

## Ovarian Cancer — Stages and Survival Rate

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Ovarian cancer is of epithelial origin in 60% of the patients. Most patients present at an advanced stage due to the lack of specific symptoms except for mucinous ovarian cancer where abdominal distension is so severe that patients present very early in the disease. Once ovarian cancer is suspected, the patient usually undergoes a transvaginal ultrasonography, abdomen-pelvic CT scan and CA-125 concentration measurement. If an ovarian cyst or mass is identified, its characteristics will be noted and a risk of malignancy index can be calculated. Treatment involves neoadjuvant platinum-based chemotherapy with or without surgery. Newer treatments include antiangiogenic antivascular endothelial growth factor bevacizumab and pazopanib.



### Definition

Ovarian cancer can be defined as a **primary malignancy of the ovaries** that is usually of **epithelial origin**. Rare forms of ovarian cancer include germ cell, sex cord, and stromal tumors.

## Epidemiology

Ovarian cancer occurs in more than 22,500 women per year in the United States and is responsible for 14,000 deaths annually. The incidence of ovarian cancer is **9.4 per 100,000**. This means that 1 out of 60 women will develop ovarian cancer in their lifetime.

Unfortunately, the majority of the patients present late to the health care system. The median age of diagnosis is estimated to be 63 years making it a disease common in women who are already experiencing **menopause**. This is true, however, only for women without genetic mutations that are known to be associated with ovarian cancer. Women with a **genetic predisposition** to ovarian cancer are usually 10 years younger than typical patients.

## Etiology

Ovarian cancer is usually of unknown cause but several **environmental and genetic risk factors** have been identified.

**Multiple pregnancies** and the use of **oral contraceptive pills** are known to result in more anovulatory cycles which are believed to lower the risk of ovarian cancer.

**Endometriosis** might increase the risk of ovarian cancer. Additionally, **tobacco smoking** and **human papillomavirus** have been linked to an increased risk of ovarian cancer in some studies.

Several genetic mutations have been linked to different types of epithelial ovarian cancers. For instance, high-grade serous cancers are found more commonly in women with **BRCA1 and 2 mutations**. KRAS mutations are linked to an increased risk of mucinous ovarian cancers, while PTEN mutations might increase the risk of endometrioid and clear cell cancer.

**Peutz-Jegher disorder**, a genetic disease associated with different forms of cancer, also increases the risk of ovarian cancer.

## Pathophysiology of Ovarian Cancer

In almost all forms of ovarian cancer, **impaired DNA repair** is implicated in the pathogenesis. To understand the different pathological changes happening in ovarian cancer, we should classify epithelial ovarian cancers according to their histological patterns.

### High-grade serous ovarian cancer

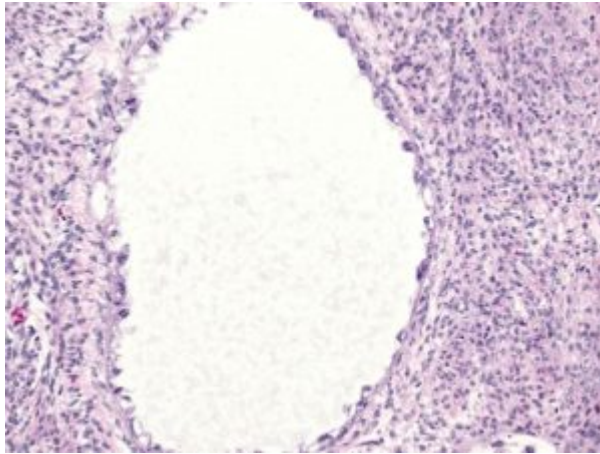
High-grade serous ovarian cancer is the most common form of epithelial ovarian cancers. All patients who have a high-grade serous ovarian cancer are expected to have **abnormalities in the p53 gene**. Mutations in the p53 gene are thought to be de novo in the majority of the cases, but **BRCA1 and BRCA2 mutations** are also known to cause high-grade serous ovarian cancer.

This type of ovarian cancer is the least differentiated and is the most malignant. High-grade serous ovarian cancer is sensitive to **chemotherapy**.

## Low-grade serous ovarian cancer

This type of ovarian cancer is not as common as high-grade serous ovarian cancer but is known to be less invasive. Several genes related to DNA repair are also impaired either de novo or due to hereditary, including PI3KCA, BRAF, and KRAS. These tumors are less responsive to chemotherapy.

## Clear-cell ovarian cancer



**Image:** "High magnification of tubulocystic clear-cell carcinoma of the ovary. Cyst is lined by hobnail cells with clear cytoplasm." by Amarvinita - Own work. License: [CC BY-SA 4.0](https://creativecommons.org/licenses/by-sa/4.0/)

**When endometriosis is** associated with ovarian cancer, it is very likely that the person has a clear-cell ovarian cancer. This form of ovarian cancer shows more differentiated cells. Unfortunately, these patients do not respond well to chemotherapy.

## Mucinous ovarian cancer

Fortunately, mucinous ovarian cancers cause more symptoms and are the earliest to be detected while in stage 1 disease. **KRAS mutations** are found in all patients with mucinous ovarian cancer.

## Risk of Malignancy Assessment in Ovarian Cancer

Many of the patients with ovarian cancer are diagnosed after the accidental finding of an **ovarian cyston ultrasonography** that was ordered for other indications; therefore, it is essential to differentiate between malignant and benign ovarian cysts.

Table 1 shows how to calculate the risk of malignancy index (RMI) for a patient with an ovarian cyst.

Parameter	Scoring Scheme	Notes
Ultrasonography of the ovarian cyst	Multilocular or solid: 0 or 1 Ascites: 0 or 1 Suspected metastasis: 0 or 1	0 is NO while 1 is YES. Total score ranges from 1 to 3
Menopausal state	Premenopause: 1 Postmenopause: 3	This score is multiplied by the previous score.
CA-125 serum concentration	Numerical value	This value is multiplied by the previous product of multiplication.

**Table 1: RMI = Ultrasonography Score X Menopausal Score X CA-125 Concentration. When RMI > 200, the risk of ovarian cancer is high.**

## Clinical Presentation

The most common presentation of ovarian cancer is **abdominal pain and distension**. The picture can highly resemble that of [irritable bowel syndrome](#) and, accordingly, any woman who presents with irritable bowel syndrome symptoms after the age of 50 years should be screened for ovarian cancer by measuring **serum CA-125 concentration**. Unfortunately, there are no specific symptoms or signs of ovarian cancer and a **pelvic ultrasound scan** is recommended whenever in doubt.

Patients with a known family history of ovarian or [breast cancer](#) should be screened for **BRCA1 or 2 mutations**. The risk of ovarian cancer in this population is really high as up to 60% of these women will develop the disease.

## Diagnostic Work-up

The first step in the assessment of a patient presenting with an ovarian cyst or with symptoms that could be explained by ovarian cancer is to measure **serum CA-125**. Cancer antigen-125 is very useful in the assessment of the risk of malignancy index described above and should always be measured in these patients.

**Transabdominal ultrasonography** is indicated to assess for possible [metastasis](#), while **pelvic transvaginal ultrasound** should be used to assess [ovarian cysts](#) and suspicious lesions.

An **abdomino-pelvic computerized tomography (CT) scan** is indicated when malignancy is suspected to assess other organ involvement and for staging purposes.

**Abdominal magnetic resonance imaging (MRI)** is indicated in a few patients also for staging purposes, but ultrasonography, combined with CA-125 concentration, remains the best diagnostic modality for ovarian cancer.

## Staging of Ovarian Cancer

The international federation of gynecology and obstetrics recently came up with the staging system for ovarian cancer that is related to the management of the condition. **Disease I** indicates cancer that is limited to the ovaries which can be unilateral (Ia), bilateral (Ib), or unilateral or bilateral but associated with ascites (Ic).

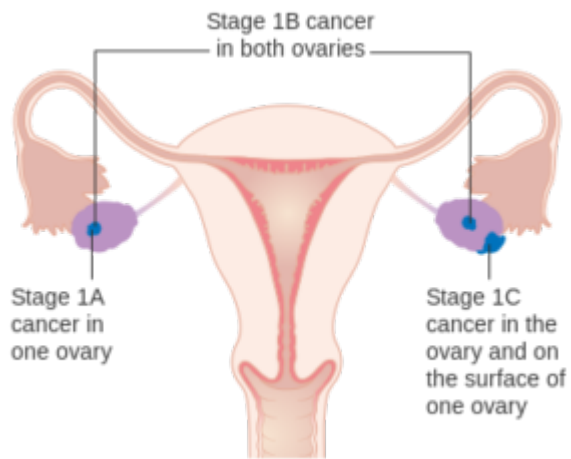


Image: "Diagram showing stage 1 ovarian cancer." by Cancer Research UK - Original email from CRUK. License: [CC BY-SA 4.0](https://creativecommons.org/licenses/by-sa/4.0/)

**Disease II** indicates cancer that involves other pelvic organs. IIa is ovarian cancer extending to the fallopian tubes or uterus. IIb disease indicates an extension to other pelvic organs such as the rectum. IIc includes IIa or IIb disease with ascites.

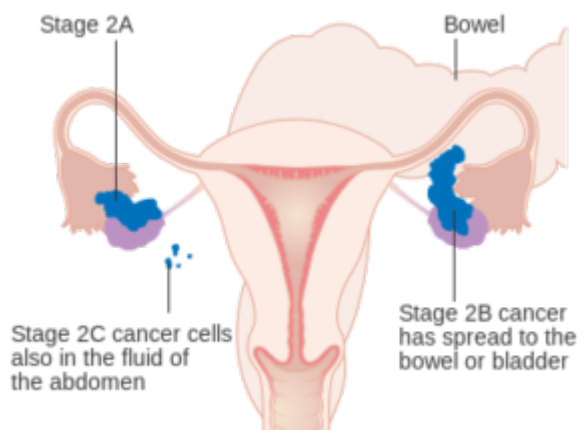


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**Disease III** indicates an involvement of the abdominal peritoneal surface IIIa, a tumor that is 2 cm in diameter IIIb, or a tumor that is above 2 cm with lymph node involvement IIIc. Disease IV disease indicates distant metastasis.

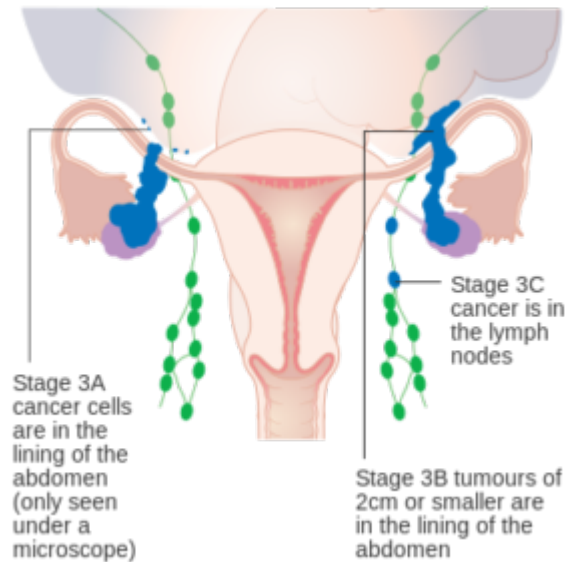


Image: "Diagram showing stage 3 ovarian cancer." by Cancer Research UK - Original email from CRUK. License: [CC BY-SA 4.0](https://creativecommons.org/licenses/by-sa/4.0/)

## Treatment of Ovarian Cancer

### Surgical Management

The purpose of the **surgery** is to provide more information for staging, provide an **excisional biopsy** for histopathological assessment and to **remove the tumor**. The surgery involves hysterectomy, bilateral salpingo-oophorectomy, tumor debulking, and removal of the omentum. Patients who are confirmed to have stage I disease do not need chemotherapy.

Patients with stage IV disease are not good surgical candidates and they might benefit from **chemotherapy** alone. In these patients, a **percutaneous biopsy** is indicated to assess the histopathological type of the tumor. Additionally, **neoadjuvant chemotherapy** may render some of these patients operable.

Premenopausal women with stage Ia disease that is confirmed to have a low-grade serous cancer or a mucinous tumor might benefit from **unilateral oophorectomy** to preserve fertility.

### Chemotherapy

**Chemotherapy** for ovarian cancer includes **carboplatin combined with either paclitaxel or docetaxel**. This regimen has been found to be successful for patients with early-stage disease and advanced disease. Newer treatments are emerging for ovarian cancer, such as the antiangiogenic antivascular endothelial growth factor **bevacizumab** and **pazopanib**.

Patients with **recurrent disease** are identified by an increase in their CA-125 concentration, double the normal upper limit. These patients usually undergo another cycle of chemotherapy as the tumor is more difficult to localize by CT scan; hence, surgical intervention is usually not possible.

## Medical Management

**Tamoxifen**, an estrogen receptor antagonist, is not useful in ovarian cancer regardless of the estrogen receptor state in the tumor. Premenopausal women who undergo bilateral ovarian removal need **estrogen-based hormonal replacement therapy**. Postmenopausal women who also have a hysterectomy can have an **estrogen-only replacement therapy**; otherwise, estrogen should be used with caution due to the increased risk of **endometrial cancer** in these women.

## References

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