**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%
- Mucinous tumor, 2%
- Mesonephroid (clear cell) tumor, 6%
- Brenner tumor, <1%
- Undifferentiated tumor, 17%
- Carcinosarcoma and mixed mesodermal tumor

Neoplasms derived from germ cells (mean age 20)

- Teratoma
  - Mature teratoma
    - Solid adult teratoma
    - Dermoid cyst
    - Struma ovarii
  - Immature (partially differentiated) teratoma
- Dysgerminoma
- Embryonal carcinoma
- Choriocarcinoma
- Gonadoblastoma
- Carcinoid

Neoplasms derived from specialized gonadal stroma

- Granulosa-theca cell tumors
  - Granulosa cell tumor
    - Inhibin, estradiol
    - Call Exner bodies
    - Coffee bean nuclei
  - Thecoma
  - Sertoli-Leydig cell tumors
    - Arrhenoblastoma
    - Sertoli tumor
  - Gynandroblastoma
  - Lipid cell tumors

Neoplasms derived from nonspecific mesenchyme

- Fibroma, hemangioma, leiomyoma, lipoma
- Lymphoma
- Sarcoma

Metastatic Neoplasms

- GI tract
- 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
  - Located on long arm of 17q
  - Carriers have a 32-84% increased risk of ovarian cancer if there is a strong family history of breast and/or ovarian cancer
  - 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%.

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


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 form 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/m², dactinomycin 0.5 mg, cyclophosphamide 5-7 mg/kg)
- Stage 2-4 CTX:
  - VBP (vinblastine 12 mg/m², bleomycin 20 u/m², cisplatin 20 mg/m²)
  - BEP (bleomycin 20 U/m², etoposide 100 mg/m², cisplatin 20 mg/m²)

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 G2 or 3 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:

<table>
<thead>
<tr>
<th>Stage</th>
<th>5yr SR</th>
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<tbody>
<tr>
<td>Stage 1</td>
<td>84%</td>
</tr>
<tr>
<td>Stage 2</td>
<td>52%</td>
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<tr>
<td>Stage 3</td>
<td>36%</td>
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</tbody>
</table>

Sources

4. Up-To-Date