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A review on clinical management strategies and treatment modalities of epithelial ovarian cancer - current scenario and future perspectives

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Abstract
Ovarian cancer is a dangerous condition that is typified by aberrant cell development in the ovaries. It is difficult to diagnose in its early stages since the illness frequently exhibits mild or vague symptoms. Ovarian cancer, one of the deadliest gynecological cancers, is usually detected at an advanced stage, making treatment more difficult and decreasing overall survival chances. The development of ovarian cancer is influenced by a number of variables, including hormones, reproductive history, and genetic predisposition. In this study, we discuss about the thorough risk assessment and screening methods. Interacting with the course material offers priceless insights into the intricacies of managing ovarian cancer. Participants gain expertise in identifying risk factors, identifying early symptoms and indicators, and successfully navigating the diagnostic and therapeutic paths. Furthermore, working with an interprofessional team improves patient outcomes by encouraging smooth coordination and communication between specialties. A holistic approach to care is assured by utilizing the combined experience of several healthcare specialists, who then customize treatment strategies to match the specific needs of each patient. By working together, we can maximize treatment results, enhance patients' quality of life, and give them more strength in the fight against ovarian cancer.

Keywords: Epithelial ovarian cancer, obesity, dyspareunia, gynaecological cancer

Introduction
Both epithelial and nonepithelial ovarian cancers are classified as ovarian cancers. More than 95% of ovarian cancer cases are of the epithelial type, with the remaining 5% being nonepithelial malignancies (Such as germ cell, sex-cord stromal and small cell ovarian cancers) [1]. Histologic categorization is used to categorise epithelial ovarian cancers into subtypes. These subtypes include high-grade serous, low-grade serous, clear cell, endometrioid and mucinous ovarian cancer. Depending on the subtype, there might be differences in diagnostic evaluation, treatment, and patient outcomes. According to the Centres for Disease Control and Prevention, ovarian cancer is the second most frequent gynaecologic malignancy in the United States and the primary cause of death among women with gynaecological cancer diagnoses. Globally, ovarian cancer is the third most prevalent kind of gynaecologic cancer [2]. In addition, ovarian cancer ranks ninth globally and fifth in the US among all cancers that claim the deaths of women [3-5]. The paucity of preventative screening techniques and the vague clinical indications of ovarian cancer, which result in a delayed diagnosis (The majority of patients are diagnosed with advanced-stage illness), are most likely to blame for the disease's high death rate [1]. The most important risk factor for ovarian cancer is advanced age, which is more common in postmenopausal women [6]. An ovarian cancer diagnosis is histologically verified. The evaluation of any ovarian mass largely comprises of clinical assessment, imaging examinations, and tumour markers to determine a patient's risk factors for malignancy and characterize the mass [7-9]. The patient's characteristics (Such as comorbidities and prior treatments), the tumor's stage and its histology all influence the treatment strategies. At the moment, systemic chemotherapy and surgical debulking are usually advised, either in conjunction with or apart from targeted treatments. Antiangiogenic bevacizumab, poly adenosine diphosphate (ADP)-ribose polymerase (PARP) inhibitors and immunotherapy are examples of targeted treatment.

Furthermore, new approaches to the management of ovarian cancer include hot intraperitoneal chemotherapy, interval surgical debulking, and neoadjuvant therapy [10, 11]. A high recurrence rate and mortality rate persist despite advancements in ovarian cancer treatment, highlighting the need for interprofessional management, effective prevention and detection strategies and novel treatment modalities founded on a deeper comprehension of the molecular features of ovarian cancer.

Etiology

1. **Ovarian Cancer Risk Factors:** Although the exact cause of ovarian cancer is unknown, a number of risk factors have been found to raise the likelihood of developing the disease. The following are risk factors for ovarian cancer: Advanced age, early onset of menarche, late onset of menopause, Family history, Nulliparity, Obesity, Perineal talc use, Smoking, Endometriosis, Hormone replacement therapy [6, 12]. Ovarian cancer risk is higher in those who have lifelong factors (Such as nulliparity, early menarche, or late menopause) that promote ovulation [13]. The precise etiologic process is unknown. Furthermore, oxidative stress and deoxyribonucleic acid damage are considered to be the secondary causes of ovarian cancer in inflammatory diseases such as obesity and endometriosis [14, 15]. A positive personal or family history of breast or ovarian cancer is a substantial risk factor for ovarian cancer. One common underlying reason of an individual's propensity to cancer is germline mutations in the BRCA1 or BRCA2 genes. Other hereditary cancer syndromes, such as Lynch syndrome, Li-Fraumeni syndrome, Peutz-Jeghers syndrome, CHEK2, RAD51, BRIP1, and PALB2, are linked to other gene mutations that also raise the risk of ovarian cancer. These diseases also include mismatch repair genes [16]. Recent findings indicate that alterations in the distal epithelium of fallopian serous tubal intraepithelial carcinoma, an HGSC precursor may be the source of high-grade serous ovarian cancer (HGSC) [17, 18]. Although studies have not shown that suggested ovarian cancer screening procedures are helpful, many organizations concur that it is reasonable to provide these high-risk people with a variety of screening options [7, 17].
2. **Ovarian Cancer Protective Factors:** A lower risk of ovarian cancer is linked to factors that inhibit ovulation, such as: Oral contraceptives, bilateral tubal ligation or salpingectomy, Breastfeeding, Multiparity [12, 19].

Epidemiology

According to study findings, a woman's lifetime chance of acquiring ovarian cancer up to the age of 95 years is only 1.1% [7]. In the United States, there were an anticipated 19000 new cases of ovarian cancer identified in 2022 and over 12000 people died from ovarian cancer. In addition age affects the incidence of different subtypes of ovarian cancer. Women between the ages of 45-50 years have the highest incidence of low-grade endometroid ovarian cancer, whereas women between the ages of 60-65 years have the highest incidence of high-grade serous ovarian cancer. Women between the ages of 55-60 years are most likely to develop clear-cell ovarian malignancies [3]. Asian/Pacific Islander women had a greater incidence of clear cell cancer, while non-Hispanic White women have the highest prevalence of high-grade serous and low-grade endometrioid tumours. All ovarian cancer subtypes had the lowest incidence in non-Hispanic Black women [3]. The stage of diagnosis also affects survival and recurrence rates. At the time of diagnosis, metastases are present in more than half of ovarian cancer patients. Early-stage ovarian cancer has a 5-year survival rate of 93.1%, whereas advanced-stage illness has a 5-year survival rate of 30.8%. Less than 10% of women with stage I ovarian cancer will experience a recurrence, whereas 90% of women with stage IV ovarian cancer will experience a recurrence [7].

Pathophysiology

1. **Ovarian Cancer Dissemination Pattern:** The physiologic lymphatic drainage of the ovaries and fallopian tube usually leads to the para-aortic and paracaval nodes as well as the external iliac, common iliac, hypogastric, and lateral sacral lymph nodes, which are the primary sites of regional lymphatic dissemination for ovarian cancer. The peritoneum comprising the omentum and visceral surfaces is the most often affected region for distal ovarian and fallopian metastases. Diaphragmatic lymphatic veins drain in this area. There is minimal evidence of a more significant haematogenous contribution, although other than in advanced-stage illness, haematogenous spread is considered to have a limited role [20]. Additionally, the findings of several researches have shown that precancerous lesions in the fallopian tube such as tubal intraepithelial neoplasia and endosalpingiosis may be the source of both high-grade and low-grade serous ovarian malignancies. The involvement of the fallopian tube in ovarian cancer staging can manifest as a tubal intraepithelial carcinoma detected histologically during risk-reducing surgery a widespread malignancy involving an ovarian and fallopian tube neoplasm, or a fallopian tube mass within the lumen that is histologically confirmed as such [21]. As a result, it might be challenging to determine with certainty if the main tumour has an ovarian, fallopian, or peritoneal origin. Tumour involvement in each of these locations is thus taken into account during staging by the International Federation of Gynaecology and Obstetrics [22].
2. **Pathophysiologic Mechanisms of Epithelial Ovarian Cancer:** Ovarian cancer has unclear etiological origins, which makes it difficult to pinpoint the precise pathophysiologic pathways that produce the illness. Genetic mutation is a recognized mechanism. DNA mutations that happen either before (Germline) or after (Somatic) fertilization might result in malignant cellular transformation. TP53 is the principal somatic mutation responsible for ovarian cancer and is frequently seen in high-grade serous carcinomas. Since the TP53 gene is also present in healthy ovarian tissue, it is not utilized as a tumour diagnostic for ovarian cancer. CSMD3, FAT3, BRCA1, BRCA2, PTEN, PIK3CA, KRAS, BRAF, CTNNB1, and PPP2R1A are somatic mutations that are less common [23]. Ovarian cancer has been linked to inherited mutations in the DNA of BRCA1 and BRCA2, ATM, BRIP1, NBN, NF1, PALB2, RAD51C, and RAD51D. Lynch syndrome, or hereditary nonpolyposis colorectal cancer is linked to

mismatch repair mutations in the MLH1, MSH2, MSH6, PMS2, and EPCAM genes, which raise the risk of ovarian cancer. Peutz-Jeghers syndrome with STK11 mutations and Cowden syndrome with a PTEN mutation are two further hereditary diseases linked to ovarian cancer [18]. The development of ovarian cancer and other malignancies is linked to epigenetic changes in gene control mechanisms such as DNA methylation, that impact genetic expression. Though their use as a tumour marker is still being investigated the results of a recent study demonstrated evidence of epigenetic methylation changes in women with early-stage ovarian malignancies [23].

Histopathology

Histological confirmation confirms the diagnosis of ovarian cancer [9]. Histologic categorisation is usually used to categorise epithelial ovarian cancers since different subtypes have different clinical behaviour, therapy and prognosis. Molecular researches, immuno-histochemical markers and cytology analysis are all included in classification. High-grade serous, low-grade serous, clear cell, endometrioid, and mucinous ovarian disease are the main categories for ovarian cancer subtypes [24]. Previously transitional cell ovarian carcinomas were also identified as a separate histologic category; however, a number of investigations revealed similarities between these tumours and high-grade serous ovarian cancer. Ovarian tumours with transitional cells are therefore categorized as belonging to the high-grade serous histologic category [25]. Rare histologic ovarian cancer subtypes include carcinosarcomas, malignant Brenner tumors and undifferentiated carcinomas [24, 25]. Furthermore, the histologic architecture of non-serious epithelial ovarian malignancies is used to grade the tumours. On the other hand, tumour biology is the basis for grading serous carcinoma [21]. The grading system for nonserous epithelial ovarian cancer uses the following classification - GX: Unable to assess grade, G1: Well differentiated, G2: Moderately differentiated, G3: Poorly differentiated [21].

1. **Immunohistochemical Classification of Epithelial Ovarian Cancers:** The histological subtypes of ovarian cancer can be distinguished with the use of immunohistochemical staining. WT_1 immunohistochemical marker distinguishes clear-cell and a mucinous subtype from high-grade and low-grade serous tumours as WT_1 is not present in these tumour types. Low-grade tumours can be distinguished from high-grade serous tumours using the p53 aberrant (p53abn) marker. While 10% to 15% of endometrioid tumours may be positive for both WT_1 and p53abn markers, the majority of endometrioid subtypes are negative for WT_1 and positive for p53 wild-type. In these situations, it is possible to do molecular tests for mismatch repair deficit (MMRd) in endometrioid tumours and homologous repair deficiency (BRCA1 and BRCA2 in high-grade serous tumours). Positive napsin A and HNF1B immunohistochemical stains together with negative progesterone receptor staining are commonly observed in clear cell tumours; endometrioid tumours are characterised by the opposite pattern of results. Mucinous ovarian carcinomas are often identified using a combination of progesterone receptor negative and napsin A negative stains. An endometrioid neoplasm is indicated by any vimentin staining. Other immunohistochemical markers such as undifferentiated carcinomas which are recognised by the absence of ARID1B, BRG1 or INI1 staining that may be used to identify rare subtypes of ovarian cancer. Histologic evaluation of serous tubal intraepithelial carcinoma reveals the presence of p53 and Ki-67 markers [6, 23, 24].
2. **High-Grade Ovarian Serous Cancer Histologic Characteristics:** The most prevalent kind of ovarian cancer is high-grade serous carcinoma [6]. Characteristic histologic features of high-grade serous carcinoma include architectural papillary and solid development, considerable nuclear atypia, hyperchromatic nucleoli and enhanced mitotic activity (Greater than 12 per 10 high-powered fields) [1]. TP53 mutation is shown by molecular testing in 96% of high-grade serous subtypes. High copy number changes and germline mutations in BRCA1 or BRCA2 are further results from molecular research [6].
3. **Low-Grade Ovarian Serous Cancer Histologic Characteristics:** Roughly 10% of ovarian epithelial tumours are low-grade serous subtypes. They are usually distinguished from high-grade serous carcinomas by the opposite cytologic characteristics such as tiny papillae with homogeneous nuclei and little mitotic activity. Psammoma bodies and hyalinised stroma are also commonly detected. Low-grade serous ovarian tumours frequently exhibit BRAF and KRAS mutations according to molecular testing results [6].
4. **Endometrioid ovarian cancer histologic characteristics:** Only 10% ovarian epithelial malignancies have endometrioid subtypes. These tumours resemble uterine endometrioid carcinoma in histology exhibiting cribriform, villous or rounded or back-to-back glands. Molecular research has revealed the presence of mutations in CTNNB1, PIK3CA, ARID1A, KRAS, PTEN, and PPP2R1A [6]. Furthermore, the molecular subtypes that are used to define endometrial cancer: POLE mutant, MMRd, no distinctive molecular profile, and p53abn which are also present in endometrioid ovarian malignancies and can be used in a similar manner to assess prognosis [24].
5. **Clear-Cell ovarian cancer histologic characteristics:** Less than 5% of ovarian carcinomas are clear-cell carcinomas which are less common. Histopathologically, they may exhibit solid regions, tubules and complicated papillae with cellular clearance a growth pattern resembling a cyst, and a growth pattern like a hobnail. In molecular investigations mutations usually affect TP53 or both ARID1A and PIK3CA [6].
6. **Mucinous ovarian cancer histologic characteristics:** Mucinous subtypes account for 2.4% of epithelial ovarian cancer cases. Given that 80% of mucinous ovarian carcinomas are detected at an earlier stage, usually stage I, this subtype often has a better prognosis than serous ovarian malignancies. Mucinous ovarian carcinomas are frequently heterogeneous, meaning that a single specimen may contain both benign and malignant tumours. Given that complicated glandular cytology and architectural characteristics of an adenocarcinoma are frequently observed on histologic inspection. This subtype of ovarian cancer is comparable to gastrointestinal tract malignancies. Stem

cell invasion varies in intensity [26]. Many gynaecologic oncologists perform regular appendectomy in patients with ovarian mucinous carcinomas because it is challenging to differentiate between original ovarian mucinous carcinomas and metastatic mucinous appendix tumours due to their close connection [27]. The most common molecular changes found in mucinous ovarian cancer subtypes are KRAS mutations. In molecular research for this subtype additional gene alterations including as HER2, CDKN2A and TP53 are less commonly discovered [1, 24].

Clinical Presentation

1. **Clinical History:** Sometimes in asymptomatic patients, epithelial ovarian cancers can be incidentally discovered; however, most patients present with nonspecific symptoms such as weight loss, abdominal fullness, bloating, nausea, abdominal distention, early satiety, fatigue, change in bowel movements, urinary symptoms, back pain and dyspareunia [26]. It is uncommon for abnormal uterine bleeding to be a sign of ovarian cancer [22]. In addition early-stage illness is usually mild or asymptomatic and is easily overlooked. As a result, early detection of ovarian cancer symptoms is usually difficult since they might be mistaken for signs of other potential disease processes. A complete clinical history including a patient's personal and family medical history, a review of symptoms, and an estimate of their genetic cancer risk, should be collected since controlling adnexal tumours entails risk classification [18, 27].
2. **Physical Examination:** To search for pelvic and abdominal masses, a comprehensive physical examination should be performed, which includes pulmonary auscultation, breast and abdominal palpation, and rectovaginal examination on an empty bladder. It is recommended to palpate the cervical, supraclavicular, axillary and groin lymph nodes. Along with a bimanual examination, the pelvic examination should include a visual inspection of the vagina, cervix, and perineum. Any hard, nodular, irregular or fixed masses or ascites should be investigated further with imaging examinations [7]. In more severe instances, there may also be a palpable pelvic mass, ascites, or reduced breath sounds as a result of pleural effusions. A solid umbilical or paraumbilical nodule also known as the Sister Mary Joseph nodule is seldom ever perceptible as a result of metastasis. The Lesar-Trelat sign which is defined as an abrupt rise in seborrhoeic keratosis cases also provides a clinical hint suggesting the possibility of concealed malignancy [28]. Ovarian cancer and paraneoplastic disorders are not always linked. Symptoms such as ataxia, dysarthria, nystagmus, vertigo and diplopia might result from subacute cerebellar degeneration caused by tumor-induced immunological reactivity against cerebellar antigens. This illness frequently manifests months or years before the main ovarian tumour does. Ovarian cancer has also been linked to Trousseau syndrome. Hypercalcemia can be brought on by elevated amounts of parathyroid hormone-releasing protein in the blood which can cause symptoms including altered mental state, exhaustion, constipation, stomach discomfort, increased thirst, and frequent urination. To prevent the diagnosis of ovarian cancer at an advanced stage where the patient might not be receptive to curative therapy, such early warning symptoms of different paraneoplastic syndromes should be taken into consideration well in advance [28, 29].

Assessment Procedures

Laboratory investigations and biomarkers: Typically serum laboratory tests should include a metabolic profile and complete blood count [7]. According to guidelines from the American Society of Clinical Oncology, all women with epithelial ovarian cancer should be provided genetic testing for BRCA1 and BRCA2, and patients with clear cell, endometrioid, or mucinous ovarian cancer subtypes should be offered MMRd molecular testing [30]. When measuring tumour markers in individuals who may have cancer, imaging investigations are typically conducted in addition to the tests. To assist rule out gastrointestinal and germ-cell cancers, human gonadotropin, alpha-fetoprotein, and carcinoembryonic antigen tumour markers should be acquired [22]. Glycoprotein generated by Mullerian epithelium, cancer antigen 125 (CA-125) is the most suggested biomarker to assess cases of probable ovarian cancer and may be found by serum laboratory investigations. The sensitivity of this biomarker is constrained since CA-125 levels are raised in the majority of instances of advanced epithelial ovarian cancer but are only up in 50% of cases of early-stage illness. Postmenopausal women had better positive predictive value and specificity than premenopausal women. An elevated risk of cancer is indicated in postmenopausal women with a CA-125 level higher than 35 U/mL. But CA-125 is not exclusive to epithelial ovarian tumours; individuals with pregnancy, nonovarian malignancies, and inflammatory pathologies (Such as acute pelvic inflammatory disease, adenomyosis, and endometriosis) can also have increased levels of this marker [9]. The epididymal epithelium contains a peptide protease inhibitor called human epididymis protein 4 (HE4). HE4 is not normally present in ovarian epithelium but it may be identified with 96% specificity in serum laboratory tests of ovarian cancer tissue. However, as HE4 is also high in other cancers (Such as endometrial cancer and lung adenocarcinomas) this biomarker cannot be used to diagnose ovarian cancer. When it comes to early-stage ovarian tumours, HE4 is more sensitive than CA-125, and when it comes to late-stage illness, it is more specific. But compared to HE4, CA-125 is more sensitive to late-stage ovarian tumours [9]. There are several diagnostic algorithms that estimate the risk of epithelial ovarian cancer by using tumour markers. To determine the risk of malignancy index (RMI), CA-125 values are employed. The RMI is a multiple of menopausal state, transvaginal ultrasound characteristics, and CA-125 to assess the likelihood that an adnexal tumour is an ovarian cancer [28]. With a specificity of greater than 96%, an RMI higher than 200 is linked to an increased risk of cancer, especially in postmenopausal women [28]. To calculate the risk of malignancy, the risk of ovarian malignancy algorithm (ROMA) uses a mathematical formula that takes into account the levels of HE4 and CA-125 after adjusting for premenopausal and postmenopausal status [31]. However, these algorithms are less accurate in predicting the malignancy of an adnexal mass than risk classification methods based on imaging data [9]. Other indicators under investigation are glycodelin, transthyretin,

CA15-3, folate receptor alpha, and CA72-4. The most useful and widely used tumour marker for assessing the risk of ovarian cancer is still CA-125. However when paired with CA-125, these other tumour markers could be more useful [9].

Transvaginal Imaging: Because transvaginal ultrasonography can show characteristics that distinguish benign from malignant illness; which is the first imaging modality of choice for characterising an adnexal tumour. Papillary or solid components, irregularity, ascites, and high-color Doppler flow are findings that are consistent with ovarian cancer. But 20% of individuals with an adnexal mass have unclear results; in these cases, further imaging is advised, usually via magnetic resonance imaging (MRI) [7, 32]. It might be difficult to determine whether an adnexal lump is cancerous. While a missed cancer diagnosis may result in higher patient morbidity and death, overdiagnosing an ovarian tumour can lead to needless procedures and psychological trauma. Based on ultrasound results, the Ovarian-Adnexal Reporting and Data System (O-RADS) ultrasound risk classification system assists doctors in managing average-risk patients, particularly when referral to an oncology expert is warranted [32, 33]. Based on recognised criteria, O-RADS stratifies adnexal masses into the following categories:

Table 1: Ovarian-Adnexal Reporting and Data System (O-RADS) Ultrasound Risk Classification

O-RADS 0	This type of transvaginal ultrasonography is used when the visualisation is poor because of technical issues (e.g., intestinal gas, adnexa, or patient intolerance). Generally, one should either use other imaging modalities or repeat an ultrasound [33].
O-RADS 1	O-RADS 1 classification is given to physiological adnexal lesions (Such as corpus luteums and follicles) that show no aberrant findings; this classification is limited to premenopausal individuals. Given the 0% chance of cancer associated with these lesions, no further treatment or imaging follow-up is necessary [33].
O-RADS 2	The masses in this group are probably benign with a risk of cancer of less than 1%. Lesions in this group are characterised by smooth walls and internal echos in the case of simple cysts or unilocular cysts that are less than 10 cm. This group also includes normal hemorrhagic cysts, dermoid cysts, hydrosalpinx of any size without any worrisome signs, endometriomas less than 10 cm or paraovarian cysts, peritoneal inclusion cysts, and endometriomas more than 10 cm. Clinical characteristics, such as lesion size, kind, and patient's menopausal state, determine the specific care (e.g., expert consultation, further imaging testing, or ongoing surveillance) [33].
O-RADS 3	This type of adenexal lesions carries a 1% to less than 10% risk of cancer. Lesions that fall under O-RADS 2 (such as simple cysts and unilocular cysts) but have a size of 10 cm or more are categorised as O-RADS 3. This group also includes avascular solid-appearing masses of any size, multilocular cysts without a solid component less than 10 cm and absent to mild colour Doppler flow, and unilocular cysts with uneven walls. Typically, a gynaecology clinician is involved in the care of lesions falling under this group. Clinical suspicion may warrant the consideration of an MRI test [33].
O-RADS 4	The probability of cancer in this group ranges from 10% to less than 50%. Consultation with a gynaecologic oncologist for care should be explored due to unclear risk factors, taking into account menopausal state, other MRI abnormalities, and serum tumour markers (e.g., CA-125). The following characteristics classify lesions in this group: Multilocular cysts that are larger than or equal to 10 cm Multilocular cysts with an irregular inner wall or septal irregularity (Less than 3 mm in height) Unilocular and multilocular cysts with a solid component or significant color Doppler flow of any size Unilocular cysts with 1 to 3 papillary projections of any size or color Doppler flow Smooth solid lesions with mild to moderate color Doppler flow [33].
O-RADS 5	The high-risk group of adnexal lesions carries a 50% or higher chance of cancer. For treatment, physicians ought to send these patients right away to a gynaecologic oncologist. The following characteristics classify lesions in this group: Irregular solid lesions of any size or color Doppler flow Smooth solid lesions of any size with high-color Doppler flow Unilocular cysts with 4 papillary projections or more of any size or color Doppler flow Multilocular cysts of any size with a solid component and high-color Doppler flow Ascites or peritoneal nodules except when associated with physiologic cysts or a benign lesion (ie, O-RADS 2) [33].

Magnetic Resonance Imaging: According to ultrasonography, up to 31% of adnexal masses are classified as having an unknown risk. Because MRI has a high sensitivity for diagnosing cancers, it may be useful in further characterizing an adnexal tumour in individuals with equivocal transvaginal ultrasound findings or a CA-125 within normal range [34]. The Ovarian-Adnexal Reporting Data System Magnetic Resonance Imaging (O-RADS MRI) also known as the AdnexMR Scoring system divides the malignancy risk of an adnexal mass into 5 groups based on MRI findings, much like the ultrasound O-RADS stratification approach. The primary goal of this stratification is to assist in guiding preoperative choices such as the necessity and amount of surgery; however, studies are now being conducted to determine treatment guidelines for each risk category [32, 35, 36]. Precontrast axial T_1-weighted and T_2-weighted images with and without fat suppression, dynamic sequence postcontrast T_1-weighted images, and perfusion and diffusion-weighted sequences are the recommended MRI techniques. If an adnexal mass was visualized with T_1-weighted and T_2-weighted images, these sequences should be performed first. For both the T_2-weighted and contrast-enhanced T_1-weighted pictures, a slice thickness of less than or equal to 3 mm is advised [32, 35]. Adnexal masses are stratified into the following groups by O-RADS MRI according to certain criteria [32]:

Table 2: Ovarian-Adnexal Reporting and Data System for Magnetic Resonance Imaging (O-RADS MRI)

AdnexMR 1	No adnexal lesion is visualized
AdnexMR 2	These lesions' features are thought to be benign. Certain defined characteristics of this group include solid tissue or solid masses with a low homogeneous signal on the T_2-weighted and the high b-value diffusion-weighted images, or exclusively adnexal cystic, endometriotic or fatty masses without wall enhancement.
AdnexMR 3	Mostly these lesions are benign. Unilocular cysts with an uneven augmenting wall and multilocular cysts containing simple, proteinaceous, hemorrhagic or endometriotic fluid which apart from merely cystic, endometriotic and fatty masses are characteristic traits. This category also includes dynamic perfusion time-intensity curve type 1 solid masses.
AdnexMR 4	The likelihood of these lesions developing into malignancies is unknown. This group is defined by solid masses with type 2 dynamic perfusion time-intensity curves.
AdnexMR 5	This type of masses carries a high risk of cancer. These lesions are characterised by solid masses, peritoneal implants, omental thickening or nodules as well as dynamic perfusion time-intensity curve type 3 [35].

Computed Tomography Imaging: MRIs are usually preceded by computed tomography (CT) scans, which are used to assess differential diagnosis in patients exhibiting vague symptoms. However, because MRI is more successful in visualising ovarian cancers than ultrasonography, it is advised as a second-line modality after ultrasound. However, because CT imaging of the belly, pelvis, and thorax is more widely available, it is frequently used for preoperative planning and to assess the degree of illness [37]. For example, in certain cases, substantial involvement of lymph nodes may rule out surgery. Since PET-CT is a more useful modality than CT alone for assessing lymph node and peritoneal metastases as well as recurrent illness, it may be taken into consideration to establish lymph node involvement [38].

Management Strategies and Treatment Modalities

Approach to Epithelial Ovarian Cancer Management: The majority of patients are discovered at an advanced stage, despite the fact that 90% of women with early-stage illness of any grade can be cured with therapy. This emphasises the need for early identification and specialised care. Based on tumour stage, biology, prior treatment and associated illnesses; each patient's optimal management strategy including the order of surgical and systemic therapy is customised. For most patients with epithelial ovarian cancer, surgical therapy is the first course of treatment in order to facilitate staging, histologic confirmation, and tumour debulking, all of which will aid in the direction of adjunct therapies. Before having surgical cytoreduction, certain patients with advanced-stage illness who are unlikely to be entirely resected or who are not treatable may benefit from neoadjuvant chemotherapy. Surgical staging with uterine preservation may be taken into consideration for younger women with stage I and low-grade ovarian malignancies that choose to have surgery that preserves their fertility. As a result, when treating ovarian cancer, physicians must take into account a number of management strategies [1, 37].

Staging and Primary Debulking Surgery: The tumour, node, metastasis (TNM) grading system and the FIGO are used in surgical staging of ovarian cancer. Research indicates that in patients with excellent surgical staging, chemotherapy is more beneficial and enhances overall prognosis. The significance of primary surgical staging and debulking for patient outcomes dictates that the surgery should be carried out by a skilled gynaecologic oncologist in a facility equipped with the required tools. A midline laparotomy with abdominal and pelvic exploration, ascites or peritoneal washing collection, bilateral salpingo-oophorectomy, assessment of the pelvic and paraaortic lymph nodes, peritoneal biopsy, and omentectomy are commonly included in surgical staging. In order to minimise tumour burden, optimal surgical debulking resects all grossly visible disease, especially in subtypes of epithelial ovarian cancer that are less susceptible to chemotherapy (Such as low-grade serous, clear cell, and mucinous carcinoma) [1]. If total resection is not feasible for patients with stage III disease or above, cytoreduction to less than 1 cm should be carried out; more complicated operations, such as upper abdominal exploration and bowel and diaphragm resection, may also be necessary. The American Society of Clinical Oncology (ASCO) advises against routine pelvic and paraaortic lymphadenectomy; however larger lymph nodes should be removed. For high-grade illness, certain professional groups do advise systematic pelvic and paraaortic lymphadenectomy [1, 37, 39]. Reproductive-sparing surgical therapy may be explored for women whose ovarian malignancies appear to be low-risk and early-stage and who prefer to maintain their reproductive possibilities. For preoperative consultation, clinicians ought to send these individuals to a reproductive endocrinologist. The National Comprehensive Cancer Network (NCCN) indicates that fertility-sparing adjustments to normal debulking surgery can involve retention of the uterus and contralateral ovary and fallopian tube or exclusively maintaining the uterus, depending on tumor stage and histology. However, surgical staging techniques should still be conducted to exclude occult illness. The risks of recurrent ovarian cancer should be extensively discussed with every patient who may be contemplating fertility-sparing surgery. Surgery to preserve fertility is not advised for any patient with clear-cell ovarian cancer regardless of stage according to the NCCN recommendations [37, 40].

Neoadjuvant Chemotherapy and Interval Debulking Surgery: Patients who have a low chance of optimal cytoreduction may get neoadjuvant chemotherapy and then interval debulking surgery. In order to maximise the chance of optimum cytoreduction, gynaecologic oncologists should assess patients with suspected advanced stage IIIC or IV epithelial ovarian cancer to see if neoadjuvant chemotherapy might be useful in decompressing the tumour burden [1, 37]. Before giving neoadjuvant chemotherapy, patients should have a histological diagnosis of invasive ovarian cancer verified by biopsy, preferable above specimens acquired from fine-needle aspiration of paracentesis [41]. Neoadjuvant chemotherapy combined with interval cytoreduction surgery has been compared to primary cytoreductive surgery in a number of clinical studies. According to these trials, individuals who received neoadjuvant chemotherapy and those who had primary cytoreduction had similar overall survival rates. Neoadjuvant treatment may lessen problems

such as the need for bowel resection and the development of stomas [42]. The best course of treatment is still being explored by more trials. Therefore, while deciding on the best course of action, interprofessional consultation including gynaecologic oncologists should individualise treatment options depending on clinical variables [6, 43]. When a patient receives neoadjuvant chemotherapy, the tumour is reevaluated using imaging to see if it may be surgically removed after three to four chemotherapy rounds [6, 43]. Studies have not shown that interval debulking surgery improves survival when tumour progression is seen after neoadjuvant treatment. For these individuals, enrolment in clinical trials or stopping therapy and starting end-of-life care may be taken into consideration [37].

Adjuvant Chemotherapy: Adjuvant chemotherapy choices should be based on surgical staging after primary debulking surgery as surgical staging may modify the disease's characterization after surgery, potentially upstaging individuals who were previously considered to have early-stage cancer. Recurrence risk is highest for stage I grade 3, clear cell, high-grade, and IC and II ovarian cancers; lowest for endometrioid, serous, or mucinous ovarian tumours in stages IA or IB grade 1. Adjuvant chemotherapy does not increase overall survival in low-grade early-stage illness. Adjuvant chemotherapy is therefore beneficial for high-risk early-stage disease, even though optimal primary cytoreduction alone may be able to treat low-risk early-stage ovarian cancers. In addition, if additional surgery is not possible, adjuvant chemotherapy should also be given for stage I ovarian cancers that are inadequately staged or suboptimally resected. The most often utilized agents are paclitaxel and carboplatin; however there are no set guidelines for the agents, dose, or duration. Chemotherapy regimens for advanced-stage cancer are tailored based on the degree of remaining disease, including the manner of delivery.

Hormone Therapy: Hormonal treatment appears to be beneficial in treating individuals with low-grade serous ovarian cancer who have both recurrence and metastases. Patient's progression-free survival was much longer in those who got adjuvant hormone treatment after primary debulking surgery and platinum-based chemotherapy than in those who were just monitored according to a research. Other research meantime, has not demonstrated a discernible distinction between adjuvant hormonal therapy and other forms of care [21]. When treating ovarian tumours that have oestrogen or progesterone receptors, some specialists advise adjuvant medication (Such as aromatase inhibitors, tamoxifen, or luteinizing hormone-releasing hormone agonists) to assist slow the tumor's pace of development [39].

Maintenance Therapy: In individuals with stage I illness, NCCN guidelines advocate observation with ongoing surveillance. But within five years, there is a significant chance of ovarian cancer recurrence for patients with stage II to IV of the illness. Because of this, maintenance therapy is widely used to lower the risk of recurrence by guaranteeing the efficient death of remaining slowly dividing cells by slowing down the turnover of cells. This prevents the dormant population of cancer cells from growing to the point where they are identified by either an increase in biomarkers or clinical evidence of recurrent disease [45]. Targeted treatments are a developing option for treating ovarian cancer among other maintenance therapy alternatives. Targeted therapy was first applied to treat ovarian cancer that returned. More recently, research has shown that targeted molecular treatments used in maintenance treatment, particularly in individuals with high-risk cancer are effective in enhancing progression-free survival in patients who responded well to adjuvant chemotherapy. The most researched targeted therapeutic medicines include PARP inhibitors and anti-angiogenic medications [43, 46]. The efficacy of different medicines has been compared in a number of randomized controlled treatment trials. The majority of recommendations for maintenance therapy based on current research include considerations for the disease stage, the initial systemic medication employed, the tumour response and the status of BRCA1 and BRCA2 mutations. Maintenance treatment options include of the following:

Table 3: Overview of Maintenance Therapy Options for Ovarian Cancer

Platinum-based chemotherapy agents	Clinical judgement historically drove the choice to start maintenance therapy in patients who had a strong response to initial cytoreduction and chemotherapy, since data from many trials indicated increased toxicity with no discernible enhanced overall survival with its usage. GOG-178, a phase 3 randomized study, assessed patients with stage III to IV ovarian cancer and compared the effects of 12 months against 3 months of paclitaxel maintenance treatment after a full clinical response to platinum/paclitaxel therapy. Following a 50% accrual interval analysis, the prolonged treatment cohort showed better progression-free survival. When compared to the same maintenance monotherapy for 22 months as opposed to 14 months, a further follow-up research revealed no overall survival advantage. When high-risk early-stage ovarian cancer patients were randomized to observational versus weekly paclitaxel 40 mg/m² for 24 weeks following the completion of 6 cycles of carboplatin and paclitaxel for 3 cycles, another trial, GOG-175, revealed no significant difference in 5-year survival or recurrence-free interval [47, 48]. GOG-0212, a 3-arm phase 3 study conducted after conventional chemotherapy, compared observation without treatment to 12 months of paclitaxel or polyglutamated paclitaxel, although the findings were underwhelming [49]. As a result, less toxic targeted treatments have taken the place of chemotherapy as medicines for maintenance therapy.
Anti-angiogenic inhibitors	Agents that target the pathways of tumorous vascular development are known as angiogenesis inhibitors. Bevacizumab, the first anti-angiogenic drug authorised in the US, is a humanised monoclonal antibody that inhibits vascular endothelial growth factor (VEGF). It has been tested in conjunction with chemotherapy [43, 46]. Patients with advanced-stage ovarian cancer demonstrated better progression-free survival in the maintenance bevacizumab cohort in 2 significant landmark studies (ICON7 and GOG-0218) when compared with surveillance alone [50]. Consequently, the NCCN recommends bevacizumab in conjunction with carboplatin and paclitaxel as maintenance therapy for patients with a complete or partial response to primary surgical debulking for stage III or IV epithelial ovarian, fallopian tube or primary peritoneal cancer. Nonetheless, the NCCN does not advise using bevacizumab for maintenance therapy if it is not taken during the first chemotherapy treatment. Furthermore, individuals with BRCA1 and BRCA2 mutations should

	not use anti-angiogenic inhibitors since other targeted medicines work better in these cases. Bevacizumab is still acceptable for individuals who are wild-type or whose BRCA1 and BRCA2 mutation status is uncertain [45]. On the other hand, ASCO recommends bevacizumab in a more cautious manner. ASCO merely recommends that bevacizumab be taken into consideration until more evidence is found, despite the fact that it greatly improves progression-free survival when used as concurrent therapy followed by single-agent maintenance therapy. No clear clinical benefit in overall survival has been demonstrated [37]. Pazopanib, sorafenib, sunitinib, cediranib, and aflibercept are other angiogenesis inhibitors; however, because of their side effects and high cost, these drugs are not commonly used [1].
Poly(ADP)-ribose polymerase inhibitors	PARP inhibitors have recently gained momentum for the maintenance treatment of ovarian cancer. PARP inhibitor agents include olaparib, niraparib, and rucaparib. Olaparib was the first Federal Drug Administration (FDA) approved drug in this subgroup indicated to treat advanced *BRCA* mutated ovarian cancer after platinum-based chemotherapy, based on SOLO-1, phase 3 randomized double-blind, placebo-controlled trial. Olaparib reduced disease progression or death by 70% (hazard ratio 0.30, 0.23 to 0.41; $p<.001$) [51]. The PAOLA-1 trial, a phase 3 randomized controlled trial of 806 women with stage III to IV high-grade serous or endometrioid ovarian cancer, showed a progression-free survival benefit of 4.5 months in the group that received olaparib and bevacizumab maintenance versus placebo and bevacizumab [52]. When used in conjunction with bevacizumab, olaparib, niraparib, or rucaparib was approved by the FDA and NCCN as a first-line maintenance treatment for patients with ovarian cancer who had responded partially or completely to initial platinum-based chemotherapy or whose tumours were associated with homologous recombination deficiency (HRD), which is defined as the presence of a deleterious BRCA mutation. In patients with newly diagnosed advanced-stage ovarian cancer who initially responded to first-line platinum-based chemotherapy, recent clinical trials such as the VELIA and PRIMA trials, which used a newer PARP inhibitor, veliparib and niraparib maintenance therapy, respectively, showed significantly improved progression-free survival compared to the placebo group [53, 54].

Immunotherapy: By provoking a patient's immune system to fight tumour cells, immunotherapy drugs have lately demonstrated notable advantages in the treatment of solid malignant tumours. Nevertheless, available data on women with ovarian malignancies to far do not indicate any advantage. Controversial findings that followed shifted attention away from combination treatments combining immune checkpoint inhibitors with PARPs, chemotherapy, anti-angiogenic drugs, and other treatments. When these medicines are combined instead of focussing on a single route, the anti-tumor activity is increased. These encouraging outcomes are from early phase studies; further findings from current phase 2 and phase 3 trials are anticipated [1, 55].

Vaccines: In an effort to stimulate the immune system and kill cancer cells, researchers are also investigating vaccinations as a potential treatment for ovarian cancer. HER-2, p53 protein, and CA-125 are possible tumor-associated antigen molecules targeted in ovarian cancer, according to ongoing research on ovarian cancer vaccines. In a particular case study, vaccination treatment was employed to boost T-cell defence mechanisms [55, 56]. The majority of currently underway pilot and phase 1 or 2 trials are examining therapeutic vaccinations in conjunction with other drugs for the treatment of ovarian cancer, as vaccine monotherapy has not proven to be beneficial. As part of future initiatives to assure lower cancer burden and enhanced life expectancy in this patient group, adoptive T-cell transfer and chimeric antigen receptor treatment are two more new medicines being examined in clinical trials [55].

Recurrent Ovarian Cancer: The majority of women (Around 80%) who have advanced-stage ovarian cancer often have tumour progression or recurrence. One of the best indicators of how well recurrent ovarian cancer will respond to further treatment is the platinum-free interval. The time between finishing the final round of platinum-based chemotherapy and experiencing a relapse is known as the platinum-free interval [57]. On the other hand, a period of time more than six months between the end of the previous cycle of platinum-based chemotherapy and the start of the next round of platinum-based chemotherapy is commonly referred to as platinum sensitivity. Surgery's place in cases of ovarian cancer that recurs is unclear. Patients with platinum-sensitive recurrent ovarian cancer were enrolled in GOG-213, a phase 3 multicenter randomized clinical trial. Patients were randomly assigned to undergo surgical cytoreduction followed by adjuvant platinum-based chemotherapy or to receive only platinum-based chemotherapy. The primary endpoint of the trial was overall survival and results indicated that patients who received chemotherapy and chemotherapy alone or secondary surgical cytoreduction followed by chemotherapy did not show any improved benefit (hazard ratio for death 1.29, 0.97 to 1.72; P =.08) [58]. Few trials evaluate chemotherapy alone against surgery followed by chemotherapy in patients with recurrent platinum-sensitive ovarian cancer. Preliminary data supported surgery followed by chemotherapy with improvements in progression-free survival and longer time intervals until the commencement of further treatment. Furthermore, two further studies are comparing surgery plus chemotherapy with surgery alone in these patient categories; the outcomes of these trials, Surgery for Ovarian Cancer Recurrence (SOCceR) and Surgery or Chemotherapy in Recurrent Ovarian Cancer (SOC 1) are still pending. Current data does not support the idea that patients with platinum-sensitive recurrent epithelial ovarian cancer who undergo second-degree surgical cytoreduction will live longer overall [59]. Bevacizumab which was investigated in conjunction with chemotherapy for the treatment of recurrent ovarian cancer as well as for maintenance therapy (GOG-218, or OCEANS and AURELIA trials), has also been approved as a result of extensive phase 3 studies [57]. Progression-free survival has objectively improved, according to the research. However, they failed to indicate an improvement in overall survival. Nonetheless, anti-angiogenic drugs have demonstrated efficacy in treating these platinum-sensitive recurrent ovarian malignancies; nonetheless, further research is required to precisely identify their advantages. Large retrospective cohort studies provide evidence for the use of aromatase inhibitors, such as letrozole, in the treatment of recurrent low-grade serous and endometrioid epithelial ovarian cancer. Clinical trials on PARP inhibitors have been conducted at different phases and their effectiveness has been demonstrated in individuals with genetic BRCA mutations. When chemotherapy failed to control ovarian cancer patients with detrimental germline

or somatic BRCA mutations, they were first authorized for use as monotherapy. Further trials revealed significant progression-free survival advantages in individuals with an initial response to bevacizumab with maintenance PARP inhibitor treatment. A longer follow-up is necessary since an overall survival benefit has not yet been demonstrated. Patients with platinum-sensitive recurrent ovarian cancer and a BRCA mutation were evaluated for maintenance monotherapy with olaparib in the SOLO-2 study. The patients who received olaparib had a significantly better progression-free survival rate, and their quality of life was not significantly affected [60]. PAOLA-1; a phase 3 study, evaluated olaparib with bevacizumab in platinum-sensitive recurrent ovarian cancer, revealing progression-free survival improvements in the patients receiving the combination. The results were consistent with those obtained in the SOLO-1 study. The safety profile of olaparib remained mostly stable throughout the trials; however, the group taking olaparib with bevacizumab saw a greater frequency of major side events than the group getting a placebo plus bevacizumab. Anaemia was the most frequent occurrence in this group [52]. Clinical advantages of PARP inhibitor maintenance treatment in patients with platinum-sensitive recurrent ovarian cancer have been demonstrated in several phase 3 studies. The study's findings however also indicate that PARP inhibitors could be harmful to patients with HRD-positive advanced recurrent ovarian cancer who had received three or more previous chemotherapy regimens. As a result, for these patients olaparib, niraparib, and rucaparib are no longer advised in the US [46]. Patients with platinum resistance have a worse prognosis; within six months of completing adjuvant chemotherapy and cytoreductive surgery, they have a recurrence of the illness. Because of this, it is critical to address treatment goals with these patients, as their overall survival chances are low. By concentrating on more recent targets such as intracellular signalling inhibition, DNA repair, tumour vasculature, and other molecular targets there may be additional opportunities to investigate and improve the therapy of ovarian cancer that recurs. As a result, platinum based chemotherapy is typically administered after initial reductive surgery for patients with advanced stage ovarian cancer. Neoadjuvant chemotherapy is advised for individuals who are not fit for surgery or who may not benefit from cytoreductive surgery. Because a lower tumour load is a strong indicator of survival, optimal cytoreductive surgery is essential. Bevacizumab and PARP inhibitors are now first-line treatments for maintenance, with PARP inhibitors being favoured for recurring patients. Targeted therapeutics are the new, developing therapy approaches.

Ancillary Treatments: Patients often have ancillary concerns that need to be treated in addition to their primary therapy for ovarian cancer. Patients who are premenopausal and undergo surgical menopause due to bilateral salpingo-oophrectomy for epithelial ovarian malignancies frequently require therapy for vasomotor symptoms. According to ASCO, oestrogen hormone treatment may be used in the majority of these individuals, with the exception of low-grade serous and endometrioid ovarian cancers, which may be treated with antiestrogen therapies [7]. Treatment may also be necessary for dyspareunia brought on by artificial menopause or problems from post-treatment vulvovaginal atrophy. Furthermore, for premenopausal individuals undergoing fertility-sparing surgery, contraception might be taken into account throughout therapy. The majority of birth control methods are deemed safe by the World Health Organisation, with the exception of intrauterine devices whose usage is limited [63].

Surveillance: The exact length of time and frequency of monitoring are yet unknown, but it is essential to keep an eye out for any signs of recurrence after initial ovarian cancer therapy. The NCCN recommendations suggest scheduling follow-up appointments with a pelvic exam for two years at a time followed by three years at a time of three to six months. A yearly follow-up can be conducted after the initial five years. Additionally, prior to therapy, individuals with high levels should have a CA-125 level evaluated. When clinically required, a full blood count, a detailed metabolic profile, and imaging should be carried out [64]. Computed tomography (CT), positron emission tomography (PET)/CT scan and chest, abdominal, and pelvic magnetic resonance imaging are examples of imaging modalities. In addition, NCCN guidelines suggest offering a referral for genetic testing if none has been done previously. Nevertheless, rather than only when clinically needed, some experts advise routinely imaging and measuring a CA-125 level in patients with stage II to IV ovarian malignancies every three months during the first year, every four months during the second year, every six months during years three to five and then every year after that. It is also advised to keep an eye on the bone mineral density of those using aromatase inhibitors [64, 65].

Differential Diagnosis

The differential diagnosis for ovarian cancer includes: Colon cancer, Embryologic remnants, Gastric adenocarcinoma, Metastatic gastrointestinal carcinoma, Ovarian torsion, Peritoneal cyst, Retroperitoneal mass, Uterine fibroids, Endometriosis, Papillary adenocarcinoma, Serous adenocarcinomas, Undifferentiated adenocarcinomas, Small-cell adenocarcinomas, Brenner tumors.

Radiation Oncology

In the past time, whole abdomen radiation was used to treat ovarian cancer; however, this modality is no longer employed for this indication due to unsatisfactory outcomes and an increased incidence of toxicity and problems. Radiation therapy is currently only used to palliate the symptoms of ovarian cancer or to treat the disease's localised spread. Since ovarian cancer usually spreads beyond the pelvis, adjuvant radiation treatment has not demonstrated any survival advantage in the early stages of clear cell carcinoma and high-risk illness [61, 62]. Radiation has been less useful and has taken a backseat in the treatment of ovarian cancer with the development of sophisticated systemic treatments. A more recent kind of palliative radiation treatment is called stereotactic body radiotherapy (SBRT). Even in cases when local control is attained, SBRT delivery is associated with high rates of distant lesion development [62]. These days, the significance of radiation treatment for locally-regionally recurrent ovarian cancer is being reevaluated due to the development of novel procedures such as SBRT, intensity-modulated radiotherapy, and low-dose hypofractionation, particularly for tumours that are resistant to chemotherapy [63, 64].

Medical Oncology

Chemotherapy after surgical cytoreduction is the conventional treatment protocol for patients with advanced illness or early-stage ovarian cancer with high-risk characteristics (i.e., stage IC and II, clear-cell histology, or high grade). Depending on the tumor's histology, stage, and whether or not optimal debulking was carried out, chemotherapy can be given intravenously (IV) or intraperitoneally. Several regimens are used, including platinum-based IV chemotherapy, platinum-based IV and intraperitoneal chemotherapy, and platinum-based intraperitoneal chemotherapy plus bevacizumab [6]. Chemotherapy with intraperitoneal carboplatin is well tolerated in patients with advanced-stage ovarian cancer. Intraperitoneal chemotherapy was believed to have an enhanced therapeutic advantage by immediately diffusing chemotherapeutic chemicals into cancer tissue, particularly for small levels of residual illness, as ovarian cancer grows mostly in the abdominal cavity at first. Intraperitoneal chemotherapy was found to improve survival in four seminal studies (GOG-104, GOG-114, and GOG-172). Nevertheless, the GOG-252 study shown that there was no gain in survival when bevacizumab and intraperitoneal chemotherapy were combined. Instead, side events such as neurotoxicity, thrombocytopenia, neutropenia, and gastrointestinal symptoms increased. This means that intraperitoneal chemotherapy is being used less now that bevacizumab has more indications [6, 65]. There are still experiments in progress that might yield further details on this therapy option [6, 66, 67]. Patients receiving a combination of paclitaxel and cisplatin had a better overall survival rate in a phase 3 study called GOG-111 than the group receiving a combination of cisplatin and cyclophosphamide. The first line chemotherapeutic drug for epithelial ovarian cancer is platinum-based cisplatin or carboplatin, combined with a taxane family agent, paclitaxel or docetaxel. Numerous research findings have indicated that carboplatin is well-tolerated and equally effective as cisplatin. Furthermore, there has been no discernible improvement in progression-free survival with weekly dose-dense treatment with paclitaxel and carboplatin compared to regular 3-weekly chemotherapy, the inclusion of a third drug, or a longer chemotherapy cycle [6, 58]. There are several efficient chemotherapy regimens available [22].

Table 4: Chemotherapy Regimen Options

Regimen	Dosage	Cycle Interval	Number of Cycles
Carboplatin	5-6 area under the curve (AUC) given IV over 30-60 min on day 1.	Every 3 weeks	6
Paclitaxel	175 mg/m^2 given IV over 3 hours.		
Carboplatin	5-6 AUC given IV over 3 hours.	Every 3 weeks	6
Paclitaxel	80 mg/m^2 given IV over 3 hours.	Every week	18 weeks
Carboplatin	5 AUC given IV over 3 hours	Every week	6
Docetaxel	75 mg/m^2 given IV over 3 hours	Every 3 weeks	
Cisplatin	75 mg/m^2 given IV over 3 hours	Every week	6
Paclitaxel	135 mg/m^2 given IV over 3 hours	Every 3 weeks	
Carboplatin (single-agent)	5 AUC given IV over 3 hours	Every 3 weeks	6

Chemotherapy in Older Adults: A randomized control study involving patients 70 years of age or older with comorbidities and stage III or IV ovarian cancer revealed that carboplatin monotherapy had lower survival outcomes than carboplatin-paclitaxel 3 weeks [58]. However, a modified dose-dense regimen of weekly carboplatin with paclitaxel is less toxic and better tolerated in patients receiving combination treatment than the standard dosage schedule of three weeks. As demonstrated by an MIT07 phase 3 study, which is also appropriate for older patients with comorbidities, progression-free survival was not extended [68, 69]. There was a reduction in high-grade neutropenia, febrile neutropenia, thrombocytopenia, and neuropathy among older persons who were fragile [21, 58, 70].

Staging

The International Federation of Gynaecology and Obstetrics (FIGO) staging method, the 8th edition of the American Joint Committee on Cancer (AJCC), and the related TNM classification are used to surgically stage ovarian cancer [21]. Tumours when the primary site cannot be distinguished should be labelled as "undesignated." This applies to cases when the primary site (peritoneum, fallopian tube, or ovary) may be identified [21].

Table 5: International Federation of Gynecology and Obstetrics Ovarian, Fallopian Tube, and Peritoneal Cancer Staging System

Stages	Sub Stages	Tumor Characteristics
I		Tumor confined to ovaries (one or both) or fallopian tubes
	IA	Tumor limited to 1 ovary (Capsule intact) or fallopian tube; no tumor on ovarian or fallopian tube surface; no malignant cells in ascites or peritoneal washings
	IB	Tumor limited to both ovaries (Capsules intact) or fallopian tubes; no tumor on ovarian or fallopian tube surface; no malignant cells in the ascites or peritoneal washings
	IC	Tumor limited to 1 or both ovaries or fallopian tubes, with any of the following: IC1: Surgical spill IC2: Capsule rupture before surgery or tumor on the ovarian or fallopian tube surface IC3: Malignant cells in ascites or peritoneal washings
II	Tumor involves 1 or both ovaries or fallopian tubes with a pelvic extension below the pelvic brim or primary peritoneal cancer	
	IIA	Extension or implants on the uterus, fallopian tubes, or ovaries
	IIB	Extension to other pelvic intraperitoneal tissue
III	Tumor involves 1 or both ovaries or fallopian tubes, or primary peritoneal cancer, with microscopically confirmed peritoneal metastasis outside the pelvis or metastasis to the retroperitoneal (pelvic or para-aortic) lymph nodes	
	IIIA1	Positive retroperitoneal lymph nodes only (cytologically or histologically proven):

		IIIA1i: Metastasis ≤10 mm in greatest dimension IIIA1ii: Metastasis >10 mm in greatest dimension
	IIIA2	Microscopic extrapelvic (above the pelvic brim) peritoneal involvement with or without positive retroperitoneal lymph nodes
	IIIB	Macroscopic peritoneal metastasis beyond pelvis ≤2 cm in greatest dimension with or without metastasis to the retroperitoneal lymph nodes
	IIIC	Macroscopic peritoneal metastasis beyond the pelvis >2 cm in greatest dimension with or without metastasis to the retroperitoneal lymph nodes (includes an extension of tumor to the capsule of liver and spleen without parenchymal involvement of either organ)
IV	Distant metastasis, excluding peritoneal metastases	
	IVA	Pleural effusion with positive cytology
	IVB	Parenchymal metastases and metastases to extra-abdominal organs (including inguinal lymph nodes and lymph nodes outside of the abdominal cavity)

Prognosis

The prognosis for ovarian cancer is typically dismal, with fewer than 50% of cases surviving for five years and about 35% for 10 years [71]. The stage of the illness at diagnosis has a direct bearing on the prognosis of ovarian cancer. Stage I ovarian cancer is thought to have a survival rate of 70% to 92%, whereas stage IV tumours have a survival rate of fewer than 6% [72]. The amount of remaining disease following initial cytoreductive surgery, baseline performance status, histologic type and grade and other parameters are also linked to prognosis. The prognosis is greatly impacted by the amount of remaining disease following primary debulking surgery, which is why recommendations advise doing this therapy for every patient who can withstand surgery [21]. The 5-year survival rate drops to 80% in women whose cancer has progressed to nearby tissues and to 25% in women whose disease has metastasised [73]. Secondary cytoreductive surgery is occasionally used to treat a subset of individuals with recurrent illness. Patients with recurrent ovarian cancer who had ascites less than 500 mL and a confined tumour recurrence location are related with improved surgical results. Patients with platinum-sensitive ovarian cancer that recurs also have a better prognosis than those with platinum-resistant ovarian cancer, which usually get palliative treatment solely [37, 72, 74].

Complications

In addition to nutritional problems, women who were not able to get therapy often experienced serious consequences such as ascites, intestinal blockage, pleural effusion, and bladder obstruction [75]. Women who die because of ovarian cancer often have a range of difficulties in the final six months of their lives, such as: Fatigue or weakness, Nausea or vomiting, Constipation, Pedal edema, Anemia [75]. Treatment for ovarian cancer may result in side effects such as neuropathy, depression, anxiety, exhaustion, nausea, dyspareunia, pelvic discomfort and dry vagina. Because of the indirect impacts on a patient's capacity to work and finances, reduced quality of life is also frequently experienced [7]. Abdominal discomfort, nausea, vomiting, dehydration, and catheter-related issues are among the common side effects resulting from chemotherapy [76]. The anti-angiogenic inhibitor bevacizumab has side effects that include rhinitis, dry skin, exfoliative dermatitis, headache, epistaxis, hypertension, proteinuria, and irregular lacrimation. Black-box warnings for the most serious side effects include bleeding, stomach perforation, and poor wound healing. Patients should be educated by clinicians about these consequences and symptoms that need to be evaluated [77].

Consultations

It is frequently erroneous to estimate the probability of malignancy only from clinical characteristics. Because of the markedly improved survival, the majority of professional societies, including the NCCN and the American College of Obstetricians and Gynaecologists (ACOG), advise referring all patients with suspected ovarian malignancies to a gynaecologic oncologist for additional assessment and treatment [7]. Additionally, ACOG has specific guidelines, recommending that practitioners visit a gynaecologic oncologist for patients with an adnexal tumour and any of the following findings:

- Ultrasound findings of ascites, a nodular or fixed pelvic mass, evidence of abdominal or distant metastasis, or other features suggestive of malignancy.
- An elevated CA-125 level in those who are postmenopausal.
- A significantly elevated CA-125 level in those who are premenopausal.
- An elevated score on a formal risk assessment test (eg, the multivariate index assay, risk of malignancy index, or the risk of ovarian malignancy algorithm) or an imaging-based scoring system [7].

Patient Counselling

The patient should be informed of all available treatment choices and their prognosis at the time of diagnosis. All patients with ovarian cancer should receive genetic testing advice from genetic counsellors and oncology physicians, particularly if they have a hereditary cancer syndrome [6]. Regardless of the stage of the cancer, the palliative care team and other relevant experts should be contacted as soon as possible to facilitate comprehensive treatment, predict the course of the disease, and have a major influence on the patient's quality of life. In the event that it applies to their specific situation, patients should also be informed about current clinical studies. Moreover, a number of research's findings have indicated a link between a lower risk of ovarian cancer and higher physical activity [15]. Diabetes and obesity have also been shown to be risk factors for ovarian cancer. Given this correlation, some recent research has shown that treating these disorders preventively may have an effect on the onset of ovarian cancer [71]. In order to lower the risk of ovarian cancer, ACOG also suggests bilateral salpingo-oophorectomy for women with BRCA1 mutations at age 35 to 40 years and for those with BRCA2 mutations at age 40 to 45 years. Salpingectomy performed at the time of a hysterectomy or as a sterilisation technique is suitable for women who have an average risk of developing ovarian cancer [7].

Discussion and Conclusion

Ovarian cancer, despite ongoing clinical trials and advancements in treatment, remains a significant challenge in women's health due to late-stage diagnosis and deviation from recommended care guidelines. Efforts are needed to develop effective strategies for early detection and optimize treatment outcomes. Experienced gynecologic oncologists are critical in achieving optimal cytoreduction surgery, a key determinant of patient survival. Interprofessional collaboration, particularly between medical and surgical oncologists, facilitates shared decision-making regarding treatment options and enrollment in clinical trials. Pathologists give critical diagnostic information through tissue samples, directing therapy recommendations. Early engagement in palliative care increases treatment effectiveness and promotes patients' quality of life. For long-term care, close observation and patient education on symptom detection for illness recurrence are essential. Ovarian cancer care demands a patient-centered approach due to its complicated nature and variety of treatment methods. This involves combining the knowledge of doctors, advanced practitioners, nurses, chemists, and other health professionals to enhance patient outcomes, safety, and teamwork.

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