OVARIAN CANCER

Epithelial Ovarian Cancer

Classification is based on histogenesis of the normal ovary with regard to its derivation from coelomic epithelium, germ cells, or mesenchymal cells. 85-90% of malignant ovarian tumors are epithelial.

Neoplasms derived from coelomic epithelium (mean age 50)		
❖ Serous tumor, 42%	CA-125	Psammoma bodies
❖ Mucinous tumor, 2%	CA 19-9	Goblet cells
❖ Mesonephroid (clear cell) tumor, 6%		Hobnail cells
❖ Brenner tumor, <1%		Warthin's nests
❖ Undifferentiated tumor, 17%		
❖ Carcinosarcoma and mixed mesodermal tumor		
Neoplasms derived from germ cells (mean age 20)		
❖ Teratoma		
o Mature teratoma		
▪ Solid adult teratoma		
▪ Dermoid cyst		Rokitansky's protuberance
▪ Struma ovarii		
o Immature (partially differentiated) teratoma		
❖ Dysgermiinoma	LDH, HCG Placental AlkPhos α_1 antitrypsin	granuloma multinucleated giant cells
❖ Embryonal carcinoma	HCG, αFP	
❖ Choriocarcinoma	HCG	
❖ Gonadoblastoma		
❖ Carcinoid		
Neoplasms derived from specialized gonadal stroma		
❖ Granulosa-theca cell tumors		
o Granulosa cell tumor	inhibin, estradiol	Call Exner bodies Coffee bean nuclei
o Thecoma		
❖ Sertoli-Leydig cell tumors		
o Arrhenoblastoma	testosterone	Crystals of Reinke
o Sertoli tumor		
❖ Gynandroblastoma		
❖ Lipid cell tumors		
Neoplasms derived from nonspecific mesenchyme		
❖ Fibroma, hemangioma, leiomyoma, lipoma		
❖ Lymphoma		
❖ Sarcoma		
Metastatic Neoplasms		
❖ GI tract		Mucin filled signet ring cells
❖ Breast		
❖ Endometrium		
❖ Lymphoma		

Borderline (LMP) epithelial ovarian neoplasms

- ❖ Account for 15% of all epithelial ovarian cancers
- ❖ High survival rate (95% at 5 years)
- ❖ Indolent course
- ❖ Occasional spontaneous regression of peritoneal implants
- ❖ Serous lesions are more common than Mucinous; Serous lesions tend not to be upgraded from frozen to final pathology; Mucinous more likely to be upgraded.
- ❖ To conclusively rule out invasion, the LMP tumor should have 1 section for every cm of size

Familial ovarian cancer

Breast-Ovarian cancer syndrome- mutation of BRCA1 or BRCA2.

- ❖ BRCA 1
  - o Located on long arm of 17q
  - o Carriers have a 32-84% increased risk of ovarian cancer if there is a strong family history of breast and/or ovarian cancer
  - o Cancer Genetics Screening Consortium: annual or semiannual CA125 and TVUS @ 25-35 for BRCA1 carriers
- ❖ BRCA 2 located on 13q12

Lynch II syndrome- inherited mutation in a family of DNA repair genes (MSH2, MLH1, PMS1, and PMS2)

Nonmalignant conditions that elevate CA-125

Acute PID
Adenomyosis
Benign ovarian neoplasm
Endometriosis
Functional ovarian cyst
Meig's syndrome
Menses
Ovarian hyperstimulation
Unexplained infertility
Uterine myoma
Hepatitis
Pancreatitis
Chronic liver disease
Cirrhosis
Colitis
CHF
Poorly controlled DM
Postoperative state
Renal disease, SLE
Nonmalignant ascites
Diverticulitis
Mesothelioma

In postmenopausal women with an adnexal mass and elevated CA-125, the PPV of CA-125 is 96%. In premenopausal women, this drops to 40%.

FIGO STAGING SYSTEM FOR OVARIAN CARCINOMA

STAGE	DESCRIPTION	5 year SR, %
I	Growth limited to the ovaries	
IA	One ovary; no ascites; capsule intact; no tumor on external surface	86.9
IB	Two ovaries; no ascites; capsule intact; no tumor on external surface	71.3
IC	One or both ovaries with either: surface tumor; ruptured capsule; or ascites or peritoneal washings with malignant cells	79.2
II	Pelvic extension	
IIA	Involvement of uterus and/or tubes	66.6
IIB	Involvement of other pelvic tissues	55.1
IIC	Stage IIA or IIB with factors as in stage IC	57.0
III	Peritoneal implants outside pelvis and/or positive retroperitoneal or inguinal nodes	
IIIA	Grossly limited to true pelvis; negative nodes; microscopic seeding of abdominal peritoneum	41.1
IIIB	Implants of abdominal peritoneum $\leq$ 2 cm; nodes negative	24.9
IIIC	Abdominal implants >2 cm and/or positive retroperitoneal or inguinal nodes	23.4
IV	Distant metastases	11.1

** Data from the New FIGO stage grouping for primary carcinoma of the ovary (1985). Gynecol Oncol 25:383, 1986.*

Staging procedure

4 peritoneal washings (diaphragm, right and left abdomen, pelvis) or ascites
Exploration
Biopsy or smear from right diaphragm
Biopsy suspicious lesions
Biopsy or resection of adhesions
Random biopsies
Selected lymphadenectomy
TAH, BSO
Debulking (largest residual mass $\leq$ 2 cm)

Incidence of pelvic node metastasis by Stage
1: 15%
2: 57%
3: 64%

Treatment

Stage 1a/b: TAH, BSO, staging unless childbearing not completed
Stage 1b/c: Surgical staging with postop CTX (platinum + alkylating agent)
Stage 2-4: Surgical staging and maximal debulking with postoperative CTX as above

- Some institutions use intraperitoneal ^{32}P instillation for Stage 2 disease.
- Survival for Stage 3 disease is related to the size of the residual tumor after surgical debulking.

Reassessment surgery
Indications
- Restaging one who probably has localized disease but has not had an optimal staging procedure
- For evaluation of effect of CTX
- For evaluation of patients who are clinically free of disease after a sufficient course of CTX and are then eligible for assessment as to possible "cure" and discontinuation of therapy

If elevated, CA-125 predicts disease @ 2nd look in 97% patients.
CT scan has a 45% false negative rate.
30% of patients without macroscopic disease will have microscopic metastases.

Salvage Therapy
Platinum sensitive
- Carboplatinum: 14-38% response rate

Platinum resistance
- Defined as disease progression or persistence while on platinum based agent or relapse within 6 months of therapy.
- Paclitaxel: response rates 22-23%

Germ Cell Tumors

Dysgerminoma
- One of two most common malignant ovarian neoplasms observed in pregnancy, the other being serous LMP
- When primary amenorrhea exists, suspect association with Gonadoblastoma
- 10-15% of cases have bilateral involvement
- In young women with unilateral encapsulated dysgerminoma, conservative surgery is indicated.
- 90%of recurrences appear within 2 years.
- CTX
  - Doxorubicin and cyclophosphamide
  - VBP (vinblastine, bleomycin, and cisplatin

Endodermal Sinus (Yolk Sac) Tumor
- 2nd most common from of malignant germ cell of the ovary
- Mean age 19
- Usually large (10-30cm)
- Insensitive to XRT
- Stage 1 CTX: VAC (vincristine 1.5 mg/m^2, dactinomycin 0.5 mg, cyclophosphamide 5-7 mg/kg
- Stage 2-4 CTX:
  - VBP (vinblastine 12 mg/m^2, bleomycin 20 u/m^2cusplatin 20 mg/m^2)
  - BEP (bleomycin 20 U/m^2, etoposide 100 mg/m^2, cisplatin 20 mg/m^2)

Embryonal Carcinoma
- One of the most malignant ovarian cancers
- Precocious puberty, irregular bleeding, amenorrhea,
- The tumors contain hCG, syncytiotrophoblast-like cells, and αFP in the large primitive cells
- CTX: VAC < VBP < VBP

Choriocarcinoma
- Rare, highly malignant, tumor associated with sexual precocity.
- MAC combination CTX (MTX, actinomycin, cyclophosphamide)

Immature teratoma
- Stage 1A G1: unilateral oophorectomy
- Stage 1A G2or3 or higher: postop VAC

Struma ovarii
- Consists predominantly of thyroid parenchyma
- 25-35% have clinical hyperthyroidism

Granulosa cell tumors
- 25% have concomitant hyperplasia
- 10% PMP women will harbor endometrial carcinoma
- Types
- Adult granulosa cell tumor, 95%
- Juvenile granulosa cell tumor
- Treatment
- Stage 1: 5 yr SR: 90-95%; no further therapy after excision
- Stage 2/3: VBP, BEP

Fallopian tube cancer

Incidence: 3.6/1,000,000 women
Classic triad (present in 15%) prominent watery vaginal discharge, pelvic pain, pelvic mass
Staging and Treatment: same as for epithelial ovarian cancer
Prognosis: Stage 1 84% 5yr SR
Stage 2 52%
Stage 3 36%

Sources

1. Clinical Oncology, 2nd ed. Abeloff MD, ed. Churchill Livingston, New York. 2000. PP 2017-36.
2. Clinical Gynecologic Oncology, 6th edition. DiSaia and Creasman, eds. Mosby Inc. St. Louis, 2002. PP 289-384.
3. Practical Gynecologic Oncology, 3rd edition. Berek JS and Hacker NF, eds. Lippincott, Williams, and Wilkins, Philadelphia, 2000. PP 457-551.
4. Up-To-Date