

CANCER ANTIGEN (CA) 125

INTRODUCTION

Ovarian cancer is the most lethal malignancy of gynecological origin. Cancer in the ovary may derive from epithelium (95% cases) or stromal supporting cells or germ cells. The most common ovarian epithelial malignancies are Serous tumors (50%); Mucinous tumors (25%); Endometrioid carcinoma (15%); Clear cell carcinoma (5%); Brenner tumor (1%). CA 125 is a marker of epithelial ovarian malignancy.

NORMAL RANGE

<35.0 U/mL

CLINICAL USE

- An aid in the management of Ovarian cancer patients. Preoperative CA 125 level of < 65 U /mL is associated with a significantly greater 5 year survival rate.
- Monitor the course of disease in patients with Invasive epithelial ovarian cancer
- Detection of residual tumor in patients with Primary epithelial ovarian cancer who have undergone first line therapy. Persistent elevation of CA 125 levels after 3 cycles of therapy indicates a poor prognosis.

STAGE OF OVARIAN CANCER	PERCENTAGE POSITIVITY OF CA 125
Stage I	50
Stage II	90
Stage III & IV	>90

INTERPRETATION

Increased Levels

Malignant disease	<ul style="list-style-type: none">• Non mucinous epithelial ovarian carcinoma (85%)• Fallopian tube tumors (100%)• Cervical adenocarcinoma (83%)• Endometrial adenocarcinoma (50%)• Squamous cell carcinoma cervix / vulva (15%)• Trophoblastic tumors (45%)• Non-Hodgkin lymphoma (40%)• Cancer of Pancreas / Liver / Lung
Endometrial conditions	<ul style="list-style-type: none">• Pregnancy (27%)• Endometriosis• Menstruation
Pleural effusion	<ul style="list-style-type: none">• Cancer• Congestive heart failure

Peritoneal effusion	<ul style="list-style-type: none"> • Pelvic inflammatory disease • Bacterial peritonitis
Non malignant conditions	<ul style="list-style-type: none"> • Cirrhosis (66%) • Disorders of GIT / Liver / Pancreas • Renal failure
Healthy individuals	1%

Decreased Levels

- Postmenopausal women
- African American & Asian women have lower normal values

HIGH RISK FACTORS FOR OVARIAN CANCER

- Epidemiologic factors – increasing age specially above 60 years. Females have approximately 1:72 lifetime risk of developing ovarian cancer.
- Genetic factors – 10% women with ovarian cancer have a somatic mutation in BRCA1 or BRCA2 & Lynch syndrome Type II caused by mutations in repair genes (MSH2, MLH1, MLH6, PMS1 & PMS2)
- Nulliparity
- Use of talc agents to the perineum
- Obesity
- Hormone Replacement Therapy (HRT)

PROTECTIVE FACTORS FOR OVARIAN CANCER

- Oral contraceptives
- Multiparity
- Breast feeding
- Fallopian tube ligation

EARLY DETECTION OF OVARIAN CANCER

- CA125 is recommended along with Transvaginal ultrasound (TVS) for early detection of ovarian cancer in women with hereditary syndromes.
- It also acts as an adjunct in distinguishing benign from malignant suspicious pelvic masses in postmenopausal women.

LABORATORY DIAGNOSIS

- Diagnosis of ovarian cancer is made on **histological examination** of tissue or **cytology** of peritoneal or pleural fluid if present. Rarely abnormal glandular cells may be seen on Pap smear which on further workup are found to originate from the ovary.
- Imaging for identifying an adnexal mass
- Blood biomarkers –
 - CA125 – CA 125 is elevated in approximately 50% patients with early stage disease and >80% patients with advanced disease. Thus serial CA 125 levels over time may be beneficial as a screening tool.
 - Human epididymis protein 4 (HE4) – helpful in diagnosing recurrent or progressive disease or in the evaluation of a suspicious adnexal mass. This is an FDA approved test for monitoring the disease.
 - ROMA (Risk of ovarian malignancy algorithm) – it is used as a supplement to the standard pre-surgical evaluation of a patient with a pelvic mass to assess likelihood of malignancy prior to surgery specially in those cases where presurgical evaluation does not indicate malignancy.
 - Carcinoembryonic antigen (CEA) – non specific marker as it is elevated in non malignant conditions also
 - OVA1 – is a panel of 5 serum biomarkers of which 2 markers are up-regulated (CA125 & Beta 2 microglobulin) & 3 markers are down-regulated (Transferrin, Transthyretin & Apolipoprotein A1). An algorithm determines the patients risk for ovarian cancer

LIMITATIONS

- CA125 level is not increased in Mucinous adenocarcinomas.
- Normal concentration of CA125 does not exclude presence of the tumor.
- Even at high concentrations, CA125 alone is not useful for distinguishing benign from malignant pelvic masses.
- Although CA125 may be increased 12 months before clinical evidence of disease, it is not recommended for screening women for Serous carcinoma ovary because it is not increased in 20% cases at the time of diagnosis and in <10% cases with Stage I / II carcinoma.
- In postoperative monitoring cases for persistent / recurrent disease, 95% patients show CA125 >35 U/mL but a negative result does not exclude residual disease.
- In 0.6% of normal women >50 years of age, CA125 levels may be increased
- Rising level of CA125 during chemotherapy is associated with tumor progression and return to normal is associated with a good response. However it may remain elevated in stable or progressive Serous carcinomas.
- Different assays do not produce equivalent values and should not be used interchangeably.