Chapter 10

Ovarian Cancer: Etiology, Clinical Features and Treatment Approaches

Mustafa Bilici[1]

Summary

Cancer has remained a significant health problem throughout human history. Despite advances in modern medicine, it remains a leading cause of death, particularly in developed countries. For example, in the United States, cancer accounts for approximately 23% of all deaths. These rates clearly demonstrate the importance of this disease to public health. The term cancer describes a broad group of pathological disorders characterized by the uncontrolled proliferation of specific cell groups in the body and their invasion of surrounding tissues. This uncontrolled proliferation develops as a result of disruption of the normally tightly regulated cell cycle through various molecular mechanisms. Normal cells balance processes such as growth, proliferation, and apoptosis through genetically regulated mechanisms. Disruptions in the cell life cycle lead to a loss of genetic stability and initiate the process of tumor formation. Ovarian cancer has one of the highest mortality rates among gynecological malignancies and is most often diagnosed in advanced stages. One of the main reasons for this is that the disease presents with vague, nonspecific symptoms in its early stages. This clinical uncertainty complicates early diagnosis and leads most patients to seek medical attention in the metastatic stage. Histopathologically, approximately 80% to 90% of ovarian cancers are epithelial carcinomas, which originate from the surface epithelium of the ovary. Diagnosing the disease at an advanced stage significantly reduces treatment response rates and long-term survival. Indeed, the 5-year survival rate in cases diagnosed at an advanced stage ranges from 30% to 40%, and cure is quite limited. Ovarian cancer is a group of malignant diseases characterized by uncontrolled cellular proliferation that occurs in the ovaries, a key organ of the female reproductive system. This type of cancer, which exhibits a clinically heterogeneous structure, often follows an insidious course and often presents no symptoms in the early

1 Van Security Collage, Van Yuzuncu Yil University, Van, Turkey
mustafabilici@yyu.edu.tr, Orcid: 0000-0002-8689-6463

https://doi.org/10.58830/ozgur.pub933.c3922

stages. Therefore, most cases are already in an advanced stage by the time they are diagnosed. According to epidemiological data, ovarian cancer is the 18th most common cancer type worldwide and the 8th most common malignancy in women. Statistics in Turkey reflect a similar picture, reporting it as the 7th most common malignancy among women.

Introduction

Cancer-Causing Factors

1. Genetic and Molecular Basis

Cancer development begins with the disruption of cellular regulation due to mutations in the genetic structure. These mutations can be congenital or develop throughout life due to various environmental and biological factors. Mutations in tumor suppressor genes and proto-oncogenes, in particular, cause the cell cycle to become uncontrolled. For example, mutations in the p53 gene have been shown to play a significant role in breast, lung, kidney, and ovarian cancers (Vogelstein & Kinzler, 2005).

2. Hereditary Factors

Hereditary predisposition plays a significant role in approximately 20% of all cancer cases. Familial transmission is particularly evident in some types of cancer, such as breast and ovarian cancer. For example, the risk of developing the disease in first-degree relatives of individuals with ovarian cancer is significantly higher than the general population average. However, hereditary ovarian cancer cases account for less than 1% of all ovarian cancer cases. (Özkılıç, 2007).

3. Radiation Effects

Ionizing radiation has destructive effects on DNA, resulting in chromosome breaks and structural abnormalities. This disrupts the genomic integrity of cells and can trigger oncogenic processes. Ultraviolet rays, in particular, have been identified as responsible for 90% of skin cancers. Similarly, naturally occurring radon gas has been identified as a significant risk factor for the development of lung cancer. (Ministry of Health, 1998; Tuncer et al., 2022; Çalışkan, 2008).

4. Chemical Exposures and Dietary Factors

Exposure to environmental carcinogens, particularly smoking, consumption of foods containing additives, and foods cooked at high temperatures, are among the primary external factors that predispose to cancer. Additives such as nitrate and nitrite can cause gastrointestinal

cancers by converting to nitrosamines in stomach acid. Toxic compounds such as acrylamide, which form at high temperatures, have also been shown to play a role in the development of colon and breast cancer. Furthermore, some nutrients may also reduce cancer risk due to their antioxidant content. (Doğan D. et al., 2025; Tuncer et al., 2022; Bilici M., 2014).

Ovarian Cancer: Overview

Ovarian cancer, one of the most common causes of death among gynecological cancers, is often diagnosed in advanced stages. The clinical picture often presents with non-specific symptoms, making early diagnosis difficult. Approximately 80-90% of ovarian cancers are epithelial carcinomas, which originate from the surface epithelium of the ovary. The 5-year survival rate for patients diagnosed at an advanced stage is around 30-40%, and the chance of cure is low. (Çalışkan, 2008; Bilici M., 2014).

Etiopathogenesis and Risk Factors

Genetic predisposition, hormonal imbalances, and environmental toxins are known to play important roles in the development of ovarian cancer. BRCA1 and BRCA2 gene mutations, in particular, have been found to significantly increase the risk of familial ovarian cancer. Among hormonal factors, increased ovulation frequency plays a significant role. Prolonged estrogen exposure can trigger proliferative effects in epithelial ovarian tissue. (Bilici M., 2014).

The Role of Nutrition and Micronutrients

The protective effects of antioxidants, trace elements, and vitamins have been investigated in ovarian cancer and some other cancer types. A study conducted in Finland found that patients with ovarian cancer who received selenium and vitamin E supplements underwent chemotherapy responded better to treatment (Sundström et al., 1989). It has also been suggested that the Cu/Zn ratio in serum may serve as a biomarker for the course of gynecological tumors (Gao & Zhonghua, 1988). Low levels of these elements reduce the activity of antioxidant enzymes such as superoxide dismutase, which facilitates cell damage (Gurusamy, 2007; Bilici M., 2014).

Epidemiological Data and the Situation in Turkey

Approximately 175,000 people are newly diagnosed with cancer each year in Turkey, and cancer cases are widespread throughout the country, with no regional differences. According to TÜİK (Turkish Statistical Institute) data, the cancer-related mortality rate rose from 12% in 2002 to 21% in 2012 (TÜİK, 2012). The World Health Organization (WHO)

predicts that cancer-related deaths will be among the leading causes of death worldwide after 2015. WHO data lists three main reasons for the increase in cancer incidence: smoking, an aging population, and rising obesity rates. Furthermore, with the development of cancer registration systems in Turkey, an increase in the number of detected cases is also observed (Bilici M., 2014).

Ovarian Cancer

Ovarian cancer is a group of malignant diseases characterized by uncontrolled cellular proliferation that occurs in the ovaries, a vital part of the female reproductive system. This type of cancer, which has a clinically heterogeneous structure, tends to be diagnosed late because it often follows an insidious course and is asymptomatic in the early stages (Memorial Medical Publications Board, 2024; Ministry of Health, 2017; Webb & Jordan, 2017). Tumors of epithelial origin account for approximately 80% of all ovarian cancers and are most commonly seen in the postmenopausal period. In contrast, germ cell tumors are more common in younger age groups—especially those under 20. Epidemiological data reveal that ovarian cancer is the 18th most common cancer type worldwide and the eighth most common cancer among women. In Türkiye, it is reported to be the seventh most common malignancy among women (Ministry of Health, 2017; Webb & Jordan, 2017).

Incidence and Mortality

According to global statistics, an average of 239,000 new cases of ovarian cancer are detected each year, and approximately 152,000 of these cases result in death (Bray et al., 2018). Ovarian cancer has the highest mortality rate among gynecological malignancies, with a five-year overall survival rate of approximately 35% (Berrino et al., 1995). Despite advanced medical technologies and treatment methods, the prognosis for ovarian cancer remains quite poor. The main reasons for this are the lack of a specific screening method, the disease's presentation with nonspecific symptoms, and its advanced stage of diagnosis (Capriglione et al., 2017; Ekinci et al., 2013). Approximately 19,710 new cases of ovarian cancer are diagnosed each year in the United States, and 13,270 people die from the disease (Sung et al., 2020). Ovarian cancer is the leading cause of all gynecologic cancer deaths in the United States, ranking fourth after breast, lung, and colorectal cancers (Siegel et al., 2023; WHO, 2020).

Early Diagnosis and Response to Treatment

Survival rates significantly increase and life expectancy increases in cases of early-stage ovarian cancer. However, only 30% of patients are diagnosed at an early stage (Quaye et al., 2008). Despite modern surgical and chemotherapy approaches, survival is low in advanced-stage cases. The combination of maximal cytoreductive surgery and platinum-based chemotherapy is among the primary treatment strategies that improve survival. Meta-analyses have demonstrated that optimal tumor burden reduction has a significant impact on survival in stage III-IV patients (Bristow, 2002; Bozkurt et al., 2024).

Risk Factors

Many genetic, hormonal, and environmental factors play a role in the etiology of ovarian cancer. Advanced age, family history, BRCA1 and BRCA2 gene mutations, and inherited conditions such as Lynch syndrome are among the most important risk factors (Colombo et al., 2006). Fertility history also plays a decisive role in the etiopathogenesis. Numerous factors such as nulliparity, early menarche, late menopause, and frequent ovulation increase the risk of ovarian cancer. In this context, certain factors such as oral contraceptive use, duration of breastfeeding, tubal ligation, and hysterectomy have been reported to reduce the risk (Beji & Bilgiç, 2015; Moysich et al., 2001). According to the "continuous ovulation hypothesis," monthly ovulation causes repetitive microtrauma to the ovarian surface, and this process can facilitate DNA damage and malignant transformation (Tortolero-Luna & Mitchell, 1995). This leads to the accumulation of genetic mutations during the repair process of epithelial cells, paving the way for tumor formation.

Genetic Factors and BRCA Mutations

BRCA1 and BRCA2 genes are tumor suppressor genes involved in DNA repair. Germline mutations in these genes significantly increase the risk of both ovarian and breast cancer. The penetrance of these autosomal dominantly inherited mutations is variable, with the risk of ovarian cancer ranging from 40-60% and breast cancer ranging from 65-85% in individuals carrying a BRCA1 mutation (Clement, 2002; Rosai, 2004).

Histopathological Subtypes and Clinical Course

Ovarian cancer is histologically divided into three main groups: epithelial, germ cell, and sex cord-stromal. The most common form is serous carcinoma, originating from the ovarian surface epithelium. These tumors are high-grade and usually diagnosed in advanced stages. Germ cell tumors are more common in young women, while sex cord-stromal tumors are rare

and may be hormone-producing. Major factors affecting the course of the disease include the stage at diagnosis, tumor grade, histological type, patient age, and the amount of tumor remaining after surgery. The minimal amount of residual tumor remaining after cytoreductive surgery is a key determinant of survival (Falcetta et al., 2016).

Preventive Effectiveness and Awareness

One of the most effective methods in combating ovarian cancer is identifying risk factors and raising public awareness. Because symptoms of the disease are often associated with the gastrointestinal system, they can be misinterpreted, leading to delays in diagnosis. Therefore, regular checkups, especially for individuals at risk, will increase the chance of early diagnosis (Eroğlu & Koç, 2013). Early cancer diagnosis not only provides physiological benefits but is also important for psychological well-being and reducing healthcare costs. Emphasizing these issues in health policies has the potential to reduce morbidity and mortality rates (Pınar et al., 2008).

Ovarian Tumors of Epithelial Origin

The most common histological subgroup of ovarian cancers is malignancy of epithelial origin. These tumors arise from the surface epithelium lining the outer surface of the ovary and are particularly prevalent in postmenopausal women. The literature reports that approximately 80% of ovarian cancers diagnosed in the postmenopausal period are epithelial in origin. Epithelial tumors are histopathologically divided into various subtypes, each with a different clinical course, prognosis, and treatment approach (Kuzey, 2007; Çalışkan, 2008).

1. Serous Carcinoma

Serous carcinoma, the most common form of epithelial ovarian cancer, accounts for approximately 40% of all ovarian cancers. It is usually seen in women between the ages of 40 and 60 and tends to be bilateral (involving both ovaries). The development of serous tumors has been associated with invagination and transformation of the ovarian surface epithelium. The tumors often form cystic structures filled with fluid, and this fluid is serous, produced by the tumor cells (Demirbağ, 2004).

2. Endometrioid Carcinoma

Endometrioid-type ovarian carcinoma accounts for approximately 20% of epithelial tumors. It can have a solid or cystic appearance. This tumor type is thought to develop from cells similar to endometrial tissue, and 15% of patients have a history of endometriosis. Furthermore, endometrial cancer

can be detected simultaneously in 15-30% of patients with endometrioid tumors. Under the microscope, the tumor may occasionally resemble sex cord-stromal structures. The rate of bilateral involvement is approximately 40%. The five-year survival rate ranges from 40-50% (Soidman et al., 2002; Kao & Norris, 1979).

3. Mucinous Carcinoma

Mucinous ovarian tumors represent approximately 25% of ovarian cancers and are usually seen in middle-aged women. These tumors are often benign or borderline, with only 15% exhibiting malignant features. Malignant forms are rarely bilateral. While macroscopically similar to serous tumors, they are larger and contain multiocular cystic structures. These cysts are filled with a glycoprotein-rich, gelatinous fluid. Microscopically, the cystic spaces are lined with highly columnar and secretory cells. Peritoneal dissemination can occur in malignant and borderline lesions. This can lead to complications such as intra-abdominal adhesions and intestinal obstruction (Clement, 2002; Adilay, 2006; Demirbağ, 2004; Guerrieri et al., 1994; Riopel et al., 1999).

4. Clear Cell Carcinoma

Clear cell tumors account for approximately 5% of epithelial ovarian cancers. This subtype is most commonly seen in women between the ages of 40 and 80 and is characterized by the clear, abundant cytoplasm of the cells. It is thought to be of Müllerian origin and a variant of endometrioid carcinoma. It can be solid or cystic. Within the solid structures, tumor cells may form islands or tubules, while cystic forms are characterized by cells lining the cyst wall. It generally has an aggressive clinical course, and the five-year survival rate is approximately 50%. Benign or borderline variants are rare (Kao & Norris, 1979; Bell & Scully, 1985).

5. Borderline Ovarian Tumors

Borderline epithelial ovarian tumors are neoplasms with low malignant potential and constitute 10-15% of all epithelial ovarian tumors. These tumors are generally confined to the ovarian surface and are not invasive. Their clinical prognosis is quite good compared to other epithelial tumors. A high cure rate can be achieved after surgical treatment (Kao & Norris, 1979; Bell & Scully, 1985).

Clinical Findings and Diagnostic Process

Because epithelial ovarian cancers develop deep within the pelvis and initially present with no specific symptoms, diagnosis is often delayed until

later in life. A significant portion of patients (70%) are in advanced stages of disease at the time of diagnosis. These tumors are often detected during routine gynecological examinations or by imaging studies of abnormal masses in the pelvic area. In advanced stages, they can spread to the peritoneal cavity, causing ascites accumulation, pressure on abdominal organs, and respiratory distress (Kao & Norris, 1979; Bell & Scully, 1985).

Ovarian Cancer Symptoms

The symptoms of ovarian cancer are often nonspecific and can mimic symptoms associated with the gastrointestinal and urinary systems. Therefore, delays in diagnosis are common. The following symptoms may be clinical indicators of ovarian cancer:

- Pain or a feeling of fullness in the pelvic or abdominal area
- Significant abdominal bloating and distension
- Change in bowel habits (e.g., constipation)
- Frequent urination
- Feeling full early after meals, loss of appetite
- Unexplained weight loss
- Vaginal bleeding (especially outside of menstrual periods)
- Pain during intercourse
- Persistent weakness and fatigue
- Nausea and indigestion

Because many of these symptoms can also be seen in other benign conditions, careful evaluation and differential diagnosis with appropriate diagnostic tests are important (Memorial Medical Publications Board, 2024; Bilici M., 2014).

Ovarian Cancer Staging

The stage of the disease at diagnosis plays a decisive role in the clinical management of ovarian cancer. Staging is critical for determining whether the tumor has spread beyond the ovary and metastasized to surrounding tissues or distant organs. The staging system recommended by the International Society for Gynecologic Cancer (FIGO) and the American Joint Committee on Cancer (AJCC) classifies tumors based on their anatomical extent (Memorial Medical Publishing Board, 2024).

1. Stage I: Ovarian-Limited Disease

• In stage I ovarian cancer, the malignancy is confined to only one or both ovaries. At this stage, cancer cells have not spread to pelvic or abdominal organs, lymph nodes, or distant parts of the body. The tumor is located solely within or on the surface of the ovaries; in some cases, malignant cells can be observed in the peritoneal fluid (ascites). Surgical treatment is the primary approach for this stage. Optimal surgery aims to completely remove the tumor; however, in some cases, the risk of recurrence can range from 5-20% due to microscopic spread (micrometastasis). The presence of micrometastatic foci indicates that small, invisible cancer cells may have spread beyond the ovary. Therefore, adjuvant treatment may be necessary after surgery (Benedet et al., 2000; Özkılıç, 2007).

Adjuvant therapy is a multidisciplinary approach that includes chemotherapy, radiotherapy, or biologic agents administered after surgery and aims to prevent disease recurrence. Platinum-based chemotherapeutic agents are generally preferred, and the treatment plan is determined by the histopathological features and risk of recurrence.

Stage I is categorized into three subgroups:

• Stage IA: The tumor is localized in only one ovary; there is no tumor formation on the external surface or disruption of capsule integrity; and no malignant cells are found in the peritoneal fluid.

• Stage IB: The tumor has involved both ovaries; capsule integrity is preserved, and there is no surface localization.

• Stage IC: The tumor has involved one or both ovaries, and there is rupture of the ovarian capsule, surface localization, or malignant cells in the peritoneal fluid (Benedet et al., 2000; Özkılıç, 2007).

2. Stage II: Spread Within the Pelvis

In Stage II, cancer has spread from the ovaries to adjacent organs such as the uterus, fallopian tubes, or other pelvic structures. However, the tumor has not yet reached the upper abdomen or distant lymph nodes. Surgical debulking (cytoreductive surgery) is the primary treatment method at this stage. However, because microscopic cancer cells that have spread to the pelvic region may not all be surgically removed, adjuvant chemotherapy becomes an absolute necessity. Intraperitoneal chemotherapy, in particular, is one of the preferred methods for effectively removing small residual tumors. Delivering chemotherapeutic agents directly to the tumor tissue increases treatment efficacy and can prolong survival. Furthermore, in some

cases, neoadjuvant chemotherapy administered before surgery is used to reduce tumor volume and facilitate surgical intervention. Studies on the effectiveness of this approach are ongoing; it is particularly preferred in patients with high tumor burden or those not suitable for surgery (Benedet et al., 2000; Özkılıç, 2007).

Stage II is further classified as follows:

• Stage IIA: The tumor has spread to the uterus or fallopian tubes.

• Stage IIB: The tumor has invaded the pelvic peritoneum or other pelvic organs.

• Stage IIC: In addition to the findings of Stages IIA or IIB, features such as malignant peritoneal fluid or rupture of the ovarian capsule are present (Benedet et al., 2000; Özkılıç, 2007).

3. Stage III: Intra-Abdominal Spread and Lymph Node Involvement

In stage III, the tumor has spread beyond the ovary, reaching the intra-abdominal peritoneal surfaces, intestines, omentum, or regional lymph nodes. However, distant organs such as the liver parenchyma have not yet been affected. Standard treatment consists of maximal cytoreductive surgery followed by systemic chemotherapy. During surgery, the tumor burden should be reduced as much as possible, and residual disease smaller than 1 cm should be targeted. However, in this stage, the risk of disease recurrence is quite high due to micrometastatic remnants. Only 30-40% of stage III patients achieve long-term survival.

Adjuvant therapy in this stage usually consists of a combination of paclitaxel and carboplatin, administered every 3 weeks for a total of 6 cycles.

Stage III substages are as follows:

• Stage IIIA: Microscopic peritoneal metastases are present outside the pelvis.

• Stage IIIB: Peritoneal metastases smaller than 2 cm are observed outside the pelvis.

• Stage IIIC: Peritoneal metastases larger than 2 cm or regional lymph node involvement is present (Benedet et al., 2000; Özkılıç, 2007).

4. Stage IV: Distant Metastasis Stage

Stage IV ovarian cancer is defined as an advanced stage in which the disease has spread beyond the abdominal region. At this stage, metastases involve distant organs such as the liver parenchyma, pleural space, or distant

lymph nodes. The treatment strategy again includes a combination of cytoreductive surgery and platinum-based systemic chemotherapy. However, the high tumor burden and the presence of chemotherapy-resistant cells at this stage significantly reduce the response rate to treatment, increasing the risk of recurrence. Although multimodal treatment approaches are being implemented to prolong life and control symptoms, survival at this stage is generally limited. Palliative approaches to improve quality of life are also important (Benedet et al., 2000).

Prevention, Screening, and Treatment Approaches in Ovarian Cancer

Ovarian cancer (ovarian cancer) continues to have high mortality rates compared to some highly treatable cancers. Although numerous treatment protocols based on surgery and chemotherapy have been developed, the overall 5-year survival rate for the disease is approximately 45%. This low survival rate is associated with most cases being diagnosed at an advanced stage (Siegel et al., 2011). The ideal treatment protocol for ovarian cancer is surgical resection to remove the tumor tissue, followed by adjuvant chemotherapy. In some cases, radiotherapy may be added to the treatment. Anatomical sites to which the disease spreads frequently include the pelvis, intra-abdominal peritoneal surfaces, and distant organs such as the lungs and liver via the systemic circulation (Siegel et al., 2011; Bilici, M., 2014).

Screening and Evaluation During Diagnosis

Suspicion of ovarian cancer often arises from the sensation of a pelvic mass, swelling, or nonspecific abdominal symptoms. Initial diagnostic evaluation includes measuring tumor markers, particularly CA-125, along with transvaginal or abdominal ultrasonography. However, an increase in CA-125 levels does not always indicate malignancy; inflammatory conditions, benign gynecological diseases, or other non-malignant causes can also cause this marker to rise. In postmenopausal women, a CA-125 level of >35 U/mL is considered more suggestive of malignancy. While this marker is not diagnostic, it is an important biological indicator for monitoring the disease during treatment and detecting recurrences (Tian et al., 2009).

Surgical Intervention

Surgery is used for both staging and treatment in ovarian cancer. During this procedure, usually performed via laparotomy, tissue samples are taken from the tumor mass along with the affected pelvic and abdominal organs for pathological examination. The primary goal of surgery is to remove the largest tumor mass possible.

Etiology and Risk Factors

The causes of ovarian cancer are not fully understood. However, as with other solid tumors, genetic and environmental factors are thought to play a role.

Genetic Risk Factors

A family history of ovarian cancer, especially in first-degree relatives, significantly increases an individual's risk of developing the disease. This condition is not limited to maternal but is also associated with paternal inheritance. BRCA1 and BRCA2 gene mutations are frequently observed in individuals with a genetic predisposition. These mutations show an autosomal dominant inheritance pattern and have variable penetrance. The risk of developing ovarian cancer in individuals carrying a BRCA1 mutation ranges from 15-60%, and the risk of developing breast cancer ranges from 35-85%. Genetic testing is now becoming more widespread in high-risk individuals, and prophylactic mastectomy and oophorectomy may be recommended for individuals with mutations (Clement, 2002; Rosai, 2004).

Nongenetic and Environmental Risk Factors

1. Age

Ovarian cancer frequently occurs in older adults. While the disease is rare in women under 40, the incidence increases significantly, especially in the postmenopausal period (Colombo et al., 2006).

2. Hormone Therapies and Ovulation Induction

Postmenopausal women using estrogen-only hormone replacement therapy have a higher risk of ovarian cancer than those using combined estrogen-progestin therapy. Furthermore, long-term use of ovulation-inducing drugs used in infertility treatments has also been associated with ovarian cancer. Conditions such as polycystic ovary syndrome, endometriosis, and amenorrhea have also been considered risk factors (Colombo et al., 2006).

3. Breast Cancer History

The risk of developing ovarian cancer is significantly increased in women who have had breast cancer. This association is particularly pronounced in individuals carrying BRCA mutations. The same genetic mutations play a role in the development of both breast and ovarian cancer (Clement, 2002; Rosai, 2004).

4. Smoking

Smoking has been associated with the development of ovarian cancer, particularly the mucinous histological type. Toxic components in cigarette smoke, such as tar, nicotine, and carbon monoxide, can cause damage at the cellular level and trigger malignant transformation (Guerrieri et al., 1994; Clement, 2002).

5. Oral Contraceptive Use

Regular use of birth control pills provides a significant reduction in the risk of ovarian cancer. This protective effect is directly proportional to the duration of use. However, the use of these medications must be under the supervision of a physician (Moysich et al., 2001).

Screening, Early Diagnosis, and Treatment Approaches in Ovarian Cancer

Although effective screening methods are currently available for some types of cancer, there is no effective screening method for the general population for ovarian cancer. Screening is recommended only for high-risk groups, such as BRCA1/2 carriers (Clement, 2002; Moysich et al., 2001).

Commonly accepted symptoms include: Significant abdominal distension, Pelvic or abdominal pain, Early satiety or loss of appetite, and Frequent urination. While these symptoms are nonspecific, they require further evaluation if they are persistent and severe. Early diagnosis is critical for successful treatment. During clinical evaluation, pelvic examination, ultrasonography, and, if necessary, Doppler ultrasound can help distinguish between solid and cystic masses. In addition to CA-125 and other tumor markers, the blood flow characteristics of the mass can be analyzed with Doppler ultrasonography. However, none of these methods are diagnostic alone. In cases with high suspicion of malignancy, a biopsy with surgical intervention is the gold standard for establishing a definitive diagnosis. (Memorial Medical Publishing Board, 2024). The primary treatment approach is surgery and chemotherapy, depending on the stage of the disease. During the surgical procedure, the uterus, ovaries, affected peritoneal tissues, and, if necessary, lymph nodes are removed. If the mass has spread to surrounding tissues or is not amenable to surgery, surgery may be performed after the tumor is reduced in size with neoadjuvant chemotherapy. Platinum-based chemotherapy protocols are commonly preferred in the postoperative period. (Memorial Medical Publications Board, 2024; Bilici, M., 2014).

Kaynaklar

Adilay, Utku., 2006. ***Glioblastoma multiforme ve benign Meningiom olgularında tümör dokusunda Ölçülen çinko, demir ve kadmiyum düzeylerinin karşılaştırılması*** (uzmanlık tezi) Bakırköy Ruh Sağlığı ve Sinir Hastalıkları Eğitim ve Araştırma Hastanesi. İstanbul.

Bilici, M., 2014. Over Kanserli Hastalarda Ameliyat Öncesi ve Sonrası Kandaki Eser Element Düzeylerinin (Zn, Cu, Mg, Pb, Mn, Cd, Co Ve Fe) İncelenmesi (Doktora tezi), Yüzüncü Yıl Üniversitesi, ***Fen Bilimleri Enstitüsü,*** Kimya Anabilim Dalı, Van.

Bell, D.A., Scully, R. E., 1985. Benign and borderline clear cell adenofibromas of the ovary. ***Cancer***, 56 : 2911 - 2931.

Benedet, J. L., Bender, H., Jones, H., 2000. 3rd, Ngan H.Y, Pecorelli S. FIGO staging classifications and clinical practise guidelines in management of gynecologic cancers. FIGO Committee on Gynecologic Oncology. ***Int J Gynecol Obstet,*** **70**:209-62.

Berrino F, De Angelis R, Sant M, Rosso S, Lasota MB, Coebergh JW, et al. 2007, Survival for eight major cancers and all cancers combined for European adults diagnosed in 1995-99: results of the EUROCARE-4 study. Lancet Oncol 2007;8:773-83.

Beji, N.K., Bilgiç, D. (2015). Over kanseri. In G, Can (Eds), Onkoloji hemşireliği (pp. 807-838). ***Nobel tıp Kitabevi.***

Bozkurt Ö, B., Göçmen A., Itır E. Z. 2024, Kliniğimizde over kanseri nedeniyle opere edilen hastaların retrospesifik analizi, ***Türk Jinekolojik Onkoloji Dergisi*** 2024, VOL. 24, NO.1, 25-33.

Bray, F., Ferlay, J., Soerjomataram, I., Siegel, R.L., Torre, L.A. ve Jemal, A. (2018). Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: ***A Cancer Journal of Clinicians,*** 68(6),394-424.

Bristow RE, Tomacruz RS, Armstrong DK, Trimble EL, Montz FJ. Survival effect of maximal cytoreductive surgery for advanced ovarian carcinoma during the platinum era; a meta-analysis. J Clin Oncol 2002 ; 20 : 1248 – 59.

Çalışkan, M.O., 2008. ***Malign Epitelyal Over Tümörlerinin Agresivitesinde Ve İlaç Dirençliliğinde Rol Oynayan Genlerin Ekspresyon Düzeylerinin Tümör Evrelerine Göre Primer Ve Metastatik Dokularda Belirlenmesi.*** (Doktora Tezi) A.Ü. Sağ. Bil. Ens. Tıbbi Biyoloji ve Genetik Anabilim Dalı, Ankara.

Capriglione, S., Luvero, D., Plotti, F., Terranova, C., Montera, R., Scaletta, G., ve diğerleri. (2017). Ovarian cancer recurrence and early detection: may HE4 play a key role in this open challenge? A systematic review of literature. Medical Oncology (Northwood, London, England), 34(9), 164.

Clement, P.B., 2002. Anatomy and Histology of the Ovary. In Kurman R (ed): Blaustein's Pathology of the Female Genital Tract, 5th ed. New York, Springer-Verlag, 649-650.

Colombo, N., Gorp T.V., Parma G., Amant F., 2006. Ovarian cancer. Critical Reviews in Oncology / Hematology, 60: 159-179.

Demirbağ, N., 2004. Over Tümörleri. Patoloji. Nobel Tıp Kitabevleri.163-165.

Doğan D., Meydan İ., Kömüroğlü A. U., 2022. ***"Protective Effect of Silymarin and Gallic Acid against Cisplatin-Induced Nephrotoxicity and Hepatotoxicity,"*** International journal of clinical practice , vol.2022, pp.6541026.

Doğan D., Okumuş E., Meydan İ. 2025. ***Ketogenic Diet and Cancer***. Van Sağlık Bilimleri Dergisi, cilt.18, sa.1, ss.80-85.

Ekinci, T., Yavuzcan, A., Ozbay, P., ve Uysal, S. (2013). Epiteryal over kanserinde sağkalımı etkileyen faktörlerin incelenmesi. Türk Jinekolojik Onkoloji Dergisi, 3,66-73.

Eroğlu, K. ve Koç, G. (2013). Jinekolojik kanser kontrolü ve hemşirelik. *Hacettepe Üniversitesi Hemşirelik Fakültesi Dergisi,1*(2),77–90.

Falcetta, F. S., Lawrie, T. A., Medeiros, L. R., da Rosa, M. I., Edelweiss, M. I., Stein, A. T., ve diğerleri. (2016). Laparoscopy versus laparotomy for FIGO stage I ovarian cancer. *The Cochrane Database of Systematic Reviews*, *10*(10), CD005344.

Gao Z.J., Zhonghua Zhong Liu Za Zhi.1988. ***Diagnostic value of serum copper/zinc ratio in gynecologic tumors.*** 10: 434-6.

Guerrieri. C., Hogberg, T., Wingren, S., Fristedt, S., Simonsen, E., Boeryd, B., 1994. Mucinous borderline and malignant tumors of the ovary. A clinicopathologic and DNA ploidy study of 92 cases***. Cancer***. 74:2329-2340.

Gurusamy, K., 2007. Trace element concentration in primary liver cancers-a systematic review. ***Biol Trace Elem Res.***118:191-206.

Kao, G.F., Norris, H.J., 1979. Unusual cystadenofibromas: endometrioid, mucinous, and clear cell types. ***Obstet Gynecol.*** **54**: 729-736.

Kuzey, G.M., 2007. Over ve Fallopian Tüp Hastalıkları Patolojisi. ***Temel Patoloji.***Güneş Kitabevi: 673-72

Memorial Tıbbi Yayın Kurulu,2024, ***Memorial Tıbbi Yayın Kurulu.*** Uzm. Dr. Yüksel Koçak. Grup Direktörü. Dr. Hakan Taşlı.

Moysich, K.B., Mettlin, C., Piver, MS., Natarajan, N., Menezes, R.J., Swede, H., 2001. Regular Use of Analgesic Drugs and Ovarian Cancer Risk. ***Cancer Epidemiology Biomarkers & Prevention:*****10,** 903-906.

Özkılıç, A. Ç., 2007. ***Over kanserli hastalarda mthfr Polimorfizmi, folat, homosistein düzeyleri ve apoptoza eğilimleri*** (Doktora Tezi), İstanbul Üni. Sağlık Bilimleri Enstitüsü, Tıbbi Biyoloji Anabilim Dalı, İstanbul.

Pınar, G., Algıer, L., Doğan, N. ve Kaya, N. (2008). Jinekolojik kanserli bireylerde risk faktörlerinin belirlenmesi. *International Journal of Hematology and Oncology*, *4*(18),208-216.).

Tuncer G. S., Demir H., Izmirli M., Cakir T., Yilmazer G., Demir C. 2022 "Effect of radiotherapy on erythrocyte catalase, and carbonic anhydrase activities, serum levels of some trace elements and heavy metals (Zn, Cu, Pb, Cd, Mn, Fe, Mg and Co) in cancer patients," *INTERNATIONAL JOURNAL OF RADIATION RESEARCH* , vol.20, no.1, pp.97-102, 2022.

Riopel, M.A., Ronnett, B.M., Kurman, R.J., 1999. Evaluation of diagnostic criteria and behavior of ovarian intestinal-type mucinous tumors: atypical proliferative tumors and intraepithelial, microinvasive, invasive and metastatic carcinomas**.** ***Am J Surg Pathol***, **23**:617-635.

Rosai, J., 2004. ***Rosai and Ackerman's Surgical Pathology.*** Vol 2, 9 th ed. Mosby.

Edinburgh, London, Oxford, 1649-1709, New York.

Sağlık Bakanlığı. Halk Sağlığı Genel Müdürlüğü Kanser Dairesi Başkanlığı. Türkiye Kanser İstatikleri (2017). Kanser rapor 2017 (https://hsgm.saglik.gov.tr/depo/birimler/kanser- db/istatistik/Turkiye_Kanser_Istatistikleri_2017.)

Sağlık Bakanlığı., 1998. ***Hemşireler için el kitabı*** (Kanserle Savaş Daire Başkanlığı Ve Onkoloji Hemşireliği Derneği Yayını) Ankara.

Schulz, W.A., 2005. Molecular Biology of Human Cancers. ***Apoptosis and replicative Senescence in Cancer***. Springer. Part 2. p.145-165.

Siegel, R., Ward, E., Brawley, O., Jemal, A., 2011. Cancer statistics, the impact of eliminating socioeconomic and racial disparities on premature cancer deaths. *CA:* ***Cancer Journal for Clinicians. 61*** **(4):** 212–236.

Siegel RL,Miller KD,Wagle NS,Jemal A,Kanser İstatistikleri,2023.CA Kanser j Clin 2023 ;73:17.

Soidman, J. D., Russel, P., Kurman, R. J., 2002. ***Surface epithelial tumors of the ovary,*** Chapter 18, Blaustein's Pathology of the Female Genital Tract Ed Kurman R. J. 5th ed. 791-904, Springer, Newyork.

Sundström H, Korpela H, Sajanti E, Kauppila A, 1989. Supplementation with selenium, vitamin E and their combination in gynaecological cancer during cytotoxic chemotherapy.***Carcinogenesis***.**10**: 273-8.

Sung H, Siegel RL,Küresel. 2020. Kanser İstatistikleri 2020.

Tian, C., Markman, M., Zaino, R., Ozols, R.F., McGuire, W.P., Muggia, F.M., Rose, P.G., Spriggs, D., Armstrong, D.K., 2009. CA-125 change after chemotherapy in prediction of treatment outcome among advanced mucinous and clear cell epithelial ovarian cancer: ***a Gynecologic Oncology Group study. Cancer.*** **115 (7):** 1395-403.

Tortolero-Luna, G., Mitchell, M. F., 1995. The epidemiology of ovarian cancer. ***Journal of Cellular Biochemistry*.** 59 (23) : 200–207

Quaye L, Gayther SA, Ramus SJ, Di Cioccio RA, McGuire V, Hogdall E, et al. The effects of common genetic variants in oncogenes on ovarian cancer survival. Clin Cancer Res 2008;14:5833-9.

Vogelstein, B., Kınzler, K., 2005. The genetic basis of human cancer. Basic Familial cancer syndromes. Familial cancer syndromes:***Role of catetaker and Gatekeepers.*** Springer Part 3: p.209-211

Tüik., 2008; 2012; 2013, Sağlık Raporları (***Türkiye İstatistik Kurumu***).

Webb, P.M. ve Jordan, S.J. (2017). Epidemiology of epithelial ovarian cancer. *Best Practice & Research Clinical Obstetrics & Gynaecology, 41*,3-14.).