

Ovarian Cancer

Hatice Banu KIROĞLU**Department of Molecular Biology and Genetics, Istanbul University, Faculty of Science, Turkey*

***Corresponding author:** Hatice Banu KIROĞLU, Department of Molecular Biology and Genetics, Istanbul University, Faculty of Science, Turkey

Received: May 30, 2023**Published:** October 11, 2023

Abstract

The ovaries are the essential organs of the female reproductive system. It is responsible for hormone production and maintains female reproductive cells, necessary for fertility. Ovarian cancer is usually seen in older women and is one of the seven most common types of cancer in women [1]. It has a progression that is asymptomatic in the early stages and is almost realized in the last stages, making early diagnosis difficult. 75% of patients III. or IV. stages consult a doctor [2]. There are two types of ovarian cancer, epithelial and non-epithelial. 90% of ovarian cancers are epithelial type. Although the exact cause is unknown, genetic inheritance and gene mutations such as BRCA1 and BRCA2 are principally risk factors for ovarian cancer. And older age, smoking, and obesity are among the risk factors for ovarian cancer as other types of cancer. Symptoms of ovarian cancer are abdominal bloating and pressure, abdominal pain, back pain, rectal and pelvic pain, appetite changes, involuntary weight loss, constipation or diarrhea, painful sexual intercourse, changes in urination frequency, vaginal bleeding without menstruation, fatigue, and weakness [3]. Ovarian cancer can be diagnosed with a gynecological examination, screening methods such as ultrasonography, Magnetic Resonance imaging (MR), Computerized Tomography (CT), and serum tests such as CA-125 pathology test, classical biopsy, and liquid biopsy. The most common treatment method for ovarian cancer is surgery. Depending on the cancer progression, chemotherapy, and radiotherapy are also widely used. Follow-up after treatment in ovarian cancer is vital because the recurrence rate is as high as 70%. Five-year survival rates are determined by the stage at which the cancer patient starts treatment. The five-year survival rate for ovarian cancer worldwide is around 45%. With early diagnosis, survival rates can increase.

Keywords: Ovarian cancer; Early diagnosis; Surgery; Recurrence

Introduction

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(MR), Computerized Tomography (CT), and serum tests such as CA-125 pathology test, classical biopsy, and liquid biopsy. The most common treatment method for ovarian cancer is surgery. Depending on the cancer progression, chemotherapy, and radiotherapy are also widely used. Follow-up after treatment in ovarian cancer is vital because the recurrence rate is as high as 70%. Five-year survival rates are determined by the stage at which the cancer patient starts treatment. The five-year survival rate for ovarian cancer worldwide is around 45%. With early diagnosis, survival rates can increase.

In this review, ovarian cancer is investigated in detail with mentioned majors.

Risk Factors

Although the exact cause of ovarian cancer is unknown, for sure related to some factors. Considered these factors:

Age is a prime risk factor for ovarian cancer. It usually occurs in women between the ages of 50-70. Advancing age and the risk of ovarian cancer are directly proportional.

Genetic inheritance and genetic mutations are the number one predicted cause of ovarian cancer. While BRCA1 and BRCA2 mutations may increase the cancer risk, HOXA gene expression changes may affect carcinogenesis in epithelial ovarian

cancer. [4] 10-20% of all ovarian cancers consist of germline mutations. [5] Mutations in the TP53 tumor suppressor gene may also increase the cancer risk.

The regularity of the menstrual cycle is also a risk factor. Early-aged menarche and late menopause increase the risk of ovarian cancer. Menstrual irregularity is a high risk of ovarian cancer, according to research. Late births also increase the risk of cancer.

Hormone therapies are taken after menopause to increase estrogen and progesterone levels. But increased hormone levels also increase the risk of ovarian cancer.

Obesity in the postmenopausal period is a risk-increasing factor.

Smoking is a factor that increases the risk of developing cancer in ovarian cancer, as in almost all types of cancer.

Women who have these risk factors may catch ovarian cancer or not. Some women can catch ovarian cancer without having any of these risk factors.

Epidemiology and Incidence

Ovarian cancer is one of the five types of cancer with the highest mortality. Around the world, approximately 300,000 women get this disease in a year. 63% of them die because of this reason. Although it frequently occurs in the older age group, it can also be seen in young women, although it is rare. The incidence is higher in women living at a low socioeconomic level. While it has a high incidence in Western countries, it also has high mortality in African geography. [6] In Asian countries, the incidence of ovarian cancer is low. It may relate to differences in incidence due to genetic factors, lifestyle, and environmental conditions. Since it is difficult to diagnose in the early stages, it is difficult to treat. Therefore ovarian cancer has high mortality rates. Regular doctor control after a certain age is necessary for diagnosis and treatment.

Symptoms and Diagnosis

It progresses with or without symptoms in the early stages, often compared to other conditions. As the disease progresses, the symptoms become more pronounced and increase. Let's take a look at the common symptoms:

1. Bloating is the feeling of swelling and fullness in the abdomen that usually occurs after eating or at the end of the day.
2. Abdominal pain is the most common symptom. It usually feels in the lower abdomen and pelvic region. Also, It may feel in the back.
3. Rectal and pelvic pain, ovarian cancer can also cause pain in these areas.
4. Appetite changes and involuntary weight loss can cause anorexia and food intolerances, so the individual may experience weight loss. Sometimes, the urge to overeat can also be seen.
5. Constipation and diarrhea, ovarian cancer can cause problems by affecting bowel movements. Constipation or diarrhea may occur with abdominal pain.
6. Pelvic pain causes painful intercourse.
7. Changes in urination frequency can cause frequent urination, urinary incontinence, difficulty, and burning while urinating
8. Recurrent unexpected bleeding without menstruation.
9. Fatigue and weakness, the body struggles with cancer without a patient's awareness. Depending on the decrease in body resistance, fatigue and weakness may appear.

Citation: Hatice Banu KIROĞLU*. Ovarian Cancer. *IJCMCR*. 2023; 30(4): 005

These symptoms are significant in the diagnosis and treatment of ovarian cancer [7].

For ovarian cancer, as in all cancers, early diagnosis is necessary, but it is usually diagnosed in the late stages since there are no understandable symptoms in the early stages.

Physical examination, imaging techniques, blood and serum tests, and biopsy applications widely use for diagnosis of ovarian cancer.

Physical examination, the abdominal region is examined to see if there is a tumor or mass in the abdomen. In addition, pelvic examination checks the tumor or cyst's size, shape, and condition.

Ultrasonography is an overhead method used to view the size, ovaries' size, and structure, and shapenetic resonance imaging is an imaging technique that provides visualization of the ovaries and pelvic region.

Computed tomography is a method that shows the pelvic region and abdominal cavity in detail.

The CA-125 test is a blood test that demonstrates the level of a protein secreted by cancerous ovarian cells. However, diagnosis alone is insufficient as it may have high rates in other diseases [8].

A tissue sample is for pathological and histological examination of the part taken from the cancerous area through biopsy, laparoscopic or open surgery.

Liquid biopsy is the molecular analysis of samples taken from biological fluids. Also, It is efficacious for the diagnosis, monitoring, treatment, and post-treatment follow-up period of the disease.

There are current diagnostic kits developed for the diagnosis of ovarian cancer. Here are some of them:

The OVA1 Test measures the levels of five proteins in a blood sample. That tests show the difference between benign and malignant tumors.

The ROCA Test determines the risk of ovarian cancer by measuring the levels of CA-125 and HE4 proteins.

The Ovarian Test is used to diagnose the early stages of ovarian cancer. It shows levels of CA-125 and five different proteins from a blood sample.

Ovarian Cancer Screen measures the levels of 14 proteins in the blood sample. It is used in the diagnosis of early stages of ovarian cancer.

Stages

Stage I:

In stage, I, only one or both ovaries are affected by cancer. The cancer has not yet spread to the ovary and lymph nodes. It is the stage where the chance of treatment is very high with early diagnosis. Usually, surgical treatment is applied, the cancerous ovary or ovaries removes, and the cancerous area is not including cancer cells. Stage I has three subgroups:

In stage, I A, cancer cells have spread to a limited area, usually only on the surface of an ovary.

Stage I B, although cancer cells metastasize in a single ovary, they exceed the surface boundaries and metastasize to the surrounding tissues.

Stage I C cancerization occurs in both the right and left ovaries but has not spread to the pelvic area or lymph nodes.

Stage II:

The cancer has spread to both the right and left ovaries. Cancer has spread to the pelvis area (womb, fallopian tubes, cervix, bladder, rectum) and lymph nodes. As a treatment approach, surgical treatment and chemotherapy can apply together. With the primary aim of controlling cancer, the cancerous areas remove with surgery, and the remaining cancer cells exterminate with chemotherapy. The subgroups of Stage II are as follows: Stage II A, cancer is found in the ovaries. It has metastasized to the uterus and fallopian tubes. There is no visible tumor image. Stage II B, metastases continue to organs in the pelvis region. A small tumor could appear.

In stage II C, the ovaries, pelvic organs, and nearby lymph nodes are cancerous.

Stage III:

Cancer begins to spread from the ovaries to the pelvis and abdomen. Approximately 70% of the patients receive the first diagnosis at this stage. The treatment plan considers the extent of cancer spread, the patient's general health status, age, and other factors. Combinations of surgical treatment, chemotherapy, and radiotherapy use as a treatment approach. The subgroups of Stage III are as follows:

In stage III A, cancer cells have spread to the peritoneum and serous membranes (the membranes surrounding the viscera).

Stage III B, the cancer has spread to the lymph nodes in the abdomen and the lymph system. Cancer may diagnose due to small nodules or ascites in the peritoneum.

Stage III C, cancer has spread to lymph nodes in the peritoneum and lymph nodes above the diaphragm.

Stage IV:

Ovarian cancer begins to metastasize to more distant parts of the body. It is the most advanced stage of cancer and is a difficult stage in terms of treatment. The treatment approach determines the patient's general health status, the location of the metastases, and the degree of spread. Palliative care applies to improve the patient's quality of life, along with surgical treatment, chemotherapy, and targeted therapy methods. The subgroups of Stage IV are as follows, according to the organs in which it spreads and the degree of spread:

Stage IV A, cancer has affected the pelvic and abdominal organs and has spread to organs in the abdomen. For instance, It has metastasized to the lungs, liver, and bone tissue.

Stage IV B is cancerous in other regions such as the brain, lymphatic system, bones, and liver.

Treatment Approaches

The treatment plan is determined by the cooperation of the doctor and the patient, depending on the stage of the disease, the age and general health of the patient, and the spread of the cancer. Surgical treatment is the most common treatment method. Chemotherapy and radiotherapy are also frequently used. Treatment methods applied in ovarian cancer, respectively:

Surgery: It is the first method applied. The tissues and organs, of cancer metastasize such as the ovaries, the fallopian tubes, the uterus, and pelvic lymph nodes removed from the body. After the treatment, the tumors and cancerous tissues analysis in the pathological examination. According to the results, treatment can plan [9].

Chemotherapy: It can apply before and after surgery. Patients use target drugs to extirpate the cancer cells. Chemotherapy is

the first method used in the advanced stages of ovarian cancer. Tumors and cysts can remove with surgery before chemotherapy [10].

Radiotherapy: It rarely uses for ovarian cancer. It is the application of high-energy radiation used to kill target cancerous cells. It can be applied after surgery or in combination with chemotherapy.

Hormone Therapy: It can use in addition to surgery and chemotherapy. Ovarian cells that secrete estrogen and progesterone are the target. However, it is not an effective method for all types of ovarian cancer.

Targeted Therapy: It targets specialized proteins and gene mutations in cancer cells.

Theranostics Therapy: These are treatments based on the patient rather than the disease. The most appropriate treatment method for the patient and the target drugs are used to determine by molecular profiling and computer modeling.

Studies on the treatment of ovarian cancer are still ongoing. A few examples of current treatment approaches, apart from classical treatments, are as follows:

Neoadjuvant Therapy: It is chemotherapy and targeted drug therapy used before surgery. It aims to shrink the tumor and facilitates surgical procedures [11].

Immunotherapy: It aims to kill cancerous cells by acting on immune cells. It can reduce the spread of cancerous cells. It is also available in the form of cancer vaccines. Cancer vaccines aim to strengthen the immune system of the patient[12].

Possible Side Effects of the Treatment

Each treatment method has its side effects.

The most common side effect of surgical treatment is pain that may occur after surgery. Some patients may be at risk of infection.

Chemotherapy has several side effects. In general, nausea, vomiting, hair loss, eyebrows, lash loss, loss of appetite, and infection. Heavy drugs used in chemotherapy can damage heart, kidney, and liver functions.

Side effects in radiotherapy treatment may vary depending on the treatment duration, dose, and area. Generally, redness, itching, and burning occur in the treatment area. Radiotherapy can also damage organs and tissues close to the target area.

During hormonal therapy, patients may experience vaginal dryness, hot flashes, sweating, and weight gain. In some cases, it can be risky by affecting blood clotting.

Targeted therapy generally has fewer side effects. Some medications used in treatment may increase the risk of blood clots.

Follow-Up After Treatment

After the end of the treatment process for ovarian cancer, it is significant to carry out regular check-ups by considering the physical and psychological needs of the patient.

The follow-up treatment process can reduce the recurrence risk and the development of another tumor. Recurrence is generally an adverse event in ovarian cancer. A recurrence is the recurrence of cancer after treatment is completed. Ovarian cancer has a high recurrence rate of 70%.

It usually occurs within the first 2-3 years after the end of the first course of treatment [13]. The symptoms of relapse are the same as those in the initial diagnosis. Treatment for recurrence varies depending on the type, location, and stage of the disease. Surgery, chemotherapy, radiotherapy, or targeted therapies can use as a treatment method.

Early diagnosis and treatment facilitate the fight against recurrence and increase survival rates. In the post-treatment follow-up, the patient can follow up with blood tests, physical examination, and imaging techniques with the joint plan of the patient and the doctor. Follow-up appointments are made frequently in the first two years and more frequently after the first two years.

Survival Rates

Survival rates in ovarian cancer may vary depending on the stage of the disease, the patient age and general health characteristics, and the patient response to treatment.

While the first five-year survival rate in early-stage ovarian cancer is approximately 80-90%, this rate falls below 30% in advanced-stage ovarian cancer. If we look at the world in general, this is about 45% [14].

Conclusion

Ovarian cancer is a disease that does not show symptoms in the early stages, progresses insidiously, is common among women, and has a high mortality. Early diagnosis can seriously affect the ovarian cancer treatment path and survival rate.[15] III. and IV. stages show symptoms such as abdominal pain and swelling, frequent urination, constipation, or diarrhea.

Physical examination, imaging techniques, and blood tests extensively use to diagnose the defect. The most commonly used treatment methods are surgery and chemotherapy. Since it is a cancer type with high recurrence rates, post-treatment follow-up is critical.

Funding: This research received no external funding.

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