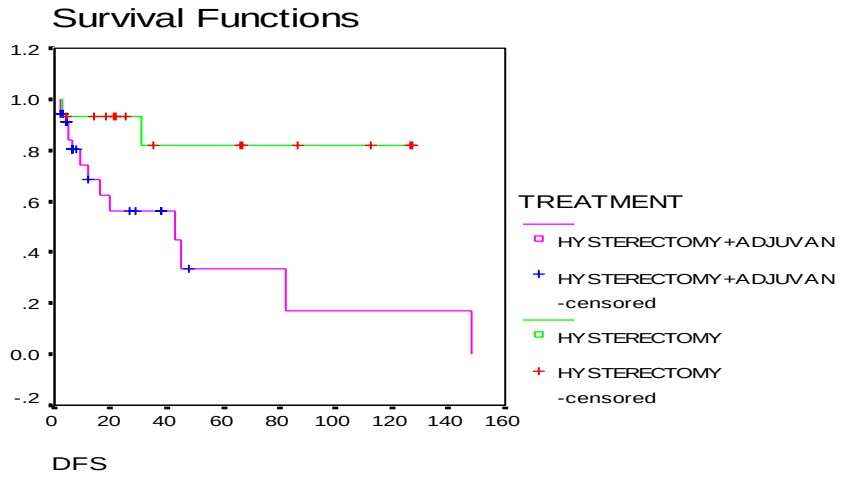


Fig-5 Kaplan-Meier overall survival curve(histology)

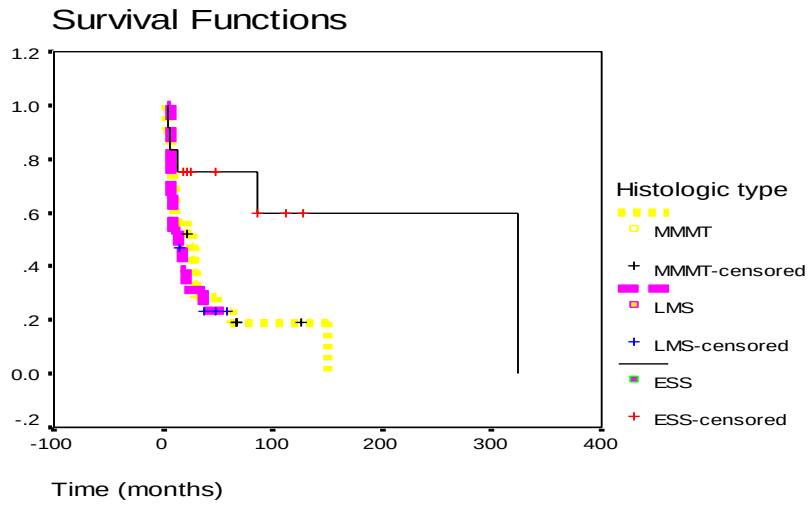
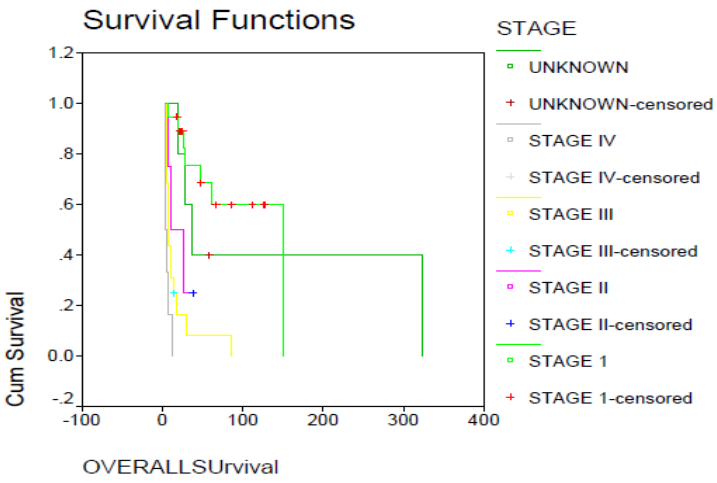


Fig -6 Kaplan-Meier overall survival curve(stage).



V. Conclusion

The incidence of uterine sarcoma in our hospital is 23.5 %(55/234) of all uterine malignancies with malignant mixed mullerian being the tumor most common histology . In comparison to LMS and MMMT, ESS tends to present as indolent disease with favorable outcomes. The histology, stage, and grade/ mitotic index;

appears established prognostic factors with the tumor stage being the major determinant. The rarity and biological diversity of the tumor variants has until date prevented the evolution of standard treatment protocols. This scenario is likely to change as better understanding of tumor behavior and uniform adaptation of newer FIGO staging is likely to encourage well designed studies to evaluate the effects of available treatment options. Presently, the standard of care for uterine sarcoma is surgery, to date however no effective adjuvant therapy regimen has a proven benefit. Radiation therapy, combination chemotherapy or bimodal management with radiation therapy and chemotherapy is unlikely to impact survival outcomes in uterine sarcoma.

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NONE

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