Review Article

Ovarian Cancer: Epidemiology, Clinical Presentation, Investigation and Treatment

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Abstract:

Global epidemiological reports indicate a steady increase in the tendency to develop ovarian cancer. Ovarian cancer is the most fatal gynecologic malignancy, primarily due to nonspecific symptoms that lead to late-stage diagnosis. This review summarizes its epidemiology, key risk factors, pathophysiology, clinical features, diagnostic approaches, staging and treatment. There is no effective screening tool. A growing body of evidence points to the role of genetic factors in the development of cancer. It is known that mutations in the BRCA1 gene are responsible for an increased risk of developing ovarian cancer. Ovarian cancer is a hormone dependent cancer and its steroid hormones are estrogens. Estrogens affect cells through the estrogen receptors ERα and ERβ. An imbalance between ERα and ERβ receptor expression may, therefore, be a key step in estrogen dependent carcinogenesis.

Key words: ovarian cancer, high grade serous carcinoma BRCA mutation CA-125, FIGO staging, cytoreductive surgery.

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Epidemiology of ovarian cancer

Ovarian cancer is the eight most common cause of cancer and cancer relative death in women worldwide.[1] Ovarian cancer, though less common than other malignancies, is the most fatal gynecologic cancer due to late stage detection.[2] Most ovarian cancer cases occur after menopause. Ovarian cancer mainly affects women aged 55-70. The peak of incidence occurs between the ages of 55 and 59.[3] About 70% of ovarian cancers are detected at an advanced stage (FIGO-III and IV) (The International Federation of Gynecology and Obstetrics).[4]

The germ cell tumor affects younger woman.[5]

Risk factors for ovarian cancer

Mutations in the BRCA1 and BRCA-2 genes is one of the most well-known risk factors for ovarian cancer, 10–15% of all ovarian cancers have a genetic basis associated with these mutations. The risk of developing ovarian cancer for BRCA1 mutation carriers is about 44%, and for BRCA-2 mutation carriers, it is about 17%.[6,7] Lynch syndrome is responsible for about 10% of ovarian cancers.[8]

The risk of developing ovarian cancer can be reduced as a result of hysterectomy, oophorectomy, the closure of the fallopian tubes, or the use of hormonal contraception.[9,10] Taking oral contraception over a shorter, five-year period has a beneficial effect reducing the incidence of ovarian cancer by 20–30%.[11] Decrease in the incidence of ovarian cancer up to 60% in women who use oral contraceptives for 10 years.

It has been proven that four births reduce the risk of developing the disease by about 40%.[12] The beneficial effect of pregnancy and childbirth is based on the inhibition of ovulation, the consequence of which is the prevention of damage to the epithelium on the surface of the ovary. As a result of this process, there is no development of inclusion cysts, and thus the start of carcinogenesis. Other explains this situation by apoptosis (as natural process of programmed cell death) induced by progesterone or progestogens.

As a result, cancer cells are removed from the ovary.[13] Those who undergo in vitro procedure, there is almost twenty fold increase the risk of developing ovarian cancer.[14]

Endometriosis increase the risk of ovarian cancer by 1.8%.[15, 16]

Other risk factors are early menarche, late menopause, nulliparity, excessive body weight.[17, 18]

Long term hormone replacement therapy slightly elevates risk, which declines after cessation.[19] Possible but unconfirmed risk factors include asbestos exposure and certain dietary habits.[20]

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Prevention of Ovarian Cancer:

The patients who had hereditary burden of breast cancer and ovarian cancer (who are carriers of the BRCA 1/2 mutation) follow up medical and imaging examinations are recommended. A detailed family history is conducted, and if there are medical indications, genetic testing is performed.[21]

For patients with known ovarian cancer susceptibility genes, prophylactic bilateral salpingo-oophorectomy is the most effective preventive measure for ovarian cancer.[22] The NCCN (The National Comprehensive Cancer Network) guidelines recommend bilateral salpingo-oophorectomy at age 35 to 40 years for BRCA1 gene variant carriers who have completed childbearing, age 40 to 45 years for BRCA2 carriers and age 45 to 50 years for women with other pathogenic gene variants such as for Lynch syndrome.[21]

Oral contraceptives reduce ovarian cancer risk for high risk younger individuals. The American College of Obstetricians and Gynecologists and International Federation of Gynecology and Obstetrics guidelines recommend considering surgical and hormonal preventive approaches to the general population to reduce ovarian cancer risk.[23, 24]

For premenopausal women not interested in childbearing who are undergoing pelvic surgery, bilateral salpingectomy (removal of the fallopian tubes) while preserving the ovaries can avoid early menopause and its potential adverse effects on health [23, 24].

Clinical Presentation and Diagnosis:

Symptoms:

Abdominal bloating or swelling, Early satiety or difficulty eating, Pelvic or abdominal pain, Changes in bowel habits (constipation/diarrhea), Urinary frequency or urgency, Fatigue, back pain, and unexplained weight loss. These symptoms are often mild and persistent. The key distinguishing feature is their new onset and daily occurrence over several weeks [25].

Diagnosis of ovarian Cancer

Pelvic Examination

A pelvic examination assesses ovarian size, shape and consistency but has limited sensitivity for early detector especially of small tumor.[17]

Imaging

- Transvaginal ultrasound (TVUS): first line imaging to differentiate benign from malignant adnexal masses by assessing morphology and blood flow.[26] Not suitable for population screening due to low specificity.[27]
- Computed Tomography (CT): Evaluates tumor spread, lymph node involvement, and guides surgical planning.[28]
- Magnetic Resonance Imaging (MRI): offers superior soft tissue contrast and helps assess local invasion or indeterminate lesions.[29]
- Positron Emission Tomography (PET): Often combined with CT, it detects metabolically active disease and is valuable for recurrence and metastasis assessment.[30]

Tumor Markers

- CA-125: Elevated in 80% of advanced and 50%of early epithelial ovarian cancers but lacks specificity due to elevation in benign conditions [31, 32]. Mainly used for monitoring treatment response, recurrence, and risk assessment.[33]
- HE4: More specific than CA-125, especially for serous and endometrioid subtypes. Combined with CA-125 in the ROMA algorithm, it improves diagnostic accuracy, particularly in premenopausal women.[34, 35]

Biopsy and Histopathology

Definitive diagnosis requires histopathological confirmation from a surgical or image-guided biopsy.[36] Tissue examination determines tumor type, grade, and molecular features, guiding therapeutic decisions. In advanced disease or pre-surgical evaluation, image-guided biopsy may precede surgery.[37]

Staging and Prognosis

Accurate staging is vital in ovarian cancer as it guides treatment and determines prognosis. The International Federation of Gynecology and Obstetrics (FIGO) system is the most accepted method for ovarian, fallopian tube, and primary peritoneal cancers.[38] Based on disease spread at surgery, FIGO staging remains the strongest prognostic indicator.[39]

Prognostic Factors

Histology and Grade: High-grade serous and clear cell carcinomas have poorer outcomes than low-grade tumors.[40]

Residual Disease: Minimal or no macroscopic residual tumor post-surgery (optimal debulking) strongly improves survival.[41]

Performance Status and Age: Younger, healthier patients show better tolerance and outcomes.[42]

Genetic and Molecular Markers: BRCA1/2mutations predict favorable response to platinum therapy and PARP inhibitors.[43] Elevated CA-125 may also indicate disease course.[33]

Treatment Modalities

Management of ovarian cancer is individualized, depending on stage, histology, patient health, and molecular profile. Standard treatment involves surgery and chemotherapy, often supplemented with targeted, hormonal, or immunotherapeutic approaches.[44]

Surgical Management

Primary Debulking Surgery: Standard for advanced disease; aims for no visible (R0) or<1 cm (R1) residual tumor. It usually includes hysterectomy, bilateral salpingo-oophorectomy, omentectomy, and lymphadenectomy, with additional organ resections if needed.[41, 45] Optimal debulking remains a key prognostic factor.[41]

Interval Debulking Surgery: For patients with extensive disease or poor performance status, neoadjuvant chemotherapy followed by interval surgery achieves comparable outcomes to primary debulking.[46, 47]

Fertility-Sparing Surgery: In selected young women with early-stage, low-grade or germ cell tumors, unilateral salpingo-oophorectomy preserves fertility while maintaining oncologic safety.[48]

Chemotherapy

Chemotherapy is essential, given post-surgery(adjuvant) or pre-surgery (neoadjuvant).[44]

Platinum-Based Regimens: The first-line regimen combines carboplatin (preferred for lower toxicity) with a taxane (paclitaxel or docetaxel), administered every three weeks for six cycles.[49, 50]

Intraperitoneal Chemotherapy: In optimally debulked stage III disease, intraperitoneal delivery enhances survival versus intravenous therapy but has greater toxicity.[51, 52]

Targeted Therapy

Targeted agents disrupt molecular pathways in tumor growth.[53]

PARP Inhibitors: Olaparib, niraparib, and rucaparib are effective in BRCA1/2-mutated or HRD-positive tumors, improving outcomes as maintenance or recurrent therapy.[54, 55]

Anti-Angiogenic Agents: Bevacizumab inhibits VEGF-mediated angiogenesis and is used with chemotherapy or as maintenance in advanced and recurrent disease.[56, 57]

Hormone Therapy

Used mainly for hormone-sensitive low-grade serous ovarian cancer. Tamoxifen or aromatase inhibitors block estrogen effects and offer a well-tolerated option for slow-growing or recurrent cases.[58, 59]

Immunotherapy

Checkpoint inhibitors such as pembrolizumab and nivolumab activate immune responses against tumor cells. While still under study, they show promise in platinum-resistant and combination therapy settings.[60, 61]

Supportive (Palliative) Care

Palliative care addresses physical, psychological and emotional needs throughout the disease course.[62]

Immunotherapy Advances

Although single-agent checkpoint inhibitors show modest results, combination strategies are improving outcomes. These include pairing immunotherapy with chemotherapy, PARP inhibitors, or anti-angiogenic agents to overcome the immunosuppressive tumor microenvironment.[63]

Gene Therapy

Gene therapy introduces or modifies genes to enhance tumor suppression or immune response. Methods include inserting TP53 tumor suppressor genes, suicide genes, or immune-enhancing genes via viral vectors like adenoviruses or AAV.[64]

Conclusion

The future of ovarian cancer care lies in personalized medicine, guided by genomic profiling, biomarker discovery, and liquid biopsies for precise diagnosis and tailored therapies. Further exploration of the fallopian tube origin of high-grade serous cancers may improve early detection and prevention. Addressing disparities in access and outcomes worldwide will be vital.

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