Ovarian Cancer

A type of cancer in which abnormal cells begin to grow in one or both of a woman's ovaries.

Diagnosis Female

Related Diagnoses:
- Polycystic ovary syndrome
- Fallopian tube blockage
- Endometriosis
- Menopause
- Hydrosalpinx
- Endometrial cancer
- Tubal ligation
- Hysterectomy

About Ovarian cancer

Ovarian cancer is a cancer that begins in an ovary. The term “ovarian cancer” encompasses several types of cancer that all arise from the cells of the ovaries in the female reproductive system. Ovarian cancer commonly manifests as three different types including:

1. epithelial (derived from the cells on the surface of the ovary or fallopian tube)
2. germ cell (derived from the cells that produce eggs)
3. cord-stromal cell (derived from the connective tissue within the ovary)

Ovarian cancer remains the leading cause of death from all gynaecological tumors due to the lack of both symptoms at an early stage and a reliable clinical test.

Cancer is a complex array of different diseases. It results in abnormal cells that have the ability to invade or spread to other parts of the body. Approximately 90% of ovarian cancers are carcinomas (malignant epithelial tumors) and, based on histopathology, immunohistochemistry, and molecular genetic analysis, at least five main types are currently distinguished:

- high-grade serous carcinoma (HGSC, 70%)
- endometrioid carcinoma (EC, 10%)
- clear-cell carcinoma (CCC, 10%)
- mucinous carcinoma (MC, 3%)
- low-grade serous carcinoma (LGSC, <5%)

The ovarian cancer stages are labelled by Roman numerals I, II, III and IV to describe how widespread a cancer is. The stages are also divided into smaller groups:

**Stage I** - Cancer is completely limited to the ovary (Pic.1).
- Stage IA - involves one ovary, capsule intact, no tumor on ovarian surface, negative washings
- Stage IB - involves both ovaries; capsule intact; no tumor on ovarian surface; negative washings
- Stage IC - tumor is present on the outer surface of one or both ovaries; the capsule has ruptured

**Stage II** - Pelvic extension of the tumor (must be confined to the pelvis) or primary peritoneal tumor, involves one or both ovaries (Pic.2).
- Stage IIA - tumor found on uterus or fallopian tubes
- Stage IIB - tumor elsewhere in the pelvis
- Stage IIC - tumor is present on the outer surface of one or both ovaries; the capsule has ruptured; and there are ascites including malignant cells or with positive peritoneal washings

**Stage III** - Cancer found outside the pelvis or in the retroperitoneal lymph nodes, involves one or both ovaries (Pic.3).
• Stage IIIA - metastasis in retroperitoneal lymph nodes or microscopic extrapelvic metastasis
• Stage IIIB - metastasis in the peritoneum less than or equal to 2 cm in diameter, regardless of retroperitoneal lymph node status; or metastasis to liver or spleen capsule
• Stage IIC - metastasis in the peritoneum greater than 2 cm in diameter, regardless of retroperitoneal lymph node status; or metastasis to liver or spleen capsule

Stage IV - Distant metastasis (i.e. outside of the peritoneum) (Pic.4). Common areas to which the cancer may spread include the lining of the abdomen, lining of the bowel and bladder, lymph nodes, lungs, and liver.

High-grade serous is most common. These tumors are believed to start in the cells covering the ovaries, though some may form at the Fallopian tubes. Since the ovaries and tubes are closely related to each other, it is thought that these fallopian cancer cells can mimic ovarian cancer. Other types may arise from the egg cells (germ cell tumor) or supporting cells. Less common types of ovarian cancer include germ cell tumors and sex cord stromal tumors.

The risk of ovarian cancer increases in women who have ovulated more over their lifetime. This includes those who have never had children, those who begin ovulation at a younger age or reach menopause at an older age.

The dismal fact is that 75% of patients are diagnosed when the tumor has spread or metastasized into the peritoneal wall or abdominal cavity. However, some tests are done if a patient is showing signs of ovarian cancer.

Some exams that are used to diagnose ovarian cancer include:

• biopsy
• physical exams, including a pelvic exam and a Pap test
• cancer antigen 125 (CA-125) test to measure amount of protein found on cancer cell surfaces
• pelvic and transvaginal ultrasounds
• pelvic or abdominal CT scan or MRI

Screening is not recommended in women who are at average risk, as evidence does not support a reduction in death and the high rate of false positive tests may lead to unneeded surgery, which is accompanied by its own risks. Those at very high risk may have their ovaries removed as a preventive measure. If caught and treated in an early stage, ovarian cancer may be curable.

Treatment usually involves chemotherapy and surgery, and sometimes radiotherapy, regardless of the subtype of ovarian cancer. Surgical treatment may be sufficient for well-differentiated malignant tumors and confined to the ovary. Addition of chemotherapy may be required for more aggressive tumors confined to the ovary. For patients with advanced disease, a combination of surgical reduction with a combination chemotherapy regimen is standard. Borderline tumors, even following spread outside of the ovary, are managed well with surgery, and chemotherapy is not seen as useful.

Associated diseases

• polycystic ovary syndrome
• endometriosis

Complications

Complications of ovarian cancer can include spread of the cancer to other organs, progressive function loss of various organs, ascites, and intestinal obstructions, which can be fatal. Intestinal obstructions in multiple sites are the most common proximate cause of death. Intestinal obstruction in ovarian cancer can either be a true obstruction, where tumor blocks the intestinal lumen, or a pseudo-obstruction, when tumor prevents normal peristalsis. Continuous accumulation of ascites can be treated by placing a drain that can be self-drained.

Risk factors

Some studies suggested an association among the use of ovulation-inducing drugs, IVF, and ovarian cancer risk, but only few cases of ovarian cancer have been described in women followed in IVF programs. Therefore the relationship between IVF and development of ovarian cancer is still under investigation.

Ovarian cancer mostly arises sporadically, but a fraction of cases are associated with mutations in BRCA1.
and BRCA2 genes. Women with BRCA gene mutations usually also have their Fallopian tubes removed at the same time (salpingo-oophorectomy), since they also have an increased risk of Fallopian tube cancer. The risk of ovarian cancer is higher for women with a high-risk BRCA1 mutation than with a BRCA2 mutation. The presence of a BRCA mutation in OC patients has been suggested as a prognostic and predictive factor. In addition, the identification of asymptomatic carriers of such mutations offers an unprecedented opportunity for OC prevention.

Women who have had children are less likely to develop ovarian cancer than women who have not, and breastfeeding may also reduce the risk of certain types of ovarian cancer. Tubal ligation and hysterectomy reduce the risk and removal of both tubes and ovaries (bilateral salpingo-oophorectomy) dramatically reduces the risk of not only ovarian cancer but breast cancer also. A hysterectomy that does not include the removal of the ovaries has a one-third reduced risk of developing ovarian cancer, it also has no higher risk of developing other types of cancer, heart disease or hip fractures.

Impact on fertility

Two possibilities have been discussed with regard to the relationship between ovarian cancer and fertility treatment. One possibility is that fertility treatment involving ovarian stimulation and controlled ovulation contributes to the development of ovarian cancer. IVF (in vitro fertilisation) requires a pharmacological ovarian hyperstimulation. Generally the intensive ovulation induction treatments are represented by injectable gonadotropins (FSH analogues), GnRH agonist and GnRH antagonist. Some studies suggested an association among the use of ovulation-inducing drugs, IVF, and ovarian cancer risk, but only few cases of ovarian cancer have been described in women followed in IVF programs.

Another possibility is the involvement of patient background factors and predisposing factors of infertility, such as ovulation disorder and endometritis. Standard surgical procedure in ovarian cancer patients leads to permanent sterility (since it includes the execution of hysterectomy plus bilateral salpingo-oophorectomy), young women who wish to preserve their childbearing potential may benefit by conservative (with uterine and contralateral andexal preservation) approach. Fertility preservation, such as ovarian tissue or oocyte cryopreservation, may also be used to prevent infertility but the proportion of patients with early ovarian cancer demanding fertility-preserving techniques is increasing. This represents a challenge to the gynecologic oncologist when setting the limits in order to not affect the prognosis and survival of these patients.

Prevention

People with strong genetic risk for ovarian cancer may consider the surgical removal of their ovaries as a preventative measure. This is often done after completion of childbearing years. This reduces the chances of developing both breast cancer (by around 50%) and ovarian cancer (by about 96%) in people at high risk. People with a significant family history for ovarian cancer are often referred to a genetic counselor to see if they should be tested for BRCA mutations.

Symptoms

In several cases, ovarian cancer is not diagnosed until it is in its later stages. However, the most common symptoms of ovarian cancer are:

- frequent bloating
- pelvic or abdominal pain
- difficulty eating or feeling full quickly
- bloating or swollen belly area

If these symptoms persist daily for more than 2 to 3 weeks, it is best to consult a doctor.

There are other symptoms that occur with ovarian cancer, but are not necessarily a sign of cancer. They consist of:
- fatigue
- indigestion
- back pain
- pain with intercourse
- constipation
- menstrual cycle changes

**Therapies**

**Self therapy**

Naturally occurring plant components from traditional herbs are a significant source of potential therapeutic compounds for cancer treatment. The use of natural products as alternative anticancer therapies tends to increase, especially in developing countries. Agents with the ability to induce apoptosis in cancer cell have the potential to be used for anticancer therapy and may candidate as alternative ovarian cancer therapy. The terpenoid bioactive compound from Papua ant nest (Pic.5) is an important traditional medicine with anticancer effects. Papua ant nest plant is a herbaceous plant that is new and has potential as an alternative therapy in treating cancer, especially the Myrmecodia species.

**Conventional medicine**

**Pharmacotherapy**

**Hormonal therapy**

Despite the fact that 60% of ovarian tumors have estrogen receptors, ovarian cancer is only rarely responsive to hormonal treatments. Estrogen alone does not have an effect on the cancer, and tamoxifen and letrozole are rarely effective.

**Surgical therapy**

Surgery is the preferred treatment and is frequently necessary to obtain a tissue specimen for differential diagnosis via its histology. The type of surgery depends upon how widespread the cancer is when diagnosed (the cancer stage), as well as the presumed type and grade of cancer. The surgeon, who is usually a specialized gynecologic oncology surgeon, may remove one (unilateral oophorectomy) or both ovaries (bilateral oophorectomy), the Fallopian tubes (salpingectomy), the uterus (hysterectomy), and the omentum (omentectomy). Typically, all of these are removed. For low-grade only the involved ovary (which must be unruptured) and Fallopian tube will be removed. This can be done especially in young people who wish to preserve their fertility. However, a risk of microscopic metastases exists and staging must be completed. If any metastases are found, a second surgery to remove the remaining ovary and uterus is needed. If a tumor in a premenopausal woman is determined to be a low malignant potential tumor during surgery, and it is clearly stage I cancer, only the affected ovary is removed. For postmenopausal women with low malignant potential tumors, hysterectomy with bilateral salpingo-oophorectomy is still the preferred option. During staging, the appendix should be examined or removed. This is particularly important with mucinous tumors. In children or adolescents with ovarian cancer, surgeons typically attempt to preserve one ovary to allow for the completion of puberty, but if the cancer has spread, this is not always possible. Dysgerminomas (a type of germ cell tumor; usually malignant and usually occurring in the ovary) in particular tend to affect both ovaries: 8-15% of dysgerminomas are present in both ovaries. People with low-grade (well-differentiated) tumors are typically treated only with surgery, which is often curative.

In advanced cancers, where complete removal is not an option, as much tumor as possible is removed in a procedure called debulking surgery. This surgery is not always successful, and is less likely to be successful in women with extensive metastases in the peritoneum, stage-IV disease, cancer in the transverse fissure of the liver, mesentry, or diaphragm, and large areas of ascites. Debubking surgery is usually only done once. More complete debulking is associated with better outcomes: women with no macroscopic evidence of disease after debulking have a median survival of 39 months, as opposed to 17 months with less complete surgery. Interval debulking surgery is another protocol used, where neoadjuvant chemotherapy is given, debulking surgery is performed,
and chemotherapy is finished after debulking.

To fully stage ovarian cancer, lymphadenectomy should be included in the surgery, but a significant survival benefit to this practice may not happen. This is particularly important in germ cell tumors because they frequently metastasize to nearby lymph nodes.

If ovarian cancer recurs, secondary surgery is sometimes a treatment option. This depends on how easily the tumor can be removed, how much fluid has accumulated in the abdomen, and overall health.

The major side effect of an oophorectomy in younger women is early menopause, which can cause osteoporosis. After surgery, hormone replacement therapy can be considered, especially in younger women. This therapy can consist of a combination of estrogen and progesterone, or estrogen alone. Estrogen alone is safe after hysterectomy; when the uterus is still present, unopposed estrogen dramatically raises the risk of endometrial cancer. People having ovarian cancer surgery are typically hospitalized afterwards for 3–4 days and spend around a month recovering at home. Surgery outcomes are best at hospitals that do a large number of ovarian cancer surgeries.

Surgery in ovarian cancer has been known to show a high success rate.

**Other therapy**

**Chemotherapy**

Chemotherapy is used after surgery to treat any residual disease, if appropriate. In some cases, there may be reason to perform chemotherapy first, followed by surgery. This is called “neoadjuvant chemotherapy”, and is common when a tumor cannot be completely removed or optimally debulked via surgery. If a unilateral salpingo-oophorectomy or other surgery is performed, additional chemotherapy, called “adjuvant chemotherapy”, can be given. Chemotherapies used in ovarian cancer include paclitaxel, cisplatin, topotecan, and gemcitabine. Germ-cell malignancies are treated differently - a regimen of bleomycin, etoposide, and cisplatin (BEP chemotherapy) is used. Adjuvant chemotherapy is used in stage 1 cancer typically if the tumor is of a high histologic grade (grade 3) or the highest substage (stage 1C).

Chemotherapy in ovarian cancer typically consists of platin, a group of platinum-based drugs. Three-drug regimens have not been found to be more effective. Chemotherapy can be given intravenously or in the peritoneal cavity.

If ovarian cancer recurs, it is considered partially platinum-sensitive or platinum-resistant, based on the time since the last recurrence treated with platin: partially platinum-sensitive cancers recurred 6–12 months after last treatment, and platinum-resistant cancers have an interval of less than 6 months. Second-line chemotherapy should be given only after the cancer becomes symptomatic, because no difference in survival is seen between treating asymptomatic (elevated CA-125) and symptomatic recurrences. For platinum-sensitive tumors, platin are the drugs of choice for second-line chemotherapy, in combination with other cytotoxic agents. Regimens include carboplatin combined with pegylated liposomal doxorubicin, gemcitabine, or paclitaxel. For platinum-resistant tumors, there are no high-efficacy chemotherapy options. Single-drug regimens (doxorubicin or topotecan) do not have high response rates, but topotecan is used in some cases. Topotecan cannot be used in people with an intestinal blockage. Paclitaxel used alone is another possible regimen, or it may be combined with liposomal doxorubicin, gemcitabine, cisplatin, topotecan, etoposide, or cyclophosphamide.

In people with BRCA mutations, platinum chemotherapy is more effective.

**Radiation therapy**

Dysgerminomas are most effectively treated with radiation, though this can cause infertility and is being phased out in favor of chemotherapy.

Radiation therapy is not effective for advanced stages because when vital organs are in the radiation field, a high dose cannot be safely delivered and does not improve survival in people with well-differentiated tumors. Radiation therapy is then commonly avoided in such stages as the vital organs may not be able to withstand the problems associated with these ovarian cancer treatments.

In stage 1C and 2 cancers, radiation therapy is used after surgery if there is the possibility of residual disease in the pelvis but the abdomen is cancer-free. Radiotherapy can also be used in palliative care.
of advanced cancers. A typical course of radiotherapy for ovarian cancer is 5 days a week for 3–4 weeks. Common side effects of radiotherapy include diarrhea, constipation, and frequent urination.

**Immunotherapy**

Immunotherapy is a topic of current research in ovarian cancer. In some cases, the antibody drug bevacizumab, though still a topic of active research, is used to treat advanced cancer along with chemotherapy.

**Assisted reproduction**

Egg freezing and ovarian tissue cryopreservation also offers women with cancer the chance to preserve their eggs so that they can have children in the future. If both of ovaries were removed, but patient still have the uterus, she may be eligible for in vitro fertilization with the intent to carry an own child. When a woman has no uterus, the embryo may be transferred to the surrogate mother’s uterus.

After the treatment of ovarian cancer genetic testing (PGS) is recommended. Preimplantation genetic screening allows studying the DNA of eggs or embryos to select those that do not carry certain damaging characteristics.

On the other hand, if a woman have no own eggs or their quality is not sufficient, donated ones may be used.

**Find more about related issues**

**Diagnoses**

- **Polycystic ovary syndrome**
  A condition in which a woman has an imbalance of female sex hormones. This may lead to changes in the menstrual cycle, cysts in the ovaries, trouble... Learn more at: [www.fertilitypedia.org/therapy/diag/polycystic-ovary-syndrome](www.fertilitypedia.org/therapy/diag/polycystic-ovary-syndrome)

- **Fallopian tube blockage**
  An obstruction prevents the egg or sperm from traveling down the tube, thus making fertilization impossible. Learn more at: [www.fertilitypedia.org/therapy/diag/fallopian-tube-blockage](www.fertilitypedia.org/therapy/diag/fallopian-tube-blockage)

- **Endometriosis**
  A state in which pieces of the tissue alike to the lining of the uterus (endometrium) grow in other parts of the body. Learn more at: [www.fertilitypedia.org/therapy/diag/endometriosis](www.fertilitypedia.org/therapy/diag/endometriosis)

- **Menopause**
  The time in most women’s lives when menstrual periods stop permanently, and the woman is no longer able to have children. Learn more at: [www.fertilitypedia.org/therapy/diag/menopause](www.fertilitypedia.org/therapy/diag/menopause)

- **Hydrosalpinx**
  A hydrosalpinx is an abnormal pouch containing liquid in a fallopian tube. Learn more at: [www.fertilitypedia.org/therapy/diag/hydrosalpinx](www.fertilitypedia.org/therapy/diag/hydrosalpinx)

- **Endometrial cancer**
  Cancer that arises from the endometrium, the lining of the uterus. Learn more at: [www.fertilitypedia.org/therapy/diag/endometrial-cancer](www.fertilitypedia.org/therapy/diag/endometrial-cancer)

- **Tubal ligation**
  A permanent form of female sterilization, in which the fallopian tubes are severed and sealed or "pinched shut", in order to prevent fertilization. Learn more at: [www.fertilitypedia.org/therapy/diag/tubal-ligation](www.fertilitypedia.org/therapy/diag/tubal-ligation)
Hysterectomy
A surgery performed to remove a woman’s uterus.
Learn more at: www.fertilitypedia.org/therapy/diag/hysterectomy

Organs

Fallopian tubes
Two very fine tubes that transport sperm toward the egg, and allow passage of the fertilized egg back to the uterus for implantation.
Learn more at: www.fertilitypedia.org/edu/organs/fallopian-tubes

Ovary
The ovum-producing organs of the internal female reproductive system
Learn more at: www.fertilitypedia.org/edu/organs/ovary

Reproductive cells

Oocyte
A female germ cell involved in reproduction.
Learn more at: www.fertilitypedia.org/edu/reproductive-cells/oocyte

Risk factors

Early onset of menses
Occurrence of menstruation in 11 years or less.
Learn more at: www.fertilitypedia.org/therapy/rf/early-onset-of-menses

Early onset of pubarche
The development of pubic hair before the age of 8 years in females and 9 years in males, without other signs of puberty.
Learn more at: www.fertilitypedia.org/therapy/rf/early-onset-of-pubarche

Early onset of thelarche
An isolated appearance of breast development, usually in girls younger than 3 years.
Learn more at: www.fertilitypedia.org/therapy/rf/early-onset-of-thelarche

Symptoms

Chronic pelvic pain
Pain in the area of the pelvis, that lasts more than six months.
Learn more at: www.fertilitypedia.org/edu/symptoms/chronic-pelvic-pain-1

Constipation
A condition where the feces are hardened because of excess water removal in the colon.
Learn more at: www.fertilitypedia.org/edu/symptoms/constipation

Early puberty for girls
The onset of puberty before the average age in girls (8 years).
Learn more at: www.fertilitypedia.org/edu/symptoms/early-puberty-for-girls

Fatigue
A subjective feeling of tiredness which is distinct from weakness, which has a gradual onset.
Learn more at: www.fertilitypedia.org/edu/symptoms/fatigue
Irregular menstruation
Irregular menstruation is a menstrual disorder whose manifestations include irregular cycle lengths as well as metrorrhagia.
Learn more at: www.fertilitypedia.org/edu/symptoms/irregular-menstruation

Lower abdominal pain
Pain that occurs in low area of abdomen, below the umbilicus.
Learn more at: www.fertilitypedia.org/edu/symptoms/lower-abdominal-pain

Lower back pain
A common painful disorder involving the muscles and bones of the back.
Learn more at: www.fertilitypedia.org/edu/symptoms/lower-back-pain

Painful sexual intercourse
The painful feelings during sexual intercourse.
Learn more at: www.fertilitypedia.org/edu/symptoms/painful-sexual-intercourse

Therapies

Chemotherapy of ovarian cancer
A treatment of ovarian cancer with chemotherapeutic agents which is often combined with surgery.
Learn more at: www.fertilitypedia.org/edu/therapies/chemotherapy-of-ovarian-cancer

Egg donation
Process by which a woman donates eggs for purposes of assisted reproduction or biomedical research.
Learn more at: www.fertilitypedia.org/edu/therapies/egg-donation

Fallopian tubes removal
Surgical removal of a Fallopian tube(s).
Learn more at: www.fertilitypedia.org/edu/therapies/fallopian-tubes-removal-1

Fertility preservation
The field of reproductive medicine, that focuses on helping reproductive-age men and women to prevent infertility and birth defects.
Learn more at: www.fertilitypedia.org/edu/therapies/fertility-preservation

Hysterectomy
Surgical removal of the uterus.
Learn more at: www.fertilitypedia.org/edu/therapies/hysterectomy

ICSI
A micromanipulative fertilization technique in which a single sperm is injected directly into an egg.
Learn more at: www.fertilitypedia.org/edu/therapies/icsi

Ovariectomy
Surgical removal of one or both ovaries.
Learn more at: www.fertilitypedia.org/edu/therapies/ovariectomy

Preimplantation genetic screening
The term PGS is used to denote procedures that do not look for a specific disease but to identify embryos at risk of de-novo occurring aneuploidies.
Learn more at: www.fertilitypedia.org/edu/therapies/preimplantation-genetic-screening-1

Radiation therapy of ovarian cancer
Used as a treatment of ovarian cancer in cases to prevent recurrence and as a palliative therapy to cease the symptoms.
Learn more at: www.fertilitypedia.org/edu/therapies/radiation-therapy-of-ovarian-cancer
Sperm donation
The procedure in which a man (sperm donor) provides his sperm for fertility treatment.
Learn more at: www.fertilitypedia.org/edu/therapies/sperm-donation

Standard IVF
A process in which an egg is fertilised by sperm outside the body: in vitro. Own or donated gametes may be used.
Learn more at: www.fertilitypedia.org/edu/therapies/standard-ivf

Surrogacy
The embryo is gestated in a third party’s (surrogate) uterus.
Learn more at: www.fertilitypedia.org/edu/therapies/surrogacy

Gallery

Clear cell carcinoma hobnail cells
Hobnail cells seen in a clear cell carcinoma sample.

Ovarian cancer
A very large ovarian cancer as seen on CT.

Ovarian carcinoma
A pathological specimen of ovarian carcinoma.
Serous carcinoma cytology
Micrograph of serous carcinoma, a type of ovarian cancer, diagnosed in peritoneal fluid.

Tumor deposit
Ovarian adenocarcinoma deposit in the mesentery of the small bowel.

Pic
Diagram showing stage 1 ovarian cancer.

Stage 1A cancer in one ovary
Stage 1C cancer in the ovary and on the surface of one ovary
Stage 1B cancer in both ovaries

Pic
Diagram showing stage 2A to 2C ovarian cancer.

Stage 2A
Stage 2C cancer cells also in the fluid of the abdomen
Stage 2B cancer has spread to the bowel or bladder

Pic
Diagram showing stage 3A to 3C ovarian cancer.

Stage 3A cancer cells are in the lining of the abdomen (only seen under a microscope)
Stage 3B tumours of 2cm or smaller are in the lining of the abdomen
Stage 3C cancer is in the lymph nodes
Diagram showing stage 4 ovarian cancer.

Sources

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