Review Article

Ovarian Cancer: Epidemiology, Clinical Presentation, Investigation and Treatment

*Ahmed S

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.

Received on:12.01.26; Revised on: 15.04.26; Accepted on:01.04.26

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]

Author's Affiliation:

1. Professor Dr. Shahana Ahmed, Department of Obstetrics & Gynaecology, Diabetic Association Medical College, Faridpur, E-mail: dr.shamolee42rmc@gmail.com.

Address of Correspondence : *Professor Dr. Shahana Ahmed, Professor, Department of Obstetrics & Gynaecology, Diabetic Association Medical College, Faridpur, Mobile: +880 1714 105201; Email: dr.shamolee42rmc@gmail.com.

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.

References

1. Bray F, Laversanne M, Sung H, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2024;74(3):229-263. doi:10.3322/caac.21834
2. World Ovarian Cancer Coalition. Ovarian cancer data briefing Internet. World Ovarian Cancer Coalition; 2024 Apr. [Crossref] [PubMed][GoogleScholar]
3. Ali, A.T.; Al-Ani, O.; Al-Ani, F. Epidemiology and risk factors for ovarian cancer. Prz. Menopauzalny 2023, 22, 93–104. [CrossRef] [PubMed]
4. Kehoe, S. FIGO staging in ovarian carcinoma and histological subtypes. J. Gynecol. Oncol. 2020, 31, e70. [CrossRef]
5. NHS. Ovarian cancer – Causes Internet. NHS. [Crossref][PubMed][Google Scholar]

6. Wojciechowska, U.; Bara´ nska, K.; Michałek, I.; Olasek, P.; Miklewska, M.; Didkowska, J.A. Nowotwory Zło´sliwe w Polsce w 2020 Roku; Krajowy Rejestr Nowotworów: Warszawa, Poland, 2022.

7. Barili, V.; Ambrosini, E.; Bortesi, B.; Minari, R.; De Sensi, E.; Cannizzaro, I.R.; Taiani, A.; Michiara, M.; Sikokis, A.; Boggiani, D.; et al. Genetic Basis of Breast and Ovarian Cancer: Approaches and Lessons Learned from Three Decades of Inherited Predisposition Testing. Genes 2024, 15, 219. [CrossRef]

8. Gambini, D.; Ferrero, S.; Kuhn, E. Lynch Syndrome: From Carcinogenesis to Prevention Interventions. Cancers 2022, 14, 4102. [CrossRef]

9. Daly, M.B.; Dresher, C.W.; Yates, M.S.; Jeter, J.M.; Karlan, B.Y.; Alberts, D.S.; Lu, K.H. Salpingectomy as a means to reduce ovarian cancer risk. Cancer Prev. Res. 2015, 8, 342–348. [CrossRef]

10. Dixon-Suen, S.C.;Webb, P.M.;Wilson, L.F.; Tuesley, K.; Stewart, L.M.; Jordan, S.J. The Association Between Hysterectomy and Ovarian Cancer Risk: A Population-Based Record-Linkage Study. J. Natl. Cancer Inst. 2019, 111, 1097–1103. [CrossRef]

11. Collaborative Group on Epidemiological Studies on Endometrial Cancer. Endometrial cancer and oral contraceptives: An individual participant meta-analysis of 27 276 women with endometrial cancer from 36 epidemiological studies. Lancet. Oncol. 2015, 16, 1061–1070. [CrossRef]

12. Norheim, O.F.; Jha, P.; Admasu, K.; Godal, T.; Hum, R.J.; Kruk, M.E.; Gómez-Dantés, O.; Mathers, C.D.; Pan, H.; Sepúlveda, J.; et al. Avoiding 40% of the premature deaths in each country, 2010–2030: Review of national mortality trends to help quantify the UN sustainable development goal for health. Lancet 2015, 385, 239–252. [CrossRef] [PubMed]

13. Stover, J.; Winfrey, W. The effects of family planning and other factors on fertility, abortion, miscarriage, and stillbirths in the Spectrum model. BMC Public. Health 2017, 17, 775. [CrossRef]

14. Wojciechowska, P.; Milska Musa, K.A. Quality of life and mental state of women trying to conceive using the in vitro method. Eur. Transl. Clin. Med. 2024, 7, 106–112. [CrossRef]

15. Sun, Y.; Liu, G. Endometriosis-associated Ovarian Clear Cell Carcinoma: A Special Entity? J. Cancer 2021, 12, 6773–6786. [CrossRef]

16. Hablase, R.; Kyrou, I.; Randeva, H.; Karteris, E.; Chatterjee, J. The “Road” to Malignant Transformation from Endometriosis to Endometriosis-Associated Ovarian Cancers (EAOCs): An mTOR-Centred Review. Cancers 2024, 16, 2160. [CrossRef]

17. Mayo Clinic Staff. Ovarian cancer – Symptomsand causes [Internet]. Mayo Clinic; 2025 May 2. [Crossref][PubMed][Google Scholar]

18. Winship Cancer Institute of Emory University. Ovarian cancer screening Internet. [Crossref] [PubMed][Google Scholar]

19. Roswell Park Comprehensive Cancer Center. Ovarian cancer survival rates Internet. [Crossref][PubMed][Google Scholar]

20. National Comprehensive Cancer Network (NCCN). Ovarian cancer/fallopian tube cancer/ primary peritoneal cancer guidelines Internet. [Crossref][PubMed][Google Scholar]

21. Daly MB, Pal T, Maxwell KN, et al. NCCN guidelines insights: genetic/familial high-risk assessment: breast, ovarian, and pancreatic, version 2.2024. J Natl Compr Canc Netw. 2023;21 (10):1000-1010. doi:10.6004/ jnccn.2023.0051

22. Walker JL, Powell CB, Chen LM, et al. Society of Gynecologic Oncology recommendations for the prevention of ovarian cancer. Cancer. 2015;121(13): 2108-2120. doi:10.1002/ cncr.29321

23. American College of Obstetricians and Gynecologists. ACOG committee opinion No. 774: opportunistic salpingectomy as a strategy for epithelial ovarian cancer prevention. Obstet Gynecol. 2019;133(4):e279-e284. doi:10.1097/ AOG.0000000000003164

24. Mor-Hadar D, Wilailak S, Berek J, McNally OM; FIGO Committee onWomen’s Cancer. FIGO position statement on opportunistic salpingectomy as an ovarian cancer prevention strategy. Int J Gynaecol Obstet. 2024;167(3):976-980. doi:10.1002/ijgo.15884

25. Target Ovarian Cancer. Symptoms of ovariancancer Internet. [Crossref][PubMed] [GoogleScholar]

26. American Cancer Society. Tests for ovariancancer Internet. 2022 Nov 17. [Crossref] [PubMed][Google Scholar]
27. U. S. Preventive Services Task Force. Screeningfor ovarian cancer: US Preventive Services TaskForce recommendation. JAMA. 2018;319(17):1791–7 [Crossref][PubMed] [Google Scholar]
28. RadiologyInfo. org. Ovarian cancer: Diagnosis,evaluation and treatment Internet. [Crossref][PubMed][Google Scholar]
29. Medscape. Malignant ovarian tumor imagingInternet. 2023 Jun 13. [Crossref] [PubMed][GoogleScholar]
30. Dana-Farber Cancer Institute. How we diagnoseovarian cancer Internet. [Crossref] [PubMed][GoogleScholar]
31. OCRA. How is ovarian cancer detected?Internet. [Crossref][PubMed][Google Scholar]
32. Mayo Clinic. CA 125 test Internet. 2025 Mar 7. [Crossref][PubMed][Google Scholar]
33. Cleveland Clinic. CA-125 blood test: Results. normal range & what to expect Internet. [Crossref][PubMed][Google Scholar]
34. HE4Test. Human Epididymis Protein 4. HE4Internet. [Crossref][PubMed][Google cholar]
35. Testing. com. Human Epididymis Protein 4 (HE4)Internet. 2020 Apr 24. [Crossref] [PubMed][GoogleScholar]
36. Cancer Treatment Centers of America. Ovarianbiopsy: Procedure. recovery & results Internet. [Crossref][PubMed][Google Scholar]
37. Cancer Research UK. Tests for ovarian cancerInternet. [Crossref][PubMed][Google cholar]
38. International Federation of Gynecology andObstetrics (FIGO). FIGO ovarian cancer stagingInternet. 2014 Jan 1. [Crossref] [PubMed][GoogleScholar]
39. Medscape. Ovarian cancer staging Internet.2024 Dec 14. [Crossref][PubMed][Google cholar]
40. Moffitt Cancer Center. Ovarian cancer survivalrate Internet. [Crossref][PubMed] [Google cholar]
41. Vergote I, et al. Neoadjuvant chemotherapy orprimary debulking surgery in advanced ovariancancer: A systematic review and meta-analysis. AnnOncol. 2010;21(7):1409–15. [Crossref][PubMed][Google Scholar]
42. Saint Luke's Health System. Ovarian cancer. Prognosis (your chances of recovery) Internet. [Crossref][PubMed][Google Scholar]
43. Ledermann JA, et al. Olaparib in platinum-sensitive relapsed serous ovarian cancer: A phase 2randomized trial. Lancet. 2014;383(9914):177–85. [Crossref][PubMed] [Google cholar]
44. Mayo Clinic Staff. Ovarian cancer – Diagnosis andtreatment [Internet]. Mayo Clinic; 2025 May 2. [Crossref][PubMed][Google Scholar]
45. Cancer Research UK. Types of surgery forovarian cancer Internet. [Crossref][PubMed] [GoogleScholar]
46. NCCN. Ovarian Cancer/Fallopian TubeCancer/ Primary Peritoneal Cancer GuidelinesInternet. [Crossref][PubMed][Google Scholar]
47. Vergote I, et al. Neoadjuvant chemotherapy orprimary debulking surgery in advanced ovariancancer: A systematic review and meta-analysis. AnnOncol. 2010;21(7):1409–15. [Crossref][PubMed][Google Scholar]
48. Pectasides D, et al. Fertility-sparing surgery inepithelial ovarian cancer. Gynecol Oncol.2008;111(1):161–7. [Crossref][PubMed] [GoogleScholar]
49. American Cancer Society. Chemotherapy forovarian cancer Internet. 2018 Apr 11. [Crossref][PubMed][Google Scholar]
50. Cancer Research UK. Chemotherapy for ovariancancer Internet. [Crossref][PubMed] [GoogleScholar]
51. Armstrong DK, Bundy B, Wenzel L, Huang HQ,Baergen R, Lele S, et al. Intraperitoneal cisplatinand paclitaxel in ovarian cancer. N Engl J Med.2006;354(1):34–43. [Crossref] [PubMed][GoogleScholar]
52. Walker JL, Brady MF, Wenzel L, Fleming GF,Huang HQ, DiSilvestro PA, et al. GOG 252:Carboplatin and paclitaxel with/ withoutbevacizumab and/or intraperitoneal chemotherapyin advanced ovarian cancer. J Clin Oncol.2019;37(29):2662–73. [Crossref] [PubMed][GoogleScholar]
53. American Cancer Society. Targeted drug therapyfor ovarian cancer Internet. 2022 Nov 17. [Crossref][PubMed][Google Scholar]

54. Lord CJ, Ashworth A. PARP inhibitors: Syntheticlethality in the clinic. Science.2017;355(6330):1152–8. [Crossref] [PubMed][Google Scholar]

55. Mirza MR, Monk BJ, Herrstedt J, Oza AM,Mahner S, Redondo A, et al. Niraparib in platinum-sensitive recurrent ovarian cancer. N Engl J Med.2016;375(22):2154–64. [Crossref] [PubMed][GoogleScholar]

56. Ferrara N, Gerber HP, LeCouter J. The biology ofVEGF and its receptors. Nat Med. 2004;10(10):107–13. [Crossref][PubMed] [Google Scholar]

57. Perren TJ, Swart AM, Pfisterer J, Ledermann JA,Pujade-Lauraine E, Kristensen G, et al. A phase 3trial of bevacizumab in ovarian cancer. N Engl J Med.2011;365(26):2484–96. [Crossref][PubMed][GoogleScholar]

58. American Cancer Society. Hormone therapy forovarian cancer Internet. 2018 Apr 11. [Crossref][PubMed][Google Scholar]

59. Ovarian Cancer Action. Hormone treatment forovarian cancer Internet. [Crossref][PubMed] [GoogleScholar]

60. Cancer Research Institute. Ovarian cancer – Immunotherapy Internet. [Crossref][PubMed] [Google Scholar]

61. Moffitt Cancer Center. Ovarian cancerimmunotherapy Internet. [Crossref] [PubMed][Google Scholar]

62. National Consensus Project for Quality PalliativeCare. Clinical practice guidelines for qualitypalliative care. 4th ed. Internet. 2018 [Crossref][PubMed][Google Scholar]

63. Nature. Immunotherapy for ovarian cancer:Towards a tailored approach Internet. 2024 Sep 4. [Crossref][PubMed][Google Scholar]

64. National Center for Biotechnology Information. Recent progress in gene therapy for ovarian cancerInternet. 2018 Aug 2. [Crossref] [PubMed][GoogleScholar]