Uterine Cancer

Epidemiology

- predominantly a disease of affluent, obese, postmenopausal (PMP) women of low parity
- US black women are at 40% lower risk of developing uterine cancer but 54% greater risk of dying from it
- Risk factors (unopposed estrogen): HRT, obesity, anovulation, estrogen secreting tumors, Tamoxifen (RR 2-3)
- Protective (decreased estrogen, increased progesterone): OCP, smoking

Screening: no ideal method

High risk women

- PMP on unopposed estrogen
- Family history of hereditary nonpolyposis colorectal cancer
- Premenopausal women with anovulatory cycles

15% of women with PMP VB have endometrial carcinoma.
90% of patients with endometrial carcinoma have abnormal VB, especially PMP. Metrorrhagia and menorrhagia should also raise suspicion.

Endometrial carcinoma should be ruled out in women with:

1. PMP bleeding
2. pyometra
3. asymptomatic with endometrial cells on PAP
    a. 6% with normal endometrial cells on PAP have endometrial carcinoma and 13% have hyperplasia.
    b. 25% with abnormal endometrial cells have endometrial carcinoma
4. perimenopausal with meno/metrorrhagia
5. premenopausal with abnormal uterine bleeding, esp. if h/o anovulation

EMBx has false negative rate of 10%. Berek recommends fractional curettage (ECC at minimum) for symptomatic women with negative EMBx.

Surgical Staging

IA	limited to endometrium
IB	invasion to < ½ myometrium
IC	invasion > ½ myometrium
IIA	endocervical glandular involvement only
IIB	cervical stromal involvement
IIIA	tumor invades serosa and/or adnexa, and/or positive peritoneal cytology
IIIB	vaginal metastasis
IVA	tumor invades bowel/bladder mucosa
IVB	distant metastasis including intrabdominal/inguinal lymph nodes

Stage at time of presentation:
I: 72.3%
II: 10.9%
III: 13.2%
IV: 3.1%

Prognostic variables

Age	<40	51-60	61-70	71-80	>80
5yr SR	96.3	87.3	78	70.7	53.6

Histologic Type

1. Endometrioid carcinoma 92% survival compared with 33% for all other types.
2. With adenosquamous carcinoma, biologic behavior is reflected in the histologic grade and depth of the glandular component.
3. Papillary serous carcinoma has poor prognosis regardless of the depth of invasion. They disseminate widely and have a predilection for the upper abdomen.
4. Clear cell carcinoma (<5% of endometrial carcinomas): vascular space invasion if more common.

Histologic Grade and Myometrial Invasion
These are associated with an increasing risk of pelvic and periaortic LN metastases, adnexal metastases, positive peritoneal cytology, local vault recurrence, and hematogenous spread.

G1: 5% or less of nonsquamous or nonmorular solid growth pattern
G2: 6-50%
G3: > 50%

Incidence of pelvic/periaortic LN involvement by Grade and Depth

	G1	G2	G3
Myometrium only	0/0	3/3	0/0
Inner 1/3	3/1	5/4	9/4
Middle 1/3	0/5	9/0	4/0
Outer 1/3	11/6	19/14	34/23

Vascular space invasion:

5yr SR with invasion: 64.5%
5yr SR without: 83.5%

Peritoneal Cytology

Gynecologic Oncology Group estimates **RR** of death with positive washing was **3**.

Hormone Receptor Status

ER and PR content are independent prognostic indicators for endometrial cancer. Patients whose tumors are positive for one or both receptors have longer survival.

Nuclear Grade

Tumor size is an independent prognostic factor predictive of LN metastasis.

	Tumor Size		
Depth of invasion	≤ 2cm	> 2cm	Entire Surface
None	0	0	0
<1/2	0	12	22
≥1/2	22	26	50

DNA Ploidy: GOG estimates RR 4.1 for disease-related death in patients with aneuploid tumors.

Method of Treatment: In contrast to cervical cancer, patients with endometrial cancer treated with hysterectomy alone or hysterectomy and radiation do significantly better than those treated with radiation alone.

	Distant mets,%	Pelvic Recurrence,%	5yr SR
TAH+XRT	13.3	8.9	78
XRT	11.5	34.6	48

Treatment

Stage I and Stage II Occult (microscopic cervical involvement by ECC)

1. TAH/BSO, usually vertical midline. TVH may be applicable in patients with Grade 1 lesions.
2. Staging for
    a. Patients with grade 3 lesions
    b. Grade 2 tumors >2cm in diameter
    c. adenosquamous, clear cell, papillary serous carcinomas
    d. > 50% myometrial invasion
    e. cervical extension
3. Negative nodes or 1 microscopically +LN: Vault irradiation
4. Bulky + pelvic LN or ≥ 2 +LN: external beam radiation, 5000 cGy ± extended (para-aortic) field, 4500 cGy
5. + peritoneal cytology: Phase II, no Rx
6. upper abdominal disease or pelvic disease outside the uterus; metastases completely resected: whole abdominal irradiation
7. Stage Ia, Ib; Grade 1; Grade 2 ≤ 2cm: no further treatment

Patient with IA or IB, grade 1 or 2 tumors have an excellent prognosis and no adjuvant radiation is necessary. These women must be closely followed so that vault recurrences can be detected early. Intracavitary vaginal radiation significantly reduces the incidence of vault recurrence.

Clinical Stage II

35 % incidence of + pelvic LN
2 main approaches:

- radical hysterectomy, BSO, bilateral lymphadenectomy
- Combined radiation and surgery (preoperative external pelvic irradiation and intracavitary Rd or Cs) followed in 6 weeks by TAH/BSO. There is no reported improvement in survival with radical vs. radiation then extrafascial hysterectomy. *This radiosurgical approach portends significant bowel morbidity*.

Clinical Stage III

Surgical eradication of all macroscopic tumor is the major prognostic factor for these patients. Surgery includes TAH, BSO, lymphadenectomy, omental biopsy, peritoneal washings.

Clinical State IV

36% have pulmonary metastases.

Pelvic exenteration may be considered is disease extension is limited to the bowel of bladder.

Endometrial carcinomas in young women
Approximately 90% are well differentiated and limited to the endometrium. If fertility is still desired, and the tumor is well-differentiated, a 2 month trial of Megace 160-320 daily or MPA 200-500 mg daily may be employed.

Recurrent Disease
34% detected within one year. 76% detected within 3 years.
Treatment usually begins with hormonal treatment. Cytotoxic agents (doxorubicin) are only palliative. The addition of cisplatin improved the response rate (66% vs. 35%) and the progression free interval (6.2 vs. 3.9 months) but not the median survival. GOG reports paclitaxel to have a 35% response rate in previously untreated women.

UTERINE SARCOMAS
3% of all uterine cancers
Pelvic radiation is thought to predispose to subsequent development of these cancers.
The number of mitoses per HPF seems to be the most reliable predictor of biologic behavior.
Classification

1. Pure: only malignant mesodermal elements are present
2. Mixed: malignant mesodermal and epithelial elements
3. Homologous: malignant mesodermal elements are usually present in the uterus
4. Heterologous: elements usually not present

	Homologous	**Heterologous**
Pure	leiomyosarcoma	rhabdomyosarcoma
	Stromal sarcoma	chondrosarcoma
	i. endolymphatic stromal myosis	osteosarcoma
	ii endometrial stromal sarcoma	lipsarcoma
Mixed	carcinosarcoma	Mixed mesodermal sarcoma

Sources

Clinical Gynecologic Oncology, 6th edition. DiSaia and Creasman, eds. Mosby Inc. St. Louis, 2002. PP 137-184.

Practical Gynecologic Oncology, 3rd edition. Berek JS and Hacker NF, eds. Lippincott, Williams, and Wilkins, Philadelphia, 2000. PP 407-455.