Ovarian Cancer

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Objectives

- Define symptoms and risk factors for ovarian cancer
- Review the evaluation for an adnexal mass
- Discuss the diagnosis and management of ovarian cancer

Initial Presentation

- 50 y/o presents with pelvic pressure and PCP ordered CT scan revealing a 15cm pelvic mass with solid and cystic components
- 43 y/o presents with pelvic pain and ultrasound shows 4cm complex adnexal mass
- 65 y/o had MRI for back pain, found to have a 9cm cystic lesion in the right adnexa

Differential diagnoses

Benign
Functional cyst
Endometriosis/Endometrioma
Benign neoplasm
- **Teratoma**
- **Cystadenoma**
- **Leiomyoma**

Pregnancy related conditions
- **Ectopic pregnancy**
- **Theca-Lutein cysts**

Embryological remnants
- **Paratubal cyst**
- **Paraovarian cyst**

Tubal processes
- **Tubo-ovarian abscess**
- **Hydrosalpinx/Pyosalpinx**

Differential Diagnoses

Malignant

- Ovarian cancer
  - Epithelial ovarian cancers
  - Germ cell tumors
  - Borderline ovarian tumors
  - Sex cord-stromal tumors
- Fallopian tube cancers
- Primary peritoneal cancer
- Uterine cancer

Differential diagnoses

Non-gynecologic causes

Gastrointestinal conditions
- Diverticular disease
- Appendiceal abscess/mucocele
- Meckel's diverticulum
- Small bowel tumors
  - Colorectal cancer

Urinary tract conditions
- Ureteral diverticulum
- Bladder diverticulum
- Pelvic kidney

Other
- Retroperitoneal tumors
- Retroperitoneal sarcomas
- Desmoid tumors
- Schwannomas
- Metastatic disease to adnexa
  - Bowel
  - Breast
  - Lymphoma

When to worry about cancer

- Symptoms
- Risk Factors
- Exam
- Labs
- Imaging

Symptoms

- Asymptomatic
- Pelvic pain
- Weight loss, early satiety, bloating
- Vaginal bleeding, breast tenderness, precocious puberty
- Hirsutism, deepening of the voice
- Flushing, diarrhea, hyperthyroid symptoms

Risk factors

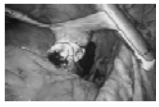
- Incessant ovulation
  - Aberrant repair process of the epithelium
  - Nulliparity/infertility
  - Early menarche/late menopause
- Inflammation
  - Endometriosis
- Genetic predisposition
  - BRCA 1 and 2
  - Hereditary NonPolyposis Colorectal Cancer (Lynch syndrome)

Genetic predisposition

- BRCA 1
  - 90% lifetime risk for breast cancer
  - 40% lifetime risk for ovarian cancer
- BRCA2
  - 20% lifetime risk for ovarian cancer
- HNPCC (Lynch Family II)
  - Endometrial, colon and ovarian cancers

Risk-reducing surgery

- Genetic predisposition
  - Risk reducing bilateral salpingo-oophorectomy
    - Recommended by age 35 or after completion of childbearing
    - Occult cancer in ~8%
    - Risk of primary peritoneal cancer ~4%



Physical Examination

- General examination: cachexia, virilization, breast tenderness, lymphadenopathy, fever
- Abdominal exam: masses, pain, ascites

Physical Examination

- **Pelvic/speculum exam: clitoromegaly, bleeding, cervical displacement**
- **Mass characteristics: contour, firmness, mobility**
- **RV exam: tenderness, nodularity, stool guaiac.**

Biomarkers

- **May aid in determining the malignant potential and histology of an adnexal mass**
- **CA-125 is most commonly used biomarker**
  - **May be elevated in benign conditions**
  - **Ordered selectively**
    - **Age**
    - **Presentation of symptoms**
    - **Findings on physical examination**
    - **Imaging**

Biomarkers

- **Cancer antigen (CA) 125**
  - **Epithelial ovarian cancer (serous)**
  - **Benign processes**
- **Alpha Fetoprotein (AFP)**
  - **Endodermal sinus tumors**
  - **Hepatocellular carcinoma**
- **Human chorionic gonadotrophin (hCG)**
  - **Choriocarcinoma, embryonal carcinoma**
  - **Pregnancy**
  - **Gestational trophoblastic disease**
- **Lactate dehydrogenase (LDH)**
  - **Dysgerminomas**
  - **Lymphomas**
- **Inhibin A and B**
  - **Granulosa cell tumors**
- **Cancer antigen (CA) 19-9**
  - **Pancreas and biliary tract**
  - **Mucinous tumors of the ovary**
- **Carcinoembryonic antigen (CEA)**
  - **Colorectal cancer**

Biomarkers

Age	**Tumor Markers**
≤30 years	AFP, hCG, LDH, Inhibin A, Inhibin B
30-50 years	Inhibin A, Inhibin B, +/- CA-125 (family history)
≥50 years	CA-125, CA 19-9, +/- Inhibin A & B (if symptoms), +/- CEA

OVA1™

- Combines five immunoassays into a single numerical result
  - CA-125
  - Transthyretin (prealbumin)
  - Apolipoprotein A1
  - ß2-microglobulin
  - Transferrin

OVA1™ Scoring

OvaCalc software uses assay results and calculates ovarian cancer risk index score

- Premenopausal
  - less than 5 = low risk
  - 5 or greater = high risk
- Postmenopausal
  - less than 4.4 = low risk
  - 4.4 or greater = high risk

HE4 and CA-125

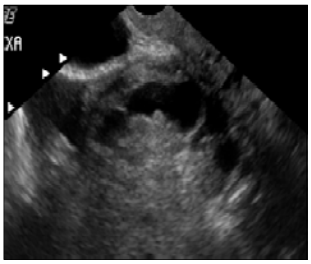
- Study of 531 patients with pelvic mass
  - Low risk: 352 cases
    - Benign ovarian tumors
  - High risk: 179 cases
    - Epithelial ovarian cancers (n=129)
    - 22 borderline tumors/6 non-epithelial ovarian cancers
    - 22 non ovarian cancers

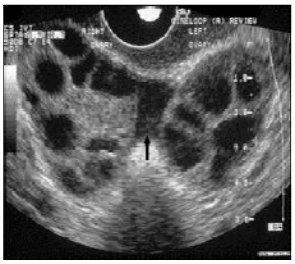
	Sensitivity	Specificity
Postmenopausal	92.3%	75.0%
Premenopausal	76.5%	74.8%

Moore RG, et al. A novel multiple marker bioassay utilizing HE4 and CA125 for the prediction of ovarian cancer in patients with a pelvic mass. Gynecol Oncol. 2009 Jan;112(1):40-6.

Radiographic imaging

- Ultrasound
  - Size, location, locularity, echogenicity, blood flow, septations, presence of ascites



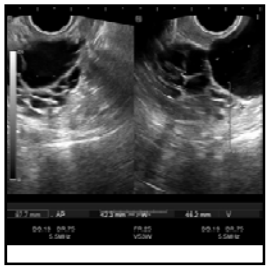


Radiographic imaging

- MRI
  - May be helpful in further assessing those masses that have an indeterminate malignant potential on ultrasound
  - Expensive, but may prevent patients from undergoing an unnecessary surgical procedure.
- CT scan
  - Ovarian cancer pre-operative and post-operative treatment planning

Concerning for Malignancy

- Complex or solid mass
- Ascites
- Presence of blood flow within papillary projection
- Diameter >10cm
- Bilateral tumors
- Septation >3mm in width



Referral Guidelines

SGO AND ACOG REFERRAL GUIDELINES FOR A NEWLY DIAGNOSED PELVIC MASS

PREMENOPAUSAL (< 50 YEARS OLD)

CA-125 > 200 U/mL
Ascites
Evidence of abdominal or distant metastasis (by exam or imaging study)
Family history of breast or ovarian cancer (in a first-degree relative)

POSTMENOPAUSAL (≥ 50 YEARS OLD)

CA-125 > 35 U/mL
Ascites
Nodular or fixed pelvic mass
Evidence of abdominal or distant metastasis (by exam or imaging study)
Family history of breast or ovarian cancer (in a first-degree relative)

Only one criterion from the list is required to recommend referral

Ovarian Cancer

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Arthur G. James Cancer Hospital and
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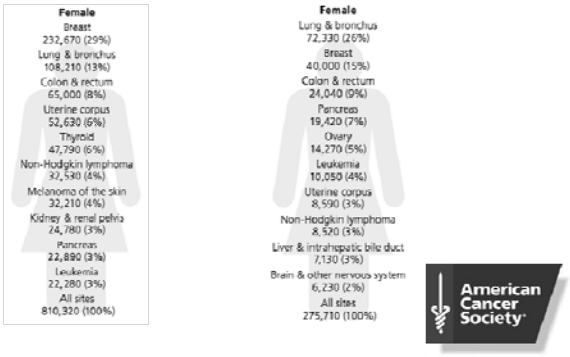
Cancer statistics 2014

Estimated new cases **Estimated deaths**



Types of ovarian cancer

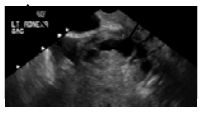
- Epithelial cancer (85%)
  - Serous
  - Mucinous
  - Clear cell
  - Endometrioid
  - Transitional cell (Brenner)
- Non-epithelial cancer
  - Germ cell tumors
  - Sex cord stromal tumors

	Ovarian cancer staging	Incidence	Survival
Stage I	Confined to the Ovary	20%	85%
I_A	Growth limited to one ovary.		
I_B	Same as I_A but involves both ovaries		
I_C	Above with positive washings or ruptured capsule		
Stage II	Extends to True Pelvis	5%	60%
II_A	Involves fallopian tube or uterus		
II_B	Extension to other pelvic tissues		
Stage III	Extends Beyond the True Pelvis	58%	26%
III_{A1}	Positive retroperitoneal nodes only		
III_{A2}	Microscopic positive biopsy outside the pelvis		
III_B	Abdominal implants up to 2 cm		
III_C	Positive lymph nodes or abdominal implants > 2 cm		
Stage IV	Distant Disease	17%	12%
IV_A	Pleural effusion with positive cytology		
IV_B	Parenchymal and extra-abdominal metastases		

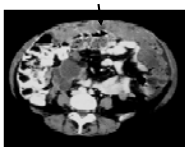
Diagnosis

- Examination
- Imaging
- CA-125 level

Septation Excrescences



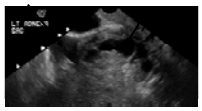
Omental Cake



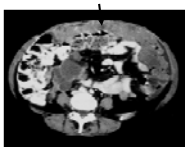
Diagnosis

- Examination
- Imaging
- CA-125 level

Septation Excrescences



Omental Cake



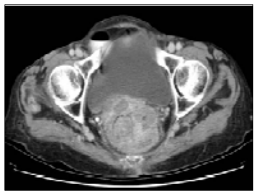
SURGERY

Role for surgery

- Establish diagnosis (surgery)
  - Laparotomy versus laparoscopy
  - Cytology only if unable to operate
- Surgical goals
  - Determine extent of disease (staging)
  - Cytoreduction (debulking)
  - Restore/preserve anatomy

Surgical staging

- Cytology
- Assessment/biopsies of peritoneal surfaces
- Hysterectomy and salpingo-oophorectomy
- Pelvic and para-aortic lymph nodes
- Appendectomy

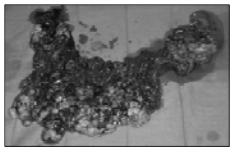


Importance of surgical staging

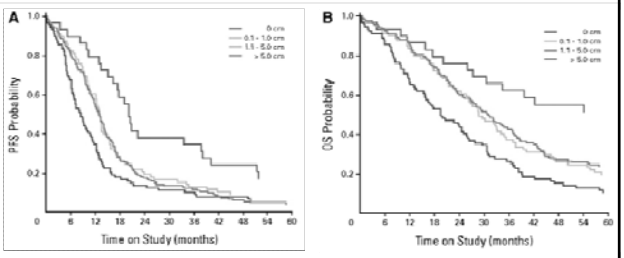
- Clinically early stage
  - Completion staging upstages 31%
- Therapeutic
  - Resection of metastatic deposits
  - Assign appropriate adjuvant treatment
  - Maximizes survival

Cytoreductive Surgery

- Goal is elimination of all tumor
  - No gross residual (microscopic)
  - Optimal (≤1 cm)
  - Suboptimal (>1 cm)
- Operative Technique
  - Radical resection



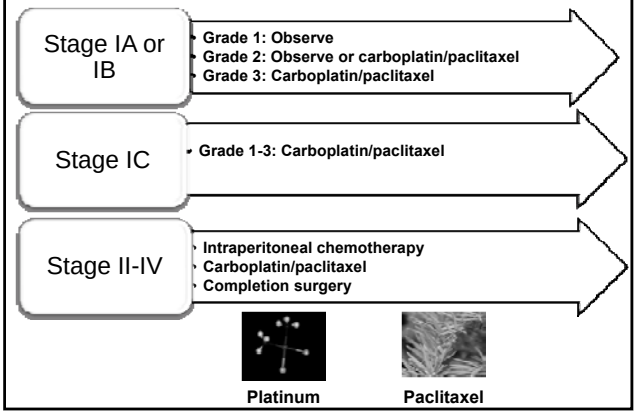
Importance of surgical debulking



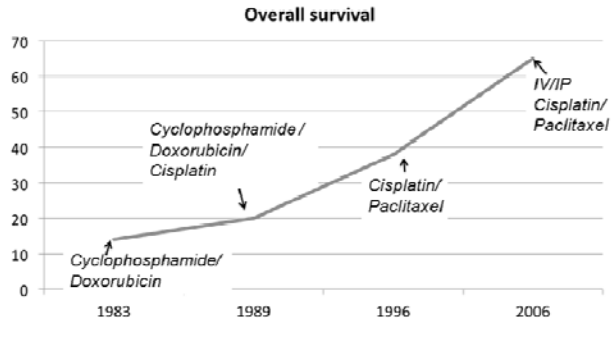
Resection of all visible disease should be the goal

Winters et al. J Clin Oncol 2008; 26(1): 83-89

Chemotherapy



Survival outcomes



Surgery and chemotherapy

- Goals of Treatment
  - Prolong survival
  - Delay time to progression
  - Control disease-related symptoms
  - Minimize treatment-related adverse events
  - Maintain or improve quality of life

Neoadjuvant chemotherapy

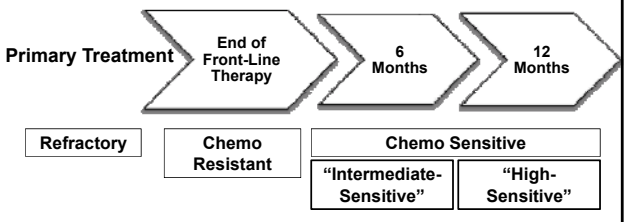
- Utilized when patients are not likely to undergo complete surgical resection
- Disease factors
- Patient factors
- Surgeon factors

Recurrent Ovarian Cancer

Stage	CR	Recurrence
Stage I	~ 100%	20-25%
Stage II	~100%	50%
Optimal stage III	> 90%	75%
Suboptimal stage III / IV	50%	> 90%

- Most patients will have disease recur within 5 years
- Retreatment challenges
  - Low response rates
  - Shortened PFS

Chemotherapy Sensitivity



Future opportunities and directions

- Screening
  - New tumor markers/Better imaging
- Referral to gynecologic oncology
  - Majority of women do not receive standard care
- Prolonging recurrence free interval
  - The role of maintenance therapy
- Improving second line therapies
  - Role of biologics

Screening

- Ultrasound
- CA-125
  - High rate of false positives
  - Often not abnormal until advanced stages

Ovarian cancer screening

- Randomization of ~78,000 low risk women to screening or routine care
  - Women aged 55 to 74 years randomized
  - Screening: annual CA-125 (cut-off ≥ 35) and ultrasound
- Results
  - False-positive rate ~10%
  - No improvement in mortality rates
  - High rate of serious complications

Screening – US and CA 125

National Health Institutes:
"…there is no evidence available yet that the current screening modalities of CA 125 and transvaginal ultrasonography can be effectively used for widespread screening to reduce mortality from ovarian cancer…"

Screening – US and CA 125

National Health Institutes:
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ROUTINE OVARIAN CANCER SCREENING IS NOT RECOMMENDED

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