ENDOMETRIAL CANCER

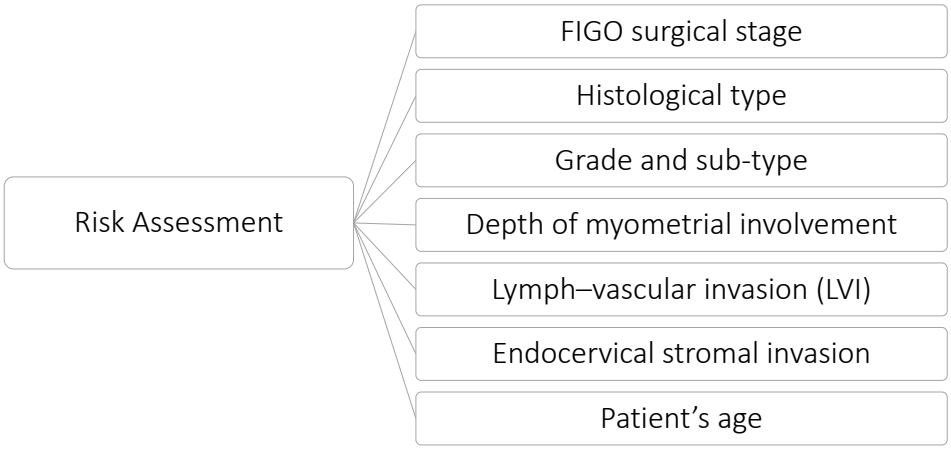
Introduction

- The diagnosis of endometrial carcinoma requires histopathological confirmation which includes:
  - Endometrioid type (80%)
  - Serous (5–10%)
  - Clear cell (1–5%)
  - Endometrial carcinosarcoma: a poor-prognosis subtype
  - Other subtypes (rarely encountered):
    - Mucinous,
    - Mixed,
    - Squamous cell,
    - Transitional cell and
    - Undifferentiated carcinomas.

Initial Workup

- **Clinical evaluation including:**
  - Performance status and
  - Gynecological examination.
- **Pathology review**
- **Laboratory Investigations:**
  - CBC,
  - Chemistry profile
- **Imaging:**
  - Chest X-ray.
  - CT scan of the abdomen and retroperitoneal nodes:
  - For determining the extra-uterine spread.
  - Contrast-enhanced dynamic MRI: It is the best way to assess the extension of the disease, in particular, the status of locoregional pelvic disease.

For risk assessment those factors should be assessed:



WHO Histological Classification of Tumors of the Uterine Corpus

Epithelial tumors	Undifferentiated carcinoma
Endometrial carcinoma	Mesenchymal tumors
Endometrioid adenocarcinoma	Endometrial stromal sarcoma,
Mucinous adenocarcinoma	Leiomyosarcoma
Serous adenocarcinoma	Miscellaneous mesenchymal tumors
Clear cell adenocarcinoma	Mixed endometrial stromal and smooth muscle tumor
Mixed cell adenocarcinoma	Mixed epithelial and mesenchymal tumors
Squamous cell carcinoma	Gestational trophoblastic disease
Transitional cell carcinoma	Miscellaneous tumors
Small cell carcinoma	

Old FIGO Staging System

IA	Tumor limited to endometrium
IB	Invasion to <50% of the myometrium
IC	Invasion to >50% of the myometrium
IIA	Endocervical glandular involvement only
IIB	Cervical stromal invasion
IIIA	Tumor invades serosa and/or adnexa and/or positive peritoneal cytology
IIIB	Vaginal metastases
IIIC	Metastases of pelvic and/or para-aortic lymph nodes
IVA	Tumor invasion of the bladder and/or bowel mucosa
IVB	Distant metastases including intra-abdominal and/or inguinal Lymph nodes.

FIGO Staging (7thedition)

Stage I (Confined to the uterus)	
Ia	Tumor limited to the endometrium with < than 50% of myometrium involvement
Ib	Invasion to > 50% of the myometrium
Stage II (Extension to the uterine cervix)	
IIa	Endocervical glandular involvement only
IIb	Cervical stromal invasion
Stage III (Extension beyond the uterus)	
IIIa	Tumor invades serosa and/or adnexa, and/or positive peritoneal cytology
IIIb	Vaginal involvement
IIIc	Metastasis to pelvic or para-aortic lymph nodes
Stage IV (Invasion in neighboring organs or distant metastases)	
IVa	Tumor invasion of the bladder and/or bowel mucosa
IVb	Distant metastases including intra-abdominal or inguinal lymph nodes

Treatment

Surgery

- Total abdominal hysterectomy and Bilateral salpingo-oophorectomy (TAH/BSO) with resection of para-aortic lymph nodes is the standard of care.

Adjuvant Treatment

Low-risk endometrial carcinoma:

- Patients with low grade (grade 1 or 2) endometrioid cancers confined to the endometrium (a subset of stage IA disease).
- No adjuvant treatment is required because their prognosis following surgery is excellent.
- Patients who wish to preserve future fertility are candidates for conservative treatment using progestin therapy.

Intermediate-risk disease:

- Patients with cancer that invades the myometrium (stage IA or IB) or demonstrates occult cervical stromal invasion (stage II).
- Other adverse prognostic factors that are used to stratify patients to be either high- or low-intermediate risk endometrial cancer include:
  - Outer one-third myometrial invasion,
  - Grade 2 or 3 differentiation and

- Presence of lymphovascular invasion within cancer.

- Such patients will be candidates for adjuvant radiation therapy (RT).
- Although there is no clear role for chemotherapy as part of an adjuvant treatment strategy, some clinicians recommend chemotherapy to women with high intermediate-risk disease.

High-risk endometrial cancer:

- Patients with any of the following features:
  - Stage III disease, regardless of histology or grade; and/or
  - Uterine serous carcinoma (USC) or
  - Clear cell carcinoma (CCC) of any stage.
- Patients in this category often receive chemotherapy with RT to prevent or minimize their high risk of both distant and locoregional relapse.

Neoadjuvant chemotherapy

- Considered for tumors advanced at diagnosis.
- This may be followed by surgery.
- Pelvic RT: considered either to palliate symptoms or as a high-dose palliative RT if it was felt it could offer a longer free-of-symptoms interval.

Chemotherapy Regimens in Adjuvant Setting

For epithelial cases:

- Carboplatin and a taxane.
- Docetaxel and paclitaxel are equally effective but differ in their toxicity profile
- (either of them can be combined with platinum)

For carcinosarcoma:

- Ifosfamide/cisplatin.
- Ifosfamide/paclitaxel.
- Docetaxel/gemcetabine

Second-line Therapy

- Single-agent Taxanes:
  - Docetaxel if not given as first-line.
- Liposomal Doxorubicin:
  - Calyx (out of supply from its manufacturer)
  - Doxil may be an alternative
- Bevacizumab may be considered in patients who have progressed on prior cytotoxic chemotherapy.

Follow Up

- Most recurrences have been noticed to occur within the first 3 years after treatment.
- Accordingly, history, physical and gynecological examination are recommended:
  - Every three months for the first 3 years
  - Every 6 months during the fourth and fifth years,
  - Annually thereafter.

- Uterine sarcoma: please refer to our `Sarcoma made easy ` Booklet for full details

References

1) Corpus Uteri. In: American Joint Committee on Cancer Staging Manual, 7th, Edge SB, Byrd DR, Compton CC, et al (Eds), Springer, New York 2010. p.403.
2) Nout RA, Smit VT, Putter H, et al. Vaginal brachytherapy versus pelvic external beam radiotherapy for patients with endometrial cancer of high-intermediate risk (PORTEC-2): an open-label, non-inferiority, randomized trial. Lancet. 2010;375(9717):816-23.
3) Creutzberg CL, Nout RA, Lybeert ML, et al. Fifteen-year radiotherapy outcomes of the randomized PORTEC-1 trial for endometrial carcinoma. Int J Radiat Oncol Biol Phys. 2011; 81(4):e631-8.
4) Greven K, Winter K, Underhill K, et al. Final analysis of RTOG 9708: adjuvant postoperative irradiation combined with cisplatin/paclitaxel chemotherapy following surgery for patients with high-risk endometrial cancer. Gynecol Oncol. 2006;103(1):155-9.
5) Lupe K, Kwon J, D'Souza D, et al. Adjuvant paclitaxel and carboplatin chemotherapy with involved field radiation in advanced endometrial cancer: a sequential approach. Int J Radiat Oncol Biol Phys. 2007; 67(1):110-6.
6) Johnson N, Bryant A, Miles T, et al. Adjuvant chemotherapy for endometrial cancer after hysterectomy. Cochrane Database Syst Rev. 2011;(10):CD003175.
7) Aghajanian C, Sill MW, Darcy KM, et al. Phase II trial of bevacizumab in recurrent or persistent endometrial cancer: a Gynecologic Oncology Group study. J Clin Oncol. 2011;29(16):2259-65.