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REVIEW ARTICLES
PREGLEDNI ČLANCI

LOW-GRADE SEROUS OVARIAN CANCER – WHAT IS NEW?

NISKODIFERENCIRANI SEROZNI KARCINOM JAJNIKA – KOJE SU NOVOSTI?

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Abstract

Introduction. Low-grade serous ovarian carcinoma is a distinct and relatively uncommon histologic subtype of epithelial ovarian cancer, characterized by unique biological and clinical features that differentiate from high-grade and other epithelial subtypes. **Material and Methods.** A comprehensive literature search was performed to identify interventional studies, systematic reviews, case reports, and meta-analyses published between 2010 and 2024, focusing on the diagnosis, management, and outcomes of low-grade serous ovarian carcinoma. **Diagnosis.** Ultrasound is the first-line imaging modality for evaluating ovarian and adnexal lesions. Computed tomography remains the preferred method for staging, treatment planning, and post-therapy monitoring, while magnetic resonance imaging is recommended for characterizing indeterminate adnexal masses or for evaluating extensive disease visualized on ultrasound or computed tomography. **Clinical management.** For patients with advanced–stage disease (FIGO stages II–IV), maximal cytoreductive surgery followed by six cycles of carboplatin and paclitaxel remains the standard of care. Optimal cytoreduction is associated with significantly improved overall and progression-free survival compared with suboptimal surgery. Given the intrinsic chemoresistance of low-grade serous ovarian carcinoma, primary cytoreductive surgery is generally favored over neoadjuvant chemotherapy. Emerging targeted therapies focusing on CDK4/6, MAPK, and PI3K/AKT/mTOR pathways, as well as hormonal treatments, are under investigation and have demonstrated encouraging preliminary results. **Conclusion.** The management of low-grade serous ovarian carcinoma increasingly necessitates an individualized, multidisciplinary approach. Future therapeutic strategies will likely integrate molecularly targeted and endocrine therapies with optimal cytoreductive surgery to improve outcomes for this chemoresistant and biologically distinct ovarian cancer subtype.

Key words: Ovarian Neoplasms; Carcinoma, Ovarian Epithelial; Diagnosis; Treatment Outcome; Cytoreduction Surgical Procedures; Survival; Molecular Targeted Therapy; Immunotherapy

Sažetak

Uvod. Niskodiferenciran serozni karcinom jajnika predstavlja poseban i relativno redak histološki podtip epitelijalnog karcinoma jajnika, sa biološkim i kliničkim karakteristikama koje se razlikuju od visokodiferenciranog i drugih epitelijalnih podtipova. **Materijal i metode.** Sprovedena je sveobuhvatna pretraga literature radi identifikacije interventnih studija, pregleda, studija slučaja i metaanaliza objavljenih između 2010. i 2024. godine, sa fokusom na dijagnostiku, lečenje i ishode niskodiferenciranog seroznog karcinoma jajnika. **Dijagnostika.** Ultrazvuk predstavlja prvi korak u dijagnostici ovarijalnih i adneksalnih lezija. Kompjuterizovana tomografija je preferirana metoda za određivanje stadijuma bolesti, planiranje terapije i praćenje nakon lečenja, dok se magnetna rezonanca preporučuje za karakterizaciju neodređenih adneksalnih masa ili za procenu opsežnih lezija uočenih ultrazvukom ili kompjuterizovanom tomografijom. **Kliničko lečenje.** Kod bolesnica sa uznapredovalim stadijumima II–IV prema Internacionalnom udruženju ginekologa i opstetičara, maksimalna citoreduktivna hirurgija praćena sa šest ciklusa karboplatine i paklitaksela i dalje predstavlja standard lečenja. Optimalna citoredukcija povezana je sa značajno boljim ukupnim preživljavanjem i preživljavanjem bez progresije bolesti u poređenju sa suboptimalnom hirurgijom. Primarna citoreduktivna hirurgija se generalno preferira u odnosu na neoadjuvantnu hemioterapiju zbog urođene hemioresistentnosti niskodiferenciranog seroznog karcinoma jajnika. Terapije koje ciljaju molekularne puteve, kao što su inhibitori CDK4/6, MAPK i PI3K/AKT/mTOR signalnih puteva, kao i hormonska terapija, trenutno su u fazi istraživanja i pokazuju obećavajuće preliminarne rezultate. **Zaključak.** Lečenje niskodiferenciranog seroznog karcinoma jajnika sve više zahteva individualizovan, multidisciplinaran pristup. Buduće strategije lečenja verovatno će integrisati molekularno ciljane terapije, endokrine tretmane i optimalnu citoreduktivnu hirurgiju kako bi se poboljšali ishodi kod ove hemiorezistentne i biološki specifične podvrste karcinoma jajnika.

Ključne reči: tumori jajnika; epitelijalni karcinom jajnika; dijagnoza; ishod lečenja; citoreduktivna hirurgija; preživljavanje; ciljana molekularna terapija; imunoterapija

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Abbreviations

LGSOC	– low-grade serous ovarian carcinomas
HGSOC	– high-grade serous ovarian cancer
FIGO	– International Federation of Gynecology and Obstetrics
IOTA	– International Ovarian Tumor Analysis
CT	– computed tomography
PET/CT	– positron emission tomography
MRI	– magnetic resonance imaging
LB	– lymph node
OS	– overall survival
PFS	– progression-free survival
RD	– residual disease
NACT	– neoadjuvant chemotherapy
BEV	– Bevacizumab
MAPK	– mitogen-activated protein kinase
MEK inhibitors	– mitogen-activated protein kinase (MAPK) enzymes 1 and/or 2 inhibitors
FDA	– Food and Drug Administration
FRα	– folate receptor alpha
DSS	– disease-specific survival

Introduction

Low-grade serous ovarian carcinoma (LGSOC) represents a distinct and relatively uncommon histologic subtype of epithelial ovarian cancer, accounting for approximately 3–9% of all diagnosed cases [1]. According to the MD Anderson two-tier grading system introduced in 2004, serous ovarian carcinomas are divided into high-grade and low-grade variants, which differ substantially in their molecular profiles and clinical behavior [2]. Unlike high-grade serous ovarian carcinoma (HGSOC), which predominantly affects older women, LGSOC is typically diagnosed in younger patients, with a median age of approximately 55 years. Its incidence rate remains low, ranging between 0.1 and 0.8 per 100,000 women annually [3]. Molecular and genetic analyses have demonstrated that LGSOC has a distinct pathogenesis. In contrast to HGSOC, which is strongly associated with *TP53* or *BRCA1/2* mutations, LGSOC rarely exhibits these genetic alterations. Instead, it is characterized by frequent mutations within the RAS-RAF-MAPK signaling pathway, particularly involving *KRAS*, *NRAS*, and *BRAF* genes [4,5]. These findings support the hypothesis that borderline serous tumors, which share similar molecular abnormalities, may represent precursor lesions to LGSOC. The *KRAS* G12V variant, in particular, has been associated with poorer clinical outcomes [4]. Biologically, most LGSOCs demonstrate hormone receptor positivity, with high expression of estrogen receptors (approximately 70%) and moderate expression of progesterone receptors (around 30%), providing a rationale for the use of endocrine therapy in selected patients [1,10]. Clinically, the majority of serous ovarian cancers – regardless of grade – are diagnosed in advanced FIGO stages (III or IV), accounting for approximately 85–90% of cases [1,3]. Compared with HGSOC, LGSOC typically follows a more indolent disease course, with a longer progression-free survival (PFS) (median ~90 months) and overall survival (OS) (median ~100 months) [1,3,4]. Serum CA-125 levels at diagnosis are generally lower in LGSOC than in HGSOC, which limits their diagnostic sensitivity but preserved their utility in disease monitoring [4]. Ascites is also less frequently observed at presentation [3]. Clinical symptoms are usually nonspecific and reflect the tumor's mass effect rather than its biological aggressiveness. Common presenting features include abdominal bloating, discomfort, early satiety, and, in advanced vases, urinary or respiratory symptoms related to peritoneal or pleural involvement [4]. Key clinical and biological differences between LGSOC and HGSOC are summarized in **Table 1** (*adapted from Zwimpfer, T.A.; Tal,*

Table 1. Clinico-pathological characteristics for low-grade and high-grade serous ovarian cancer

	LGSOC	HGSOC
Median age (years)	55	63
Frequency (%)	3–9%	90%
Presumed precursor	Serous borderline	STIC of fallopian tube
CA 125	Not clinical useful	Clinical useful
Positive family history	Rare	10-22%
Chemosensitivity	Rare	90%
Clinical course	Slow	Rapid
Median progression-free survival (PFS)	92	35
Median overall survival (OS)	97	72
Gene mutation reported (%)		
BRAF	5%	<1%
KRAS	19-55%	<1%
TP53	8%	>95%
BRCA	1-5%	15%

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Although the biological and clinical distinctions between LGSOC and HGSOC are well established, the first-line therapeutic approach for advanced-stage disease (FIGO II–IV) remains largely similar – maximal cytoreductive surgery followed by six cycles of adjuvant platinum-based chemotherapy, most commonly a carboplatin/paclitaxel regimen [1,10].

Material and Methods

A comprehensive literature search was conducted in the PubMed and Cochrane Central Register of Controlled Trials databases to identify studies addressing the management and clinical outcomes of women with low-grade serous ovarian carcinoma (LGSOC). The search covered publications from 2010 to 2024 and included clinical trials, meta-analyses, systematic reviews, case reports, and clinical practice guidelines. The search strategy incorporated the following key terms and their combinations: low-grade serous ovarian cancer, ovarian carcinoma, surgery, chemotherapy, and immunotherapy. The initial search retrieved over 600 records. After screening titles, abstracts, and full texts, 42 studies met the inclusion criteria, focusing specifically on the diagnosis, treatment, and outcomes of LGSOC. Among the included studies, 20 were reviews or meta-analysis, 9 clinical trials, 4 practical guidelines, 3 comparative studies, 3 retrospective analyses, 2 original research reports, and 1 multicenter study. The final selection was based on the level of clinical detail, methodological quality, and relevance to the research topic.

Diagnosis

Ultrasound represents the first-line imaging modality for the evaluation of ovarian and adnexal lesions. The International Ovarian Tumor Analysis (IOTA) group recommends the use of the Assessment of Different Neoplasias in the Adnexa (ADNEX) model, which integrates clinical and sonographic parameters to estimate the risk of malignancy [4]. According to Flicek et al. [5], the proportion of solid areas and papillary projections increases progressively from borderline tumors to LGSOC, reaching its peak in HGSOC. On ultrasound, LGSOC typically appears as a multilocular cystic lesion containing more solid elements than borderline tumors but fewer than HGSOC. The presence of echogenic calcified foci – representing psammoma bodies – is characteristic and may be accompanied by mild to moderate vascularization, as LGSOC generally exhibits lower vascularity compared with HGSOC [5,6].

Contrast-enhanced computed tomography (CT) remains the preferred imaging method for staging, treatment planning, and post-therapy surveillance of ovarian malignancies [7–9]. CT provides valuable information on lymph node involvement and peritoneal dissemination, with a reported diagnostic accuracy approaching 90% [8]. The use of oral contrast can enhance visualization in patients with low body mass index or in perimenopausal women, in whom adnexal structures may be difficult to delineate [8]. However, CT sensitivity for peritoneal disease is size-dependent and decreases markedly for implants smaller than 1 cm [7]. Typical CT findings of LGSOC include a complex cystic mass with well-defined septations, papillary projections, and solid components, which may be unilateral or bilateral [7,8,10]. The identification of calcified psammoma bodies – present in up to 90% of cases – can aid differentiation from other calcified adnexal entities such as fibromas, Brenner tumors, or teratomas [7,10–13]. Ascites is uncommon in this tumor subtype [5,7].

PET/CT has limited value in primary diagnosis due to reduced sensitivity for borderline and low-grade lesions. However, it becomes more informative in advanced disease stages or when CT findings are inconclusive. In cases of recurrent or residual disease, PET/CT shows high diagnostic performance, with reported sensitivity between 95–97% and specificity between 80–100% [7,9].

MRI is particularly recommended for characterizing indeterminate adnexal masses or for evaluating extensive lesions detected on ultrasound or CT. It provides excellent tissue contrast and demonstrated high sensitivity (approximately 83%) and specificity (84%) in distinguishing benign from malignant processes [5,7]. Malignant serous tumors usually display mixed solid and cystic morphology, irregular internal septations, and poorly defined margins [5]. The Ovarian-Adnexal Reporting and Data System (O-RADS) MRI risk stratification score has been validated in multicenter studies, providing standardized risk assessment and follow-up recommendations. Its reported sensitivity is 93% and specificity 91% for identifying malignant lesions that are indeterminate on ultrasound [14–16]. In patients with iodine contrast allergy, as well as young or pregnant women, MRI is preferred over CT. MRI is also useful for evaluating post-treatment response and excluding recurrent disease [7,8]. In women with LGSOC, peritoneal metastases often appear as foci of high signal intensity on MRI, allowing detection of even small implants, particularly in the pouch of Douglas and the left upper quadrant [6].

Clinical management

Surgery

The role of systematic lymphadenectomy in early-stage LGSOC remains controversial. Minig et al. [17] conducted a multicenter retrospective study (2000-2016) involving nine institutions across Europe and the United States, assessing the frequency of lymph node metastases and their impact on oncologic outcomes in stage I disease. All patients underwent both pelvic and para-aortic lymphadenectomy, with surgical adequacy defined as the removal of at least ten lymph nodes from each region. The study demonstrated an extremely low incidence of lymph node involvement (<1%), suggesting minimal benefit from extensive lymphadenectomy in this subgroup. These results are consistent with those of Heitz et al. [18], who reported that the likelihood of retroperitoneal lymph node metastases in epithelial ovarian cancer varies by tumor stage and histologic type. In early-stage LGSOC, lymphatic spread appears negligible, and reoperation for staging purposes should therefore be reserved tor carefully selected patients.

In advanced-stage LGSOC, optimal cytoreductive surgery remains the cornerstone of treatment. The extent of residual disease (RD) after surgery has a decisive effect on long-term survival. A retrospective analysis by Di Lorenzo et al. [2], published in 2022, including 92 FIGO stage III–IV patients treated between 1994 and 2018 demonstrated significantly longer OS in those achieving complete cytoreduction (RD <10 mm), with a median OS of 142.3 months compared to 86.4 months in patients with RD > 10 mm. PFS followed a similar pattern (38.3 vs. 23.3 months). These findings underscore that primary cytoreductive surgery achieving RD less than 10 mm markedly improves OS and PFS, whereas suboptimal debulking is associated with inferior outcomes. Therefore, maximal primary cytoreductive remains the preferred initial approach for patients with advanced LGSOC.

Chemotherapy

Platinum-based chemotherapy, typically carboplatin-paclitaxel combination administered after maximal cytoreduction, con remains the conventional standard of care for LGSOC [19,20]. Despite its widespread use, its clinical benefit is modest. Data from the Arbeitsgemeinschaft für Gynäkologische Onkologie (AGO) meta-database, which included more than 5,000 women with epithelial ovarian cancer, demonstrated markedly lower response rates in LGSOC (approximately 23%) compared with high-grade serous disease (approximately 90%) [19]. For early-stages (FIGO I–II), adjuvant chemotherapy is generally recommended, although its role in the lowest-risk categories remains debated. Specifically, adjuvant treatment may be omitted for patients with stage IA disease, while its use in stage IB/IC cases should be considered individually based on histopathologic and clinical risk factors [21]. Given the limited chemosensitivity of LGSOC, recent trials have explored targeted therapies. In 2020, Monk et al. [22] compared the MEK1/2 inhibitor binimetinib with standard single-agent chemotherapy (pegylated liposomal doxorubicin, paclitaxel, or topotecan) and found compatible median PFS (9.1 months for binimetinib vs. 10.6 months in the control arm) but with a distinct mechanism of action. A subsequent international phase II/III trial by Gershenson et al. [23], published in 2022, demonstrated a clear PFS benefit with trametinib over standard regimens (paclitaxel, pegylated liposomal doxorubicin, topotecan, letrozole, or tamoxifen) (13.0 vs. 7.2 months), establishing MEK inhibition as a promising therapeutic avenue in this chemoresistant subtype. Overall, while carboplatin–paclitaxel remains the backbone of therapy, emerging molecularly targeted options necessitate reevaluation of conventional chemotherapy paradigms.

Neoadjuvant chemotherapy (NACT)

Evidence for neoadjuvant chemotherapy in LGSOC remains limited to retrospective studies. Matsuo et al. [24] conducted a 2023 multicenter analysis of stage III–IV patients treated with multimodal therapy, demonstrating significantly inferior OS in those receiving NACT compared to primary debulking surgery (PDS) followed by adjuvant chemotherapy (4-year OS: 56.4% vs. 81%; HR 2.12; 95% CI, 1.55–2.90). Similarly, Scott et al. [25] reported only a 36% response rate to NACT, with shorter PFS relative to the PDS cohort, suggesting that early exposure to chemotherapy may delay effective cytoreduction. Alternative neoadjuvant strategies, particularly hormonal therapy, are being explored. Cobb et al. [26] reported encouraging preliminary results from a pilot trial using neoadjuvant endocrine therapies, achieving an overall response rate of almost 47%. These findings suggest that hormonal modulation may be more effective and biologically appropriate than cytotoxic regimens in this setting. Collectively, available evidence supports LGSOC's intrinsic chemoresistance and reinforces primary cytoreductive surgery as the optimal initial strategy whenever feasible. Patients with extensive or unresectable disease should undergo multidisciplinary evaluation within specialized gynecologic oncology centers [27].

Chemotherapy and bevacizumab

Bevacizumab (BEV), a monoclonal antibody against vascular endothelial growth factor (VEGF), is approved for ovarian cancer in patients at high risk of relapse (FIGO stage IV or stage III with residual disease ≥10 mm after cytoreduction) [20]. Retrospective analyses indicate that BEV, either alone or combined with chemotherapy, can induce partial and complete responses in LGSOC, both in primary and recurrent settings, with reported response rates between 47.5% and 55% [3]. The MITO 22 trial (2023) evaluated BEV in advanced LGSOC (FIGO stage III–IV), comparing combination therapy with chemotherapy alone. PFS was significantly longer in the BEV group in both first-line (47.9 vs. 22.6 months) and recurrent settings 37.1 vs. 11.2 months), suggesting a potential benefit of anti-angiogenic therapy in this population, although further prospective studies are warranted to confirm these results [28].

Hormonal therapy

Endocrine therapy has demonstrated clinical benefit in both primary and maintenance treatment for LGSOC. Approximately 70% of tumors express estrogen (ER) receptors and 30% express progesterone receptors (PR), though no clear correlation between receptor level and treatment response has been established. In a 2017 retrospective study, Gershenson et al. [29] reported a 9% objective response and 61% disease stabilization rate in patients with FIGO stage II–IV LGSOC with hormonal therapy following primary chemotherapy, with exhibited significantly longer PFS (65 vs. 26 months) compared to observation. Similarly, studies with anastrozole showed a 6-month clinical benefit rate of approximately 60% and a partial response rate of 14% [30]. Fader et al. [31] investigated the effect of hormonal monotherapy after cytoreductive surgery in stage II–IV LGSOC. Their preliminary data indicated comparable survival outcomes, with a 3-year PFS and OS of 79% for patients receiving hormonal therapy versus 92.6% for those treated with chemotherapy. These findings suggest that, in selected advanced-stage cases, hormonal therapy may represent an effective alternative to adjuvant chemotherapy. In recurrent disease, endocrine therapy alone generally yields modest response rates but can provide meaningful clinical benefit. Most clinicians advocate for maintenance hormonal therapy until disease progression or the development of unacceptable toxicity [26]. Given the molecular parallels between LGSOC and luminal breast cancer, CDK4/6 inhibitors are being explored in combination with endocrine agents. The ongoing GOG 3026 trial evaluates ribociclib plus letrozole in recurrent LGSOC, while a phase II pilot study of abemaciclib with fulvestrant in unresectable stage III–IV LGSOC, fallopian tube, or primary peritoneal carcinoma, showed a 60% objective response at ASCO 2022. The PARAGON II trial is further assessing aromatase inhibitors combined with PI3K inhibitors (alpelisib) or CDK4/6 inhibitors (ribociclib) in women with hormone receptor-positive recurrent or metastatic gynecologic malignancies. This study aims to determine whether these combinations improve overall response rates compared with historical controls from the original PARAGON trial, stratifying patients by PIK3CA mutation status. The trial is currently enrolling participants in Australia and New Zealand [30].

MEK inhibitors

Mitogen-activated protein kinase (MAPK) pathway inhibitors, specifically targeting MEK1 and MEK2, have emerged as a promising therapeutic option for patients with LGSOC. This approach is supported by frequent genomic alterations observed in LGSOC, particularly mutations in the RAS and RAF genes, including KRAS (19–55%) and BRAF (5%) [1]. The first clinical trial exploring this approach, GOG-0239, evaluated selumetinib in patients with advanced or recurrent LGSOC and reported an overall response rate of 15%, with disease stabilization in 65% of participants [32]. Subsequent investigations have examined other MEK inhibitors. Monk et al. [22] compared binimetinib with physician's choice chemotherapy and, although the trial did not meet its primary endpoint, binimetinib demonstrated notable activity, with a response rate of 16% versus 13% and a median overall survival (OS) of 25.3 months compared to 20.8 months. KRAS mutation status may serve as a predictive biomarker, guiding patient selection for MEK-targeted therapies. The phase II/III GOG-0281 trial evaluated trametinib in a similar patient population. Trametinib significantly improved PFS to 13 months compared with 7.2 months in the chemotherapy control group. Response rates were also higher with trametinib (26.2% vs. 6.2%), and median OS was extended to 37 months versus 29.2 months in the control arm [23]. Resistance mechanisms to MEK inhibitors, such as activation of phosphorylated FAK (p-FAK), have prompted the development of combination strategies. The ongoing ENGOT-ov60/NCRI/GOG-3052 phase II trial investigates a dual RAF/MEK inhibitor alone versus its combination with defactinib, a FAK inhibitor, in recurrent LGSOC, incorporating KRAS mutation status as a stratification factor [33]. Early findings suggest that MEK inhibition may meaningfully improve clinical outcomes in LGSOC, although additional trials are required to confirm efficacy and optimize patient selection.

BRAF inhibitors

Mutations in the BRAF protein, a regulating component of the MAPK pathway, are found in up to 6% of patients with LGSOC [34]. These mutations are often associated with early-stage disease and a more favorable prognosis. In 2018, Moujaber et al. [35] reported a case series of two patients harboring BRAF mutations who received BRAF inhibitors at relapse, with both achieving durable responses. Desai et al. [36] conducted a phase I, open-label trial evaluating lifirafenib, a novel reversible BRAF inhibitor, in patients with solid tumors, including one with LGSOC, demonstrating antitumor activity and an acceptable safety profile. Another BRAF-targeting agent, ABM-1310, is currently being tested in a phase I trial for locally advanced or metastatic LGSOC. Several BRAF inhibitors have already received U.S. Food and Drug Administration (FDA) approval for other melanoma, primarily metastatic melanoma, although their role in ovarian cancer remains under investigation [37].

PI3K/AKT/mTOR pathway inhibitors

Mutations in the PI3K/AKT/mTOR signaling pathway are uncommon in patients with LGSOC. However, studies have reported a considerably higher prevalence among Japanese patients (~60%) compared to Western populations (4–5.2%), suggesting possible ethnicity-related differences in pathway activation [38]. Based on these findings, Ghoneum et al. [39] investigated PI3K/AKT/mTOR inhibitors, both alone and in combination with agents targeting other signaling pathways, in patients with ovarian cancer. Metformin is of particular interest due to its inhibition of mTOR phosphorylation, thereby reducing cellular proliferation [40]. Its effect was evaluated in a retrospective control study including women with epithelial ovarian cancer, among whom those treated with metformin (for diabetes) showed significantly improved 5-year disease-specific survival (DSS) – 67% vs. 47%. In the low-grade ovarian cancer subtype, the 5-year DSS was 60% compared with 38% [41]. In 2020, Arend et al. [42] published phase II results exploring the combination of primasertib (a MEK inhibitor) and voxtalisib (a PI3K inhibitor) versus primasertib alone in patients with recurrent LGSOC. No differences in response rate were observed between the two groups. These findings highlight the need for further investigations.

Secondary cytoreductive surgery in recurrent disease

Due to the chemotherapy observed in patients with LGSOC, secondary and even tertiary cytoreductive surgeries are not uncommon. In 2022, Goldberg et al. [43] published results from a systematic review and meta-analysis demonstrating a significant improvement in OS among patients who achieved complete resection (no residual disease) during secondary cytoreductive surgery. Nevertheless, platinum-based regimens remain the standard of care for platinum-sensitive LGSOC, while non-platinum regimens, with or without bevacizumab, are preferred in platinum-resistant cases. Indications for secondary or tertiary cytoreductive surgery should be determined individually by a multidisciplinary team.

Conclusion

Since the recognition of low-grade serous ovarian carcinoma as a biologically distinct entity from high-grade serous ovarian carcinoma, understanding of its clinical behavior and therapeutic response has advanced considerably. Primary cytoreductive surgery remains the treatment of choice when complete resection is feasible, but unresectable cases and recurrent cases continue to pose major challenges due to chemoresistance. Ongoing research into hormonal, targeted, and immunotherapeutic strategies offer promising alternatives. The management of low-grade serous ovarian carcinoma increasingly requires an individualized, multidisciplinary approach, with future strategies likely to combine molecularly targeted agents, endocrine therapy, and optimal cytoreduction to improve survival outcomes in this chemoresistant and biologically distinct ovarian cancer subtype.

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