Review article

Diagnostics and Treatment of Malignant Ovarian Tumors

Ivana Maurac Pašalić [1, 2], Sara Šota [2], Miriam Šoletić [2], Mato Pavić [1, 2]

[1] Department of Obstetrics and Gynaecology, University Hospital Centre Zagreb, Croatia
[2] School of Medicine, University of Zagreb, Croatia

*Corresponding author: Ivana Maurac Pašalić, imaurac@yahoo.com

Abstract

Malignant ovarian tumors represent a heterogeneous group of neoplasms and a significant clinical challenge. Due to non-specific symptoms in the early stages, they are often diagnosed late, resulting in poor prognosis. Diagnostic evaluation involves a combination of medical history, physical examination, tumor marker assessment, and imaging techniques. Transvaginal ultrasound is the first-line imaging modality, followed by CT, MRI, or PET/CT as needed. Accurate staging is essential for choosing the optimal therapeutic approach. Standard treatment consists of surgery and platinum-based chemotherapy, with PARP inhibitors and anti-angiogenic therapies used in maintenance. In selected young patients, fertility-sparing surgery may be considered. The management of recurrent disease is individualized based on patient characteristics, tumor biology and previous response to therapy.

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Introduction

Ovarian cancer remains one of the most lethal gynecological malignancies worldwide, primarily due to its asymptomatic presentation in early stages and a lack of effective screening tools. As a result, the majority of cases are diagnosed at an advanced stage, when treatment options are limited, and prognosis is poor. Despite recent advances in diagnostics and therapeutics, the five-year survival rates remain low, primarily because over 70% of patients are diagnosed at FIGO stage III or IV (1). Ovarian malignancies are a heterogeneous group of tumors classified by their histological origin, with epithelial ovarian carcinomas accounting for over 90% of cases. Other less common subtypes include germ cell tumors and sex cord-stromal tumors, which typically present in younger patients and have a better prognosis (2). Given the biological complexity of ovarian cancer, timely diagnosis and individualized treatment are essential. Modern diagnostic approaches involve a combination of clinical examination, tumor marker evaluation, and imaging techniques such as transvaginal ultrasonography, CT, MRI, or PET/CT. Treatment strategies are based on surgical cytoreduction followed by platinum-based chemotherapy and increasingly include targeted therapies such as PARP inhibitors and antiangiogenic agents.

This review aims to provide a comprehensive overview of the current knowledge regarding diagnostic strategies, staging, treatment options, and prognosis of malignant ovarian tumors, with particular emphasis on evidence-based approaches and personalized medicine.

Diagnostic Methods

The diagnostic process for malignant ovarian tumors involves a combination of clinical assessment, laboratory tests, and imaging modalities. Due to the lack of specific symptoms and ineffective screening methods, early detection remains challenging, and diagnosis is often delayed. Medical history and physical examination are the initial steps in evaluating suspected cases. Patients may present with nonspecific abdominal symptoms, such as bloating, pelvic discomfort, constipation or early satiety. A detailed gynecologic and family history is essential, particularly regarding ovarian, breast, or colorectal cancer. On physical examination, findings such as an adnexal mass, ascites, or abdominal distension may raise suspicion (2). Tumor markers are routinely used in the initial evaluation. Cancer antigen 125 (CA-125) is the most commonly used biomarker, elevated in approximately 85% of women with advanced-stage epithelial ovarian cancer. However, it lacks specificity and sensitivity in early stages and may also be elevated in benign conditions such as endometriosis or pelvic inflammatory disease (2). Human epididymal protein 4 (HE4) is a more specific marker that may improve diagnostic accuracy when combined with CA-125 (3). The Risk of Ovarian Malignancy Algorithm (ROMA), which incorporates CA-125, HE4, and menopausal status, improves diagnostic accuracy. Additional biomarkers such as β-hCG, AFP, LDH, and inhibin are useful in evaluating germ cell and sex cord-stromal tumors. Novel molecular markers under investigation include circulating tumor DNA (ctDNA), TP53 autoantibodies, and microRNA profiles, which may enhance early detection in the future (4).

Imaging techniques are essential in the assessment of adnexal masses. Transvaginal ultrasonography (TVUS) is the first-line modality due to its availability and high sensitivity. Malignant features on ultrasound include irregular solid areas, papillary projections, multilocular cysts, thick septations, and the presence of ascites (5). Doppler ultrasound can evaluate tumor vascularity and help differentiate benign from malignant lesions. For staging and further evaluation, computed tomography (CT) of the abdomen and pelvis are recommended, especially prior to surgery. Magnetic resonance imaging (MRI) is reserved for indeterminate masses or when fertility preservation is considered (2). PET/CT is not used routinely but may be useful in detecting recurrence or distant metastases. In selected cases, cytological analysis of ascites or peritoneal washings can support the diagnosis and staging, although its

role has declined with the advancement of imaging. Altogether, accurate diagnosis relies on a multimodal approach that combines clinical, biochemical, and radiologic findings to guide optimal management.

Table 1. FIGO classification of ovarian cancer (2014.)

Stage	Description
Stage I	Tumor limited to ovaries or fallopian tubes
Stage IA	Tumor limited to one ovary or fallopian tube; capsule intact, no tumor on surface, negative washings
Stage IB	Tumor involves both ovaries or fallopian tubes; otherwise like IA
Stage IC	Tumor limited to one or both ovaries/fallopian tubes, with any of: IC1 – surgical spill, IC2 – capsule rupture or surface involvement, IC3 – malignant cells in ascites or washings
Stage II	Tumor involves one or both ovaries/fallopian tubes with pelvic extension (below pelvic brim) or primary peritoneal cancer
Stage IIA	Extension and/or implants on uterus and/or fallopian tubes and/or ovaries
Stage IIB	Extension to other pelvic intraperitoneal tissues
Stage III	Tumor involves one or both ovaries/fallopian tubes or primary peritoneal cancer with cytologically/histologically confirmed spread to the peritoneum outside the pelvis and/or metastasis to retroperitoneal lymph nodes
Stage IIIA1	Positive retroperitoneal lymph nodes only (without peritoneal metastases outside pelvis); IIIA1(i): ≤10 mm, IIIA1(ii): >10 mm
Stage IIIA2	Microscopic peritoneal metastases beyond the pelvis ± positive retroperitoneal lymph nodes
Stage IIIB	Macroscopic peritoneal metastases beyond pelvis ≤2 cm ± retroperitoneal lymph nodes
Stage IIIC	Macroscopic peritoneal metastases >2 cm ± retroperitoneal lymph nodes; includes extension to capsule of liver or spleen without parenchymal involvement
Stage IV	Distant metastases excluding peritoneal metastases
Stage IVA	Pleural effusion with positive cytology
Stage IVB	Parenchymal metastases and metastases to extra-abdominal organs (e.g. inguinal lymph nodes, liver/spleen parenchyma)

Staging and Spread of Disease

Accurate staging of ovarian cancer is essential for determining prognosis and directly influences treatment planning and survival outcomes. The disease often spreads beyond the ovaries at the time of diagnosis, making comprehensive staging essential. The current standard classification system is based on the 2014 revision by the International Federation of Gynecology and Obstetrics (FIGO), which applies to epithelial ovarian, fallopian tube, and primary peritoneal carcinomas. Surgical staging remains the gold standard and is typically performed during the initial procedure. It includes peritoneal washings, inspection and palpation of the abdominal cavity, bilateral salpingo-oophorectomy, hysterectomy, omentectomy, peritoneal biopsies, and pelvic and para-aortic lymphadenectomy. Laparotomy is the preferred approach, although laparoscopy may be considered in selected early-stage cases (6). The FIGO system categorizes the disease into four main stages, each with subgroups based on the extent of tumor spread. A detailed overview of the FIGO 2014 staging is presented in Table 1.

Ovarian cancer spreads through several distinct mechanisms. Direct extension to adjacent pelvic organs such as the uterus, fallopian tubes, and rectosigmoid colon. Peritoneal dissemination, a hallmark of epithelial ovarian cancer, involves exfoliation of tumor cells into the peritoneal cavity. These cells can implant on peritoneal surfaces, particularly the omentum, diaphragm, and bowel serosa (7). Malignant ascites is a common finding. Lymphatic spread typically affects pelvic and para-aortic lymph nodes. In advanced disease, supradiaphragmatic and inguinal lymph nodes may also be involved (8). Hematogenous metastasis is relatively rare but may occur in recurrent or late-stage disease. Common distant sites include the liver, lungs, and brain (2).

Treatment Options

The treatment of malignant ovarian tumors is multidisciplinary and depends on tumor histology, stage, patient age, performance status, and fertility considerations. The primary modalities include surgery, chemotherapy, and in selected cases, targeted therapies. Treatment plans should be individualized and made by a multidisciplinary oncology team.

Surgical treatment remains the cornerstone of therapy. In early-stage disease (FIGO I–II), the goal is accurate staging and complete cytoreduction. The standard procedure includes total hysterectomy, bilateral salpingo-oophorectomy, infracolic omentectomy, peritoneal biopsies, and lymphadenectomy. For young women with early-stage disease and a strong desire for fertility preservation, unilateral salpingo-oophorectomy with comprehensive staging may be considered. Minimally invasive (laparoscopic) approaches are acceptable in selected cases, although open surgery is preferred for complete tumor assessment and resection (6).

In advanced-stage disease (FIGO III–IV), the primary goal is optimal cytoreduction, defined as no residual macroscopic disease. Complete debulking surgery is associated with significantly improved survival (9). If optimal cytoreduction is not feasible due to tumor burden or patient condition, neoadjuvant chemotherapy followed by interval debulking surgery may be performed (6).

Adjuvant chemotherapy is indicated for most patients following surgical treatment, except for those with early-stage, low-risk tumors. The standard regimen consists of intravenous carboplatin and paclitaxel, administered every three weeks for six cycles (6). In selected patients with optimal debulking, intraperitoneal chemotherapy may offer higher local drug concentrations, although it is associated with higher toxicity (2). Neoadjuvant chemotherapy is reserved for patients unfit for primary surgery, with the aim of reducing tumor burden and improving surgical outcomes.

Targeted therapy has emerged as an important component of ovarian cancer management. PARP inhibitors (e.g., olaparib) are used in maintenance therapy for patients with BRCA mutations and homologous recombination deficiency (HRD). Bevacizumab, an

antiangiogenic agent, may be added to chemotherapy in both first line and recurrent settings (9).

Treatment of non-epithelial ovarian tumors differs significantly. Germ cell tumors typically occur in younger women and are often highly chemosensitive. Surgical resection with fertility preservation is usually followed by adjuvant chemotherapy using the BEP regimen (bleomycin, etoposide, cisplatin). Sex cord-stromal tumors are generally managed with surgery alone in early stages, with chemotherapy reserved for advanced or recurrent cases (9).

The treatment landscape continues to evolve with the integration of molecular profiling, immunotherapy trials, and personalized treatment strategies.

Follow-up and Prognosis

The follow-up of patients with malignant ovarian tumors plays a critical role in the early detection of recurrence and the management of long-term treatment-related side effects. Although there is no universally accepted surveillance protocol, most guidelines recommend a structured approach based on clinical examination and selective use of diagnostic tools.

Follow-up typically includes physical and pelvic examinations every 3–6 months during the first two years, and then every 6–12 months for up to five years (10). CA-125 levels may be measured in patients whose tumors previously expressed this marker, although its routine use remains controversial in asymptomatic patients. Imaging studies, such as ultrasound or CT scans, are generally reserved for cases with suspicious clinical findings or elevated tumor markers.

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Prognosis depends on several factors, with FIGO stage at diagnosis being the most significant. Patients diagnosed at an early stage (I–II) have a 5-year survival rate exceeding 80–90%, whereas for advanced stages (III–IV), the rate drops to approximately 30–50%. Other prognostic factors include tumor grade, histological subtype, residual disease after surgery, BRCA mutation status, and response to platinum-based chemotherapy (2).

Conclusion

Malignant ovarian tumors remain a major challenge in gynecologic oncology due to their asymptomatic presentation in early stages and the lack of effective screening tools. Most cases are diagnosed at an advanced stage, where therapeutic outcomes are significantly worse despite advancements in treatment modalities. A multidisciplinary approach involving accurate staging, optimal cytoreductive surgery, and platinum-based chemotherapy remains the foundation of care. The incorporation of targeted therapies, particularly PARP inhibitors and antiangiogenic agents, has improved progression-free survival in selected patient populations. In young women with early-stage disease, fertility-sparing surgery may be considered without compromising oncologic safety. Future progress in ovarian cancer management will depend on improved early detection strategies, molecular profiling, and personalized treatment plans. Raising awareness among healthcare providers and the public, as well as ensuring access to specialized oncologic care, is essential for improving survival rates and quality of life for patients affected by this aggressive disease.

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Acquisition of data: IMM, SŠ, MŠ, MP
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Dijagnostika i liječenje zloćudnih novotvorina jajnika

Sažetak

Zloćudne novotvorine jajnika vrlo su heterogena skupina tumora i predstavljaju značajan klinički izazov. Zbog nespecifičnih simptoma u ranom stadiju bolesti, karakterizira ih kasno otkrivanje i loša ukupna prognoza. Dijagnostički postupak uključuje temeljito uzimanje anamneze, fizikalni pregled, mjerenje tumorskih markera te slikovnu obradu. Transvaginalni ultrazvuk prva je metoda izbora u slikovnoj dijagnostici, a nakon njega slijede CT, MR, ili PET CT. Točno određivanje stadija ključni je korak u odabiru optimalnog terapijskog postupka. Liječenje se temelji na kirurškom zahvatu i kemoterapiji, a u terapiji održavanja mogu se primjenjivati inhibitori PARP enzima i antiangiogena terapija. Kod mladih žena u fertilnoj dobi, ukoliko je moguće, izvode se poštedni zahvati u svrhu očuvanja plodnosti. U slučaju recidiva bolesti, terapija se individualno prilagođava, ovisno o dobi i općem stanju pacijentice te vremenu pojave relapsa i prethodnom odgovoru na terapiju.

Ključne riječi: zloćudne novotvorine jajnika, transvaginalni ultrazvuk, kirurški zahvat, kemoterapija, recidiv