OVARIAN CANCER

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OVARIAN CANCER

IMPORTANT

- 27% of gynecologic cancers
- 53% of all gynecologic cancer deaths

- **Ovarian cancer is among the most malignant tumors in women**
- **Mortality overcomes the sum of mortalities of all other gynecologic malignancies**

EPIDEMIOLOGY

Ovarian cancer

leading cause of death of all gynecologic malignancies (in the USA)

Most common between 75 - 79 years

Risk factors for ovarian cancer

	Relative risk	Lifetime probability, percent*
Familial ovarian cancer syndrome	Unknown	30 to 50
Two or three relatives with ovarian cancer	4.6	5.5 (15 if first degree)
One relative (first or second degree) with ovarian cancer	3.1	3.7 (5 if first degree)
No risk factors	1.0	1.8
Past oral contraceptive use	0.65	0.8
Past pregnancy	0.5	0.6
Infertility	2.6	
Nulligravity	1.6	
Past breast feeding	0.61	
Tubal ligation	0.59	

* Indicates probability for ovarian cancer in a 50-year-old woman.
Adapted from data in Carlson, KJ, Skates, SJ, Singer, DE, Ann Intern Med 1994; 121:124 and Whittemore AS, R Harris, J Intyre, and the Collaborative Ovarian Cancer Group. Am J Epidemiol 1992; 136: 1184 and Gotlieb, WH, Baruch, GB, Friedman, E. Semin Surg Oncol 2000; 19:20 and Ness, RB, Cramer, DW, Goodman, MT, et al. Infertility, fertility drugs, and ovarian cancer: a pooled analysis of case-control studies. Am J Epidemiol 2002; 155:217.

ETIOLOGY

CAUSE
WE DON' KNOW

RISK / PROTECTIVE FACTORS WE KNOW

HYPOTHESES

ETIOPATHOGENESIS

- HYPOTHESIS OF CONSTANT OVULATION
- GONADOTROPIN HYPOTHESIS
- THEORY OF PELVIC CONTAMINATION (RETROGRADE TRANSPORT)
- TUBAL HYPOTHESIS

ETIOPATHOGENESIS

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ETIOPATHOGENESIS

HYPOTHESIS OF CONSTANT OVULATION

- Repeated mini traumas of epithelial surface
- The disruption of repairation of epithelial surface of the ovary that ruptures and repairs during ovulation
- More ovulation - ↑ risk: nulliparas, stim. ov., infertility
- Less ovulations - ↓ risk: ↑ parity, lactation, OC

ETIOPATHOGENESIS

HYPOTHESIS OF CONSTANT OVULATIONS

- **nulliparas – increased risk**
- **30% of all affected women are nulliparas**

ETIOPATHOGENESIS

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- TUBAR HYPOTHESIS

ETIOPATHOGENESIS

GONADOTROPINE HYPOTHESIS

- ↑ level of gonadotropines (↑E2) ↑ risk:
  - ↑ risk: nulliparas, stim. ov., infertility
- ↓level gonadotropines: ↓ R
  - ↑ parity, breast feeding, OC

ETIOPATOGENEZA

- HYPOTHESIS OF CONSTANT OVULATIONS
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ETIOPATHOGENESIS

THEORY OF PELVIC CONTAMINATION (RETROGRADNOG TRANSPORTA)

- Carcinogene through uterus and tubes ↑ R
- ↓ R 10-80% in women with ligated tubes (or after salpingectomy) the protective effect lasts up to 20 years
- Irritation / inflammation / carcinogenesis
- asbest (mesothelioma on animal models)
- talc (serous and undifferentiated)

ETIOPATHOGENESIS

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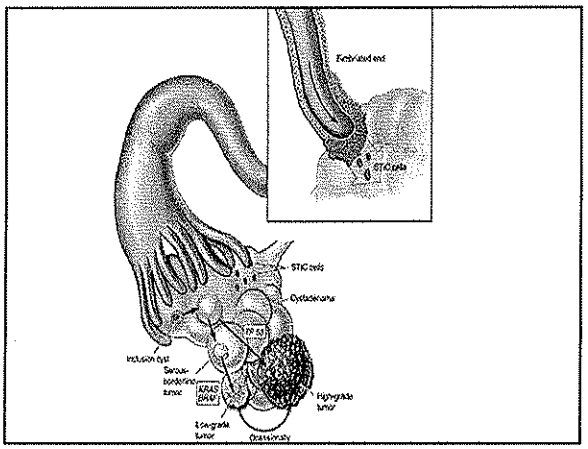
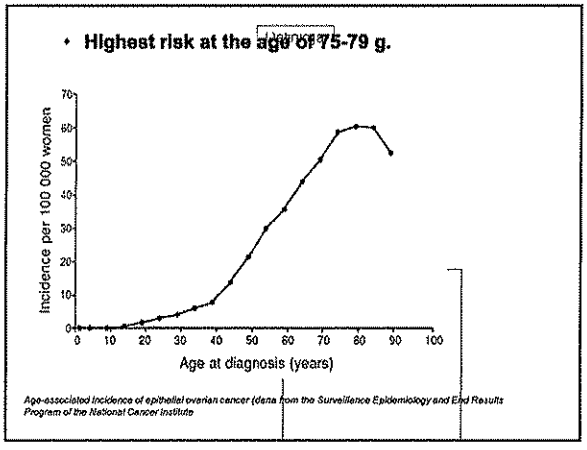
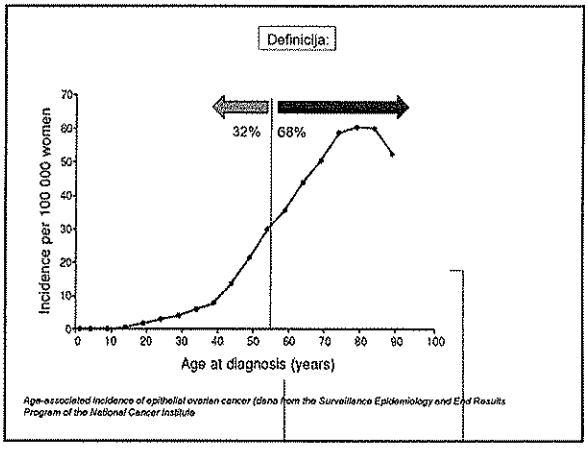


RISK FACTORS

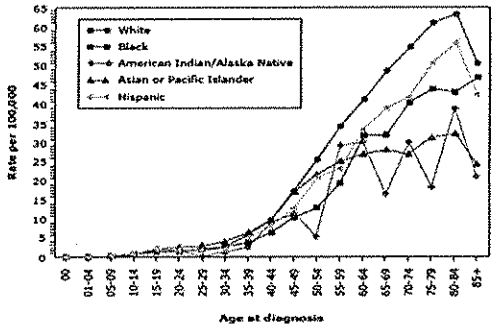
➢50% of all cases of ovarian cancer may be explainded by established risk factors

AGE





US ovarian cancer incidence by age and race, 1992-2002



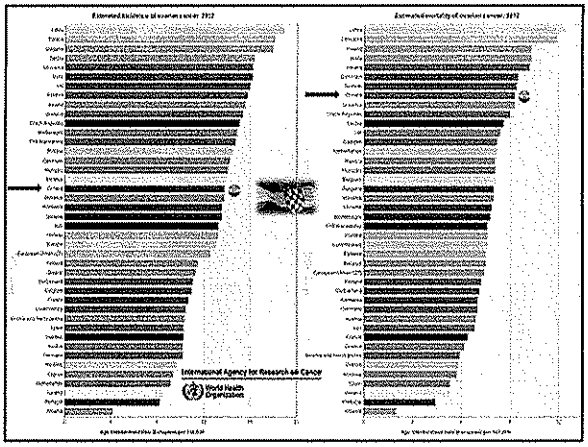
GEOGRAPHY

BELONGING TO GEOGRAPHIC REGION

- THE CONTINUOUS LIGHT INCREASE OF INCIDENCE (large increase in older age groups)
- 5% of all malign tumors in women
- 23% MALIGNANT TUMORS of female genital tract (highest mortality among genital neoplasias)

FREQUENCY:

- LOWEST in Japan and India 2/100000
- Sweden 25/100000, Croatia 13,8/100000
- SAD and Canada 15/100000
- 1999. in Croatia 540 newly diagnosed



REPRODUCTIVE AND HORMONAL FACTORS

PARITY

Whittemore and coll. su analysed 12 studies

- First birth ↓ risk for 40%
- Next deliveries ↓ rizik – 10% each

Whittemore AS, Harris R, Itnyre J. Characteristics relating to ovarian cancer risk: collaborative analysis of 12 US case-control studies. II. Invasive epithelial ovarian cancers in white women. Collaborative Ovarian Cancer Group. *Am J Epidemiol* 1992; 136: 1184–1203.

BREAST FEEDING

- A lot less of protective effect
- 0,6-0,9

COMBINED ORAL CONTRACEPTIVES

- ↓ risk (non-mucinous)
- ↓ ovulations + ↓ gonadotropines
- 10-12% ↓ risk for one year
- 50% ↓ risk for 5 y.
- ↓ risk even 25 years after cessation of OC
- COC ≥5 y. + 2 deliveries = 70% ↓R
- High dosage COC slightly more ↓R
- BRCA mutation+COC≥6Y=60% ↓R
- even gestagen contraception ↓ risk

HRT

- **Women's Health Initiative, double-blind randomized study performed on 17000 women: after 5,6 y.of follow up, unsignificantly ↑R**
  Anderson GL, Judd HL, Kaunitz AM, Barad DH, Beresford SA, Pettinger M, *et al.* Effects of estrogen plus progestin on gynecologic cancers and associated diagnostic procedures: the Women's Health Initiative randomized trial. JAMA 2003; 290: 1739–1748.
- **HRT 20 yrs – RR 3,2**
  Lacey JV Jr, Mink PJ, Lubin JH, Sherman ME, Troisi R, Hartge P, et al. Menopausal hormone replacement therapy and risk of ovarian cancer. JAMA 2002; 288: 334–341.

INFERTILITY

- infrt.+nulliparas+Assisted pregnancy Procedures =27x ↑ risk
- Badly designed studies
- Scientifically questionable

HISTORY OF CANCER

- **Ovarian cancer in closest family (mother, daughter, sister) increases the risk 3x**
- **5-10 % of patients have a hereditary (familial) genesis**
- **2 x ↑ risk of ovarian cancer in women that suffered from breast cancer**
- **3-4 x ↑ risk of breast cancer in women that had ovarian cancer**
- **Endometrial cancer ↑ risk**

SMOKING

- ↑ risk of mucinous ovarian cancer (RR 2,22)
- ↑ borderline ovarian tumor
- smoking=↑gonadotropine and androgen levels

Zhang et al, 2004
Rossing et al, 2008.

COFFEE

- ↑ risk of mucinous cancer (RR 2,22)
- ↑ borderline ovarian tumors

Zhang et al, 2004

Rossing et al, 2008.

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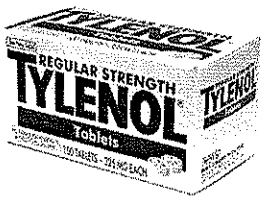
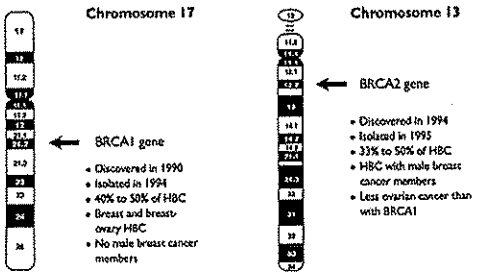
acetaminophen daily - death rate from ovarian cancer 45% lower



Cancer Prevention Study
Rodriguez and coworkers

GENETICS



Familial ovarian cancers

***Hereditary breast and ovarian cancer* - HBOC**
- **Mutation of tumor-supressor genes BRCA 1 (17. chromosome) and BRCA 2 (13. c.)**
- **47. - 50. g.**

Lynch syndrome II
- **Hereditary non-polipoid colorectal cancer and ovarian cancer**
- **↑R for colorectal/gastric and endometrial cancer**
- **Mutation for genes that repair the DNA, on 2. and 3. chr.)**
- **Risk of developing ovarian cancer is 10%**
- **44. g.**

Hereditary
- **Exclusively ovarian cancer.**
- **59. g.**

All three syndromes are autosomal dominant

Familial Ovarian Cancer

Procedure:

- 2 x / yr. CA125, US
- COC
- Delivery and then ovariectomy

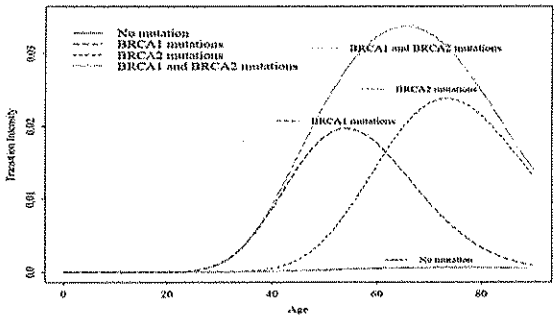
Estimated cancer risks associated with BRCA1 and BRCA2 mutations

Type of cancer	Estimated lifetime risk in BRCA1 mutation carriers	Estimated lifetime risk in BRCA2 mutation carriers	Lifetime risk in general population
Breast cancer[2]	47 to 66 percent*	40 to 57 percent*	12.5 percent
Contralateral breast cancer[1]	Up to 65 percent	Up to 50 percent	0.5 to 1 percent per year
Ovarian cancer[2]	35 to 46 percent	13 to 23 percent	1.5 percent
Colon cancer[1]	Not increased, or increased very slightly	Not increased, or increased very slightly	5 percent
Prostate cancer[1]	Elevated (risk unknown)	35 to 40 percent	15 percent
Male breast cancer[3]	0.2 to 2.8 percent	3.2 to 12 percent	0.1 percent
Pancreatic cancer[1]	<10 percent	<10 percent	1.3 percent

* These ranges represent 95 percent confidence intervals derived from a meta-analysis of 10 individual studies representing both high-risk and population-based cohorts. Many genetic specialists quote a broader range of lifetime risk for breast cancer (BRCA1 (35 to 85 percent) and BRCA2 (30 to 85 percent) carriers

1. Data compiled from Ford, D, et al. Am J Hum Genet 1998; 62:676, Struewing, JP, et al. N Engl J Med 1997; 336:1401, Antoniou, A, et al. Am J Hum Genet. 2003; 72:1117, Brose, MS, et al. J Natl Cancer Inst 2002; 94:1365, King, MC, et al. Science 2003; 302:643, Ford, D, et al. Lancet 1994; 343:692, Breast Cancer Linkage Consortium. J Natl Cancer Inst 1999; 91:1310, Thompson , D, et al. J Natl Cancer Inst 2002; 94:1358, Garber, JE, et al. J Natl Cancer Inst 2004; 96:2, and Levie A, et al. J Clin Oncol 2004; 22:735.
2. Data from: Chen, S, et al. J Clin Oncol 2007; 25:1329.
3. Data from: Tai, YC, et al. J Natl Inst 2007; 99:1811.

Modelled incidence rates of OC depending on the presence of BRCA1 and/or BRCA2 mutations



OTHER FACTORS

ENDOMETIOSIS

- ↑ R
- **endometrioid (60%) and clear cell (15%)**
- **endom. is found in 5-10% operated from ovarian cancer I-IV grade**
- **endom. is found in 40% operated from ovarian cancer I grade**

Vercellini P, Parazzini F, Bolis G, Carinelli S, Dindelli M, Vendola N, et al. Endometriosis and ovarian cancer. Am J Obstet Gynecol 1993; 169: 181–2.

BMI

WOMEN WITH OVARIAN CANCER:

- **30% overweight**
- **12% obese**
- **Metaanalyses of 28 studies found a consistent ↑ risk of ovarian and breast cancer and ↑BMI 1.3 (95% CI, 1.1-1.5)**

Olsen CM, Green AC, Whiteman DC, Sadeghi S, Kolahdooz F, Webb PM. Obesity and the risk of epithelial ovarian cancer: a systematic review and meta-analysis. *Eur J Cancer*. 2007;43(4):690-709.

PROTECTIVE FACTORS

- **Oral contraceptives**
- **Gestagens**
- **Multiparity**
- **Breast feeding**
- **Tube ligation / salpingectomy**
- **Vitamin D / sun bathing-mediterranean countries**
- **Vegetarians – less esgtrogens (less satrurated fatty acids)**

http://healthcare.utah.edu/healthlibrary/related/doc.php?type=42&id=OvarianCancerRisk

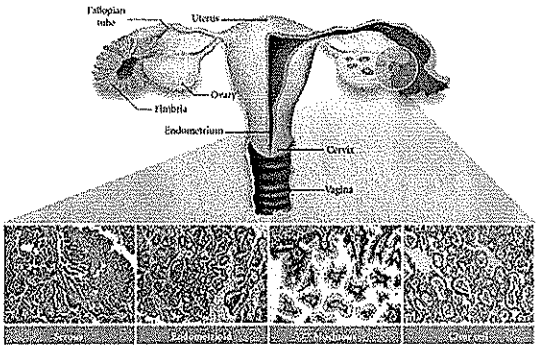
Ovarian Cancer Risk Assessment

According to 2013 statistics from the American Cancer Society, ovarian cancer accounts for 3% of all cancers in U.S. women. Ovarian cancer is most common in older women. It is a little more common in white women than in women of other ethnic groups. The risk of getting ovarian cancer during a woman's lifetime is about 1 in 72. This tool will help you determine if you are at risk for ovarian cancer. It is not a complete assessment of all risks. For a complete evaluation of your risks, see your health care provider.

1. Have you had one or more children?
   - Yes
   - No
2. If you have had a child, how old were you when your first child was born? [ ]
3. Have you taken a fertility medication to help you get pregnant?
   - Yes
   - No
4. Has your mother, sister, or daughter been diagnosed with any of the following cancers?
   - Colon or rectum cancer
   - Breast cancer
   - Ovarian cancer
   - Uterine cancer
   - None
5. Do you have more than one blood relative on your mother's side or father's side of the family who has been diagnosed with ovarian cancer?
   - Yes
   - No
6. Have you ever been diagnosed with any of the following medical conditions?
   - Breast cancer
   - Uterine cancer
   - Colon or rectum cancer
   - Infertility
   - Obesity
   - None

Calculate

PATHOLOGY



Pathology of epithelial ovarian tumors

Histologic type	Cellular type
Serous	
Benign	Endosalpingeal
Borderline	
Malignant	
Mucinous	
Benign	Endocervical
Borderline	
Malignant	
Endometrioid	
Benign	
Borderline	Endometrial
Malignant	
Epithelial-stromal and stromal	
Clear cell	
Benign	Müllerian
Borderline	
Malignant	
Transitional cell	
Benign Brenner	
Borderline Brenner	Transitional
Malignant Brenner	
Non-Brenner transitional cell	
Squamous cell tumors	Squamous
Mixed epithelial	?
Benign	Mixed
Borderline	
Malignant	
Undifferentiated	Anaplastic
Undefined	Mesotheliomas, etc.

Adapted from Serov, SF, RE Scully, IH Sobin: International Histological Classification of Tumors No. 9. Histological Typing of Ovarian Tumours. Geneva: World Health Organization, 1973.

PHD: 14 groups

Epithelial Ovarian Cancer

2/3 of all:

- **SEROUS 50% are benign, 35% is malign and 15% is borderline. Benign are usually unilocullar and adenoca in 60% bilateral**
- **MUCINOUS (larger, 15% malign, cystic with yellow mucus, more often unilocullar with better prognosis than serous – Pseudomyxoma peritonei = mucinous peritoneal fluid – may also be Mucocelle appendicis- that's why it is mandatory to remove appendix.)**
- **ENDOMETRIOID (20% of malign surface, rarely benign, 15-30% also has endometrial cancer, and 10-15% ovarian endometriosis, survival 40-50%)**
- **CLEAR CELL (develops from surface epithelium but also from endometriosis, most frequently malign, survival is 50%)**
- **TRANSITION CELLS = Brenner's (rare, smal, unilocullar, solid, most often benign)**
- **MIXED**

Stromal

- 10% of ovarian tumors, most often hormone active:
- Granulosa cells (Rokitansky described it in 1885. all malign, but low grade malignancy , rare, at any age;
- Adult and juvenile which produce estrogens in 80% - Pubertas praecox, endometrial hyperplasia, ca endometrial cancer, metrorrhagia, solid, unilateral, prognosis for luvenilie is great, core as coffee bean, slow growth),
- Teca cell (tecoma, rarely pure, most often in combination with fibrous tissue= fibro-tecoma, with granulosa cells =granuloza teca cellular; more often in post menopausis, unilocular, solid, benign; in 50% produces estrogen and in 15% androgens, in 20% there is also endometrial cancer;
- Maigs sy= ZM j, ascites, hydrothorax)
- fibroma (solid, firm consistency, in older women, grey-white, regularly Meigs sy), fibrosarcoma
- androblastoma (Sertoli-Leydig; rare, u 50% produces androgens – virilization, often benign, in 20s and 30s; solid, around 10 cm yellow-ish)
- hilar (Leydigoma, rare, solid, unilateral, benign, poligonal cells with lipids, yellow, secrete ketosteroides)

Germ (sex-cord) cells

- 25% of ovarian tumors
- Most often benign teratomas 99%, till the age of 25), in 1% they become malign; monodermal from one germinative leave – most often struma ovarii and rarest, carcinoids as gastrointestinal tissue, they produce 5-hydroxitriptine –carcinoid syndrome), disgerminoma (most often in 21. yrs malignant, most often in women with disgenetig gonades, in pseudohermafrodism, when disgerminoma develops from gonadoblasoma: areas of sinciciotrophoblast – which produces HCG, 15 cm, white yellow and pink in color, most often la, sensitive to chemotherapy and radiation), yolk sac (most often around 19 yrs: large, unilateral, solid, produces AFP, extremely malignant), choriocarcinoma (more often form placental tissue after pregnancy than from germinative cells; very rare; in young women and children; very malignant, early hematologic metastases in lungs, liver, bones. Trophoblastic cells produce HCG > 200 000),

Metastatic

- 5% of ovarian tumors and 10% malignancies from uterus, other ovary, tube, breast, digestive tract (Krukenberg from gastric cancer, stamp ring cells, secret mucus)
- in 70% billateral, nodular
- Gonadoblastoma (rare, benig, made from germinative cells, sarrounded by stroma, u 50% co-exists with disgerminoma which forms from gonadoblastoma, most often in women with disgenetic gonades, in pseudohermafrodismus)

Gynecologic Oncology Group Criteria for Diagnosis of Extraovarian Peritoneal Carcinoma

Both ovaries must be either physiologically normal in size or enlarged by benign process.
Involvement in extraovarian sites must be greater than involvement on the surface of either ovary.
Microscopically, the ovarian involvement must be:
Nonexistent
Confined to ovarian surface epithelium, or underlying cortical stromal involvement of no more than 5 mm
Histologic characteristics are primarily serous type, similar or identical to ovarian serous papillary adenocarcinoma.

Borderline Malignant Epithelial Neoplasms
Ovarian tumors of borderline malignancy,
Low malignant potential,
Atypical, Epithelial Proliferative ovarian TM

- Histologically, tumors with atypical epithelial proliferation, without stromal invasion, but still able to metastasize.
- Usually form 15 years sooner – most often before 50 yrs.
- Most often in grade I. 80%.
- The worst prognosis is in micropapillary serous carcinoma.
- They make 15% of ovarian cancers of surface epithelium (40-60 yrs.)
- Dg. in I grade in 70%.
- Most often serous, rarely mucous.
- CA125 in 50% normal.

Borderline,
Ovarian tumors of borderline malignancy,
Low malignant potential,
Atypical, Epithelial Proliferative ovarian TM

- Th.
- surgery
  - less radical (TAH-BSO) and ipsilateral lymphadenectomy
  - in mucinous appendectomy
- chemo and radio therapy have no effect on survival, and more patients die due to complications
  - For higher grades, chemotherapy prolongs the disease free interval, but not the survival
  - kemoth. if it is: serous, with implants on peritoneum (III.), or an incomplete surgical procedure, recidives.
- In case of relapse, citoreduction

Borderline,
Ovarian tumors of borderline malignancy,
Low malignant potential,
Atypical, Epithelial Proliferative ovarian TM

5 AND 10 YEAR RELATIVE SURVIVAL RATES:

- **Stage I 99, 97 %**
- **Stage II 98, 90 %**
- **Stage III 96, 88 %**
- **Stage IV 77, 69 %**

CLASSIFICATION

FIGO

FIGO Primary Tumor (T)

TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	I Tumor limited to ovaries (one or both)
T1a	IA Tumor limited to one ovary; capsule intact, no tumor on ovarian surface. No malignant cells in ascites or peritoneal washings
T1b	IB Tumor limited to both ovaries; capsules intact, no tumor on ovarian surface. No malignant cells in ascites or peritoneal washings
T1c	IC Tumor limited to one or both ovaries with any of the following: capsule ruptured, tumor on ovarian surface, malignant cells in ascites or peritoneal washings
T2	II Tumor involves one or both ovaries with pelvic extension
T2a	IIA Extension and/or implants on uterus and/or tube(s). No malignant cells in ascites or peritoneal washings
T2b	IIB Extension to and/or implants on other pelvic tissues. No malignant cells in ascites or peritoneal washings
T2c	IIC Pelvic extension and/or implants (T2a or T2b) with malignant cells in ascites or peritoneal washings
T3	III Tumor involves one or both ovaries with microscopically confirmed peritoneal metastasis outside the pelvis
T3a	IIIA Microscopic peritoneal metastasis beyond pelvis (no macroscopic tumor)
T3b	IIIB Macroscopic peritoneal metastasis beyond pelvis 2 cm or less in greatest dimension
T3c	IIIC Peritoneal metastasis beyond pelvis more than 2 cm in greatest dimension and/or regional lymph node metastasis

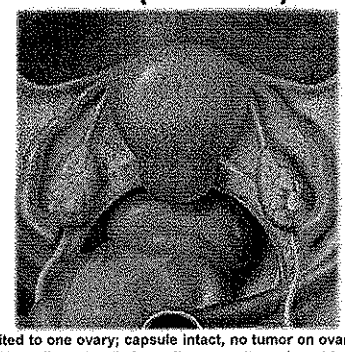
Regional Lymph Nodes (N)

TNM FIGO
Categories Stages
NX - Regional lymph nodes cannot be assessed
N0 - No regional lymph node metastasis
N1 - IIIC Regional lymph node metastasis

Distant Metastasis (M)

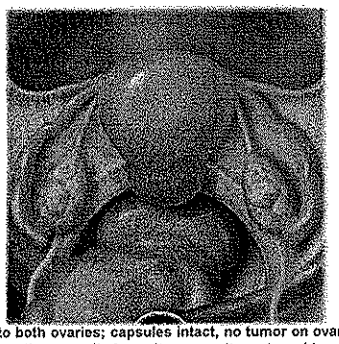
TNM FIGO
Categories Stages
M0 - No distant metastasis
M1 - IV Distant metastasis
(excludes peritoneal metastasis)

T1a (FIGO IA)



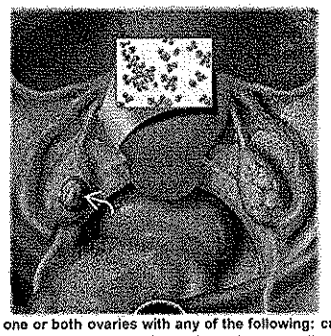
Tumor limited to one ovary; capsule intact, no tumor on ovarian surface.
No malignant cells in ascites or peritoneal washings

T1b (FIGO IB)



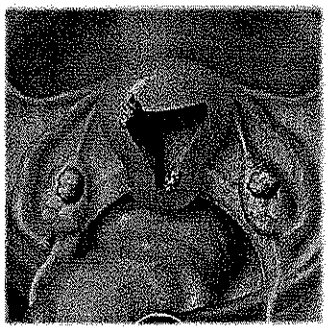
Tumor limited to both ovaries; capsules intact, no tumor on ovarian surface. No malignant cells in ascites or peritoneal washings

T1c (FIGO IC)



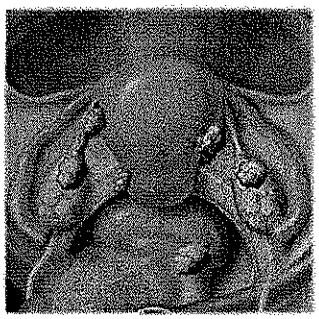
Tumor limited to one or both ovaries with any of the following: capsule ruptured, tumor on ovarian surface, malignant cells in ascites or peritoneal washings

T2a (FIGO IIA)



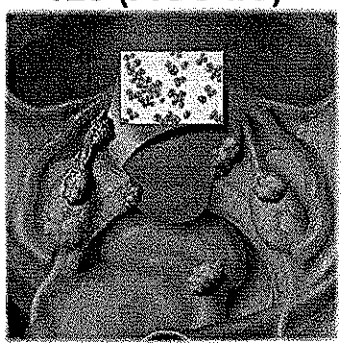
Extension and/or implants on uterus and/or tube(s). No malignant cells in ascites or peritoneal washings

T2b (FIGO IIB)



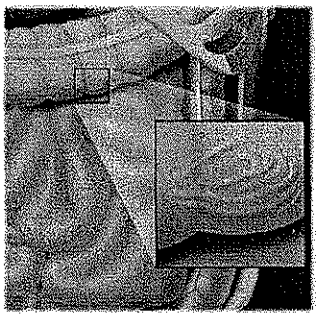
Extension to and/or implants on other pelvic tissues. No malignant cells in ascites or peritoneal washings

T2c (FIGO IIC)



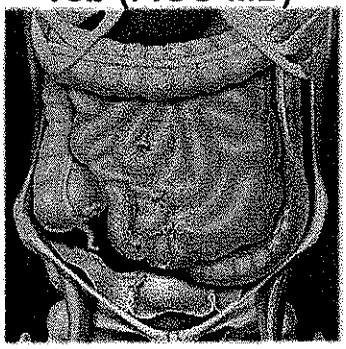
Pelvic extension and/or implants (T2a or T2b) with malignant cells in ascites or peritoneal washings

T3a (FIGO IIIA)



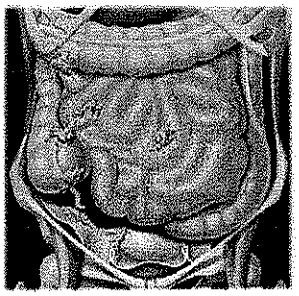
Microscopic peritoneal metastasis beyond pelvis (no macroscopic tumor)

T3b (FIGO IIIB)



Macroscopic peritoneal metastasis beyond pelvis 2 cm or less in greatest dimension

T3c (FIGO IIIC)



Peritoneal metastasis beyond pelvis more than 2 cm in greatest dimension and/or regional lymph node metastasis

METASTASES, ORGAN FREQUENCY	
Liver	45-48%
Lung	34-39%
Pleura	25%
Adrenal gland	15-21%
Spleen	15-20%
Bone	11%
Kidney	7-10%
Skin and subcutaneous tissue	5%
Brain	3-6%

FIGO IV

distant metastasis; pleural effusion with positive cytologic test results; parenchymal liver metastasis

Distant metastasis (excludes peritoneal metastasis)

SPREAD

RUTES OF SPREAD:

- LOCAL
- PETRITONEAL
- LYMPHATIC
- HEMATOGENOUS

CLINICAL ISSUES

Most Frequent Presenting Symptoms of Ovarian Cancer

Symptom	Relative Frequency
Abdominal swelling	XXXX
Abdominal pain	XXX
Dyspepsia	XX
Urinary frequency	XX
Weight change	X

- Discomfort and pressure in abdomen
- Abdominal swelling (ascites), abdominal pain
- Respiratory problems
- Sickness, nausea, weight loss
- Exhaustion

DIAGNOSTICS

DIAGNOSTICS

- History (family)
- Gynecological examination
- Ultrasound examination of the pelvis and abdomen
- Markers
- IVU, intestinal passage, lung X-ray, CT, MRI colonoscopy, puncture of ascites, cytodiagnostics LPSC, biopsy, PHA

Routine pelvic examinations detect only 1 ovarian cancer in 10,000 asymptomatic women.

MARKERS

In juvenile and adolescence:
- LDH
- alfa feto protein
- HCG

In reproductive age:
- CA-125
- CA 19-9
- CEA

In postmenopausal
- CA-125

Conditions associated with an elevated serum CA 125 concentration

Gynecologic malignancies
- Epithelial ovarian and endometrial cancers
- Fallopian tube cancers and germ cell tumors
- Adenocarcinoma of the cervix
- Sertoli-Leydig cell tumors of the ovary

Benign ovarian neoplasms
- Endometriosis
- Functional ovarian cysts
- Leiomyomata
- Meigs' syndrome
- Menstruation
- Pregnancy
- Ovarian hyperstimulation
- Pelvic inflammation

Nongynecologic conditions
- Liver disease and cirrhosis
- Colitis
- Heart failure
- Diabetes
- Diverticulitis
- Lupus
- Mesothelioma
- Pericarditis
- Polyarteritis nodosa
- Postoperative period
- Previous irradiation
- Renal disease
- Sarcoidosis
- Tuberculosis
- Pleural effusion
- Ascites

Nongynecologic cancers
- Breast
- Colon
- Lung
- Pancreas

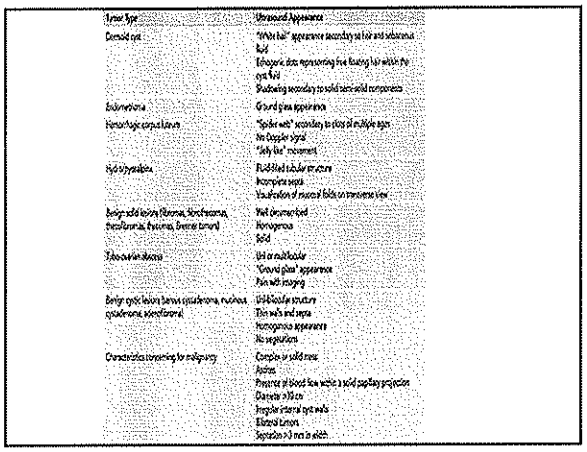
The main criteria that indicate malignancy

- **Age**
- **Tumor size**
- **TV ultrasound CD**
- **CA-125 value**
- **Symptoms**
- **Unilaterally or bilaterally**
- **...**

CA ovarii - risk ??
AGE

- In premenopausal women 4/1000
- In postmenopausal women in 20-30%

Nezhat et al, Am J Ob Gyn 1992
Rulin and Preston, Ob Gyn 1987



OVARIAN CANCER

Ultrasound factors suggesting malignancy of ovarian tumors

- **A solid component (nodular, papillary)**
- **Sep thickness of 3 mm or more**
- **Doppler shows flow in a solid mass**
- **Ascites**
- **Irregular arrangement of blood vessels**
- **Blood vessels varied in diameter**
- **Walls of blood vessels do not have any muscle**
- **Low values of resistance index (RI <0.42)**
- **Tumor lakes and arteriovenous shunts**

DIFFERENTIAL DIAGNOSIS

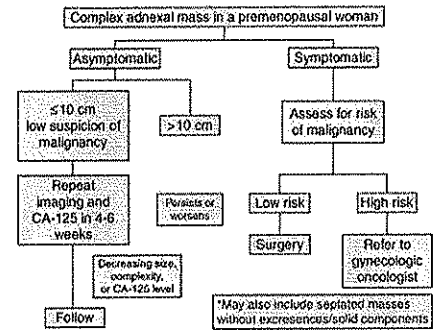
Differential diagnosis of adnexal masses in women

Extraovarian mass
• Ectopic pregnancy
• Hydrosalpinx or tuboovarian abscess
• Paraovarian cyst
• Peritoneal inclusion cyst
• Pedunculated fibroid
• Diverticular abscess
• Appendiceal abscess or tumor
• Fallopian tube cancer
• Inflammatory or malignant bowel disease
• Pelvic kidney
Ovarian mass
• Simple or hemorrhagic physiologic cyste (eg, follicular, corpus luteum)
• Endometrioma
• Theca lutein cysts
• Benign, malignant, or borderline neoplasms (eg, epithelial, germ cell, sex-cord)
• Metastatic carcinoma (eg, breast, colon, endometrium)

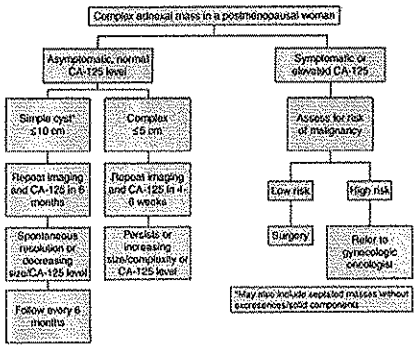
DD

TREATMENT

Schema for the management of a complex adnexal mass in a premenopausal woman



Schema for the management of a complex adnexal mass in a postmenopausal woman



First-line Therapy – Standard Treatment Options

Surgery with maximum cytoreduction effort <1cm residual disease

↓

Platinum + Taxane Chemotherapy (Carboplatin + Paclitaxel)

Guidelines for Staging in Epithelial Ovarian Cancer

- Peritoneal cytology
- Careful and systematic abdominal exploration – inspect and
- palpate all peritoneal surfaces
- Omentectomy
- Total abdominal hysterectomy and bilateral salpingooophorectomy
- Pelvic and para-aortic lymphadenectomy
- Random and directed peritoneal biopsies – posterior cul-desac, bladder reflection, both pelvic sidewalls and both paracolic spaces
- Biopsy or scrapings from the undersurface of both diaphragms
- Appendectomy in selected cases (for example, mucinous histology)

The goal of "complete resection to no residual disease" is the most optimal postoperative status

RT-5-god preživljenje:

0 cm - 60%;
< 2cm - 25%;
biopsija - 9%

Low-risk Early-Stage Disease

1. No adjuvant chemotherapy is recommended for these patients.

High-risk Early-Stage Disease

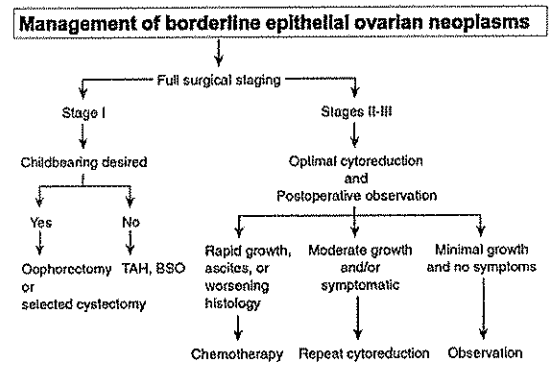
1. Patients with high-risk stage I epithelial ovarian cancer should be given adjuvant chemotherapy. The type depends on the patient's overall health and the presence of medical comorbidities.

2. Treatment with *carboplatin* and *paclitaxel* chemotherapy for three to six cycles is used in most patients, although single-agent *carboplatin* may be preferable for women with significant medical comorbidities.

3. Consideration should also be given to the addition of pelvic radiation in selected patients with clear cell and endometrioid cancers at risk for local recurrence.

Second-Look Operation (Reassessment Surgery)

- Only in FIGO stage III and IV
- after 6 cycles of chemo th clinical and radiographic disease-free
- did not demonstrate a survival benefit



FOLLOW UP

- 1 / 2 - 4 months - 2 y.
- 1 / 3-6 months - 3 y.
- 1 / year

- EXAMINATION
- US
- CA125
- KKS
- BIOKEMIJA
- CT
- MRI
- PET-CT
- RTG PL.

1.kontrola – nakon 2 mj/ UZV-CT abd, urea, kreatinin, KKS, urin/sed, PAPA
Svaka 3 mj/ 2 godine
Rtg pluća svakih 6 mj/ 2 godine
PAPA svaka 3 mj/ 2 godine
Nakon 2 god-svakih 6 mj (UZV-CT tg)
Nakon 5 godina – kontrola 1 godišnje

FOLLOW UP"- radikalna op. i zračenje
= + *INFUZIJSKA UROGRAFIJA NAKON 3 MJESECA*

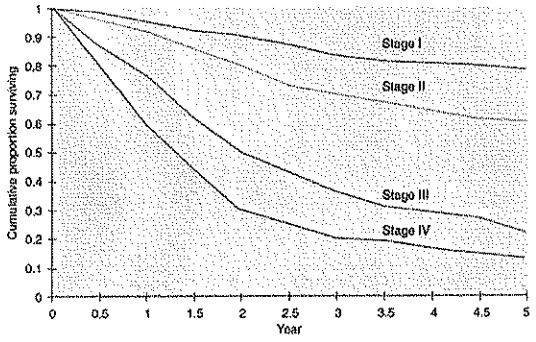
PROGNOSIS

Carcinoma of the ovary: FIGO stage and overall survival

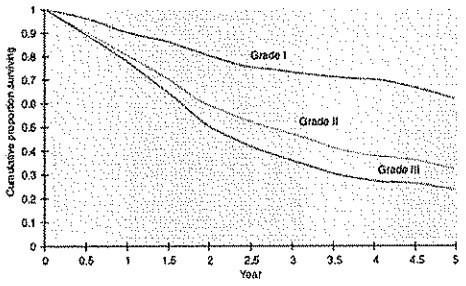
FIGO stage	Number of patients	Overall survival, percent		
		1 year	2 years	5 years
IA	632	98.4	96.2	89.6
IB	69	100	93.9	86.1
IC	663	96.3	91.4	83.4
IIA	72	93.0	87.2	70.7
IIB	93	93.4	84.5	65.5
IIC	241	93.6	85.6	71.4
IIIA	128	88.1	72.6	46.7
IIIB	271	85.7	70.6	41.5
IIIC	2030	84.8	64.5	32.5
IV	626	72.4	48.4	18.6

Original table modified for this publication. From: Heintz, AP, Odicino, F, Maisonneuve, P, et al. Carcinoma of the ovary. Int J Gynaecol Obstet 2006; 95:S161. Table used with the permission of Elsevier Inc. All rights reserved.

Cumulative proportion surviving by stage

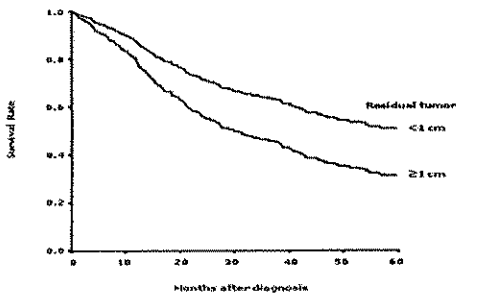


Histologic grade is an important independent prognostic factor in patients with epithelial tumors of the ovary



Serous cystadenocarcinoma of the ovary. Cumulative proportion surviving by degree of differentiation

Estimated 5-year survival by residual tumor volume after adjusting for age and international federation of gynecology and obstetrics (FIGO) stage



Data from: Tingulstad, S, Skjeldestad, E, Halvorsen, TB, Hagen, B, Survival and prognostic factors in patients with ovarian cancer. Obstet Gynecol 2003; 101:885.

Survival in patients with stage IIIc disease by completeness of surgery (*n* = 1059)