Volume 26 I January 2026 I Monthly Issue 9

AOGD BULLETIN

"Women's wellness-From tiny heartbeats to timeless strength"

THEME: BEYOND THE MASK: MODERN FRONTIERS IN OVARIAN CANCER DIAGNOSIS & CARE

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AOGD Bulletin

Volume 25 • Monthly Issue 9 • January 2026

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Published from
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Lady Hardinge Medical College, New Delhi-110001

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Wishing all AOGD Members a very Happy and Glorious New Year 2026! May this year bring academic laurels, fulfilment of personal goals and above all improvement in women's health through conscientious efforts of the members.

The subcommittees organized quite a few interesting activities in December 2025. A CME on Elimination of Vertical Transmission of HIV & Syphilis was organized by Safe motherhood subcommittee, Webinar on Mission Adolescent Health and CME on Enhancing Maternal & Fetal Health were organized by the respective subcommittees. The year has ended but never has there been a halt in our academic pursuits or social commitments.

The 68th AICOG is round the corner and AOGD members are deeply committed towards making the event a grand success. I urge all the members to attend the conference in large numbers and also contribute by fulfilling the duties assigned to them. I am confident that our members will be the star performers in the paper and poster presentation.

This month's bulletin is centred on Modern Frontier's in Ovarian Cancer Diagnosis & Care and covers all aspects of this topic. Advanced Ovarian Cancer is difficult to treat and has significant recurrences. Optimal surgical clearance and multimodal therapies is the way forward. Let's all go through the contents of this journal to be better aware of the emerging therapeutics for cancer cure. I congratulate Dr Pikee and her team for thoughtfully choosing this important topic and perfectly covering all aspects of it.

AOGD Secretariat

From the President's desk

Greetings from AOGD

I extend my warm wishes for health and happiness to everyone in this newyear 2026. January is cold and chilly, so keep yourself protected by woolens. Attendence is still an issue in monthly online clinical meeting which again I urge to AOGD members to please attend it regularly in large numbers. Important and rare cases are discussed and it is informative and also add to our knowledge.

AICOG is round the corner, hope to meet you to all there.

This January issue is focused on Ovarian cancer. The title is 'Beyond the mask: Modern frontiers in Ovarian cancer Diagnosis & care. Topics have been well written by experts. Kudos to Dr Pikee and her team for bringing out this issue.

Happy reading'

President AOGD

From the Editor's Desk

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Dear Readers,

We are pleased to present the January 2026 issue of the AOGD Bulletin, themed "**Beyond the Mask: Modern Frontiers in Ovarian Cancer Diagnosis & Care**." Ovarian cancer continues to represent a significant challenge in gynaecologic oncology owing to its insidious onset, late-stage diagnosis, and high rates of recurrence. This special issue has been curated to address these challenges through a comprehensive, contemporary, and evidence-based academic approach.

Recent advances in molecular diagnostics, imaging modalities, surgical techniques, and targeted therapies have substantially transformed the management of ovarian cancer. This issue encompasses a wide spectrum of topics, including emerging strategies in early detection, precision medicine with PARP inhibitors, advanced cytoreductive surgical approaches with HIPEC, management of recurrent disease, hereditary risk assessment, and global guideline-based practices. Together, these contributions provide a balanced and in-depth overview of current and evolving standards of care.

The scholarly strength of this Bulletin lies in the valuable contributions of the authors, whose expertise and commitment have enriched this edition. Their work reflects a collective endeavour to translate scientific progress into meaningful clinical practice, with the ultimate aim of improving outcomes for women with ovarian cancer. I would like to place on record our sincere appreciation to Dr Sharda Patra for her pivotal role in conceptualizing and coordinating this special edition.

We extend our gratitude to all contributors, the AOGD Secretariat, and our readership for their continued support and engagement. We trust that this special issue will serve as a useful academic resource and stimulate evidence-based clinical practice and further research in the field of gynaecologic oncology.

With kind regards,

The Editorial Team

Unmasking the Silent Threat: Advances in Early Detection of Ovarian Cancer

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Background

Ovarian cancer remains a leading cause of gynaecologic cancer mortality worldwide with nearly 314,000 new cases and 207,000 deaths globally, as per GLOBOCAN 2020.[1] Crucially, most ovarian cancers are diagnosed at advanced stages where five-year survival is dismal (~30%) for late-stage disease but exceeds 90% if detected early.[2] Early detection thus has enormous potential to improve outcomes. However, current screening methods (e.g. CA-125 blood tests, ultrasound) have failed to reduce mortality with screening trials (PLCO, UKCTOCS) showed no survival benefit and are not recommended for average-risk women.[3] Against this backdrop, global research efforts over the years have focused on novel biomarkers, advanced imaging, and AI driven tools to "unmask" early ovarian cancer and with molecular and genetic advancements, early detection of ovarian cancer is becoming a possibility and may lead to improved prognostication and early treatment of the same in the near future.

Conventional Screening Paradigms: Evidence, Expectations, and Limitations:

CA-125 and transvaginal ultrasound (TVUS) have long been the basis of ovarian cancer screening, but both have major limitations. CA-125 is elevated in most advanced cancers yet detects only about half of early-stage disease and lacks specificity, while TVUS identifies adnexal masses but poorly discriminates benign from malignant lesions. Large randomized trials have been disappointing: UKCTOCS (approximately 200,000 women) showed no significant mortality reduction with multimodal screening, and the PLCO trial (approximately 78,000 women) reported no difference in ovarian cancer mortality between screened and unscreened groups, with substantial false positives and unnecessary surgeries[3]. Consequently, major guidelines advise against population screening outside clinical trials.

Even with intensive screening strategies, early-stage detection remains limited. Only about 15% of screen-detected cancers in UKCTOCS study were stage I–II. Algorithms such as ROCA (risk of ovarian cancer algorithm) and studies like Normal-Risk Ovarian Screening Study (NROSS) have improved specificity and positive predictive value, but have not yet demonstrated a clear survival benefit[4]. These limitations have driven a shift toward molecular and computational approaches, including liquid biopsies, advanced imaging, and AI-based diagnostics, to enable earlier and more accurate detection.

Current Imaging Modalities used for detection of Ovarian Cancer

The diagnosis of ovarian cancer at an early stage has always been a challenge and currently imaging combined with biomarker testing is used to diagnose and categorize ovarian masses. The initial evaluation of any adnexal mass is done by a pelvic ultrasound. Transvaginal ultrasonography has shown improved sensitivity and specificity time and again when done by expert sonologists and when this modality is combined with use of CA125 biomarker[5,6]. Also, the utilization of ORADS (Ovarian-Adnexal Reporting and Data System) for categorization of ovarian masses has shown a sensitivity and specificity of 52% and 84% respectively[7]. TVS has reported a diagnostic accuracy of 89% for detection of ovarian carcinomatosis in a prospective analysis.[8]

CT scans are commonly used across the world for evaluation of ovarian malignancies. Their sensitivity varies from 40.7% to 92.16% and specificity from 57.14 to 89.1%.[9,10] When CT scans are used in collaboration with laparoscopy; it has been seen to increase the sensitivity to 87.5% from 56.7%.[11]

MRI has been reported to have a higher diagnostic accuracy in differentiation of benign from malignant ovarian masses[12]. Especially diffusion weighed MRI scans give better delineation of soft tissues and thus lend a helping hand in staging of ovarian cancers[13]. MRI scan along with gadolinium enhancement have reported a sensitivity and specificity of 91% and 87% respectively for diagnosis of residual tumor in treated patients of carcinoma ovary.[14] ORADS-MRI scoring system has also been used time and again for diagnosing ovarian tumors.

Another scoring system that has shown high diagnostic accuracy is the RMI or risk of malignancy index. It combines the ultrasound features along with CA125 values and menopausal status of the woman for predicting the chance of malignancy in an ovarian mass.[15]

PET scans are not commonly used as a first line investigation for evaluation of adnexal masses but it has proved to have the highest capability of detecting malignancy[16]. The sensitivity for diagnosing recurrence with PET scans is around 84.6% to 90% with a specificity of 100%[17]. The drawback of PET scans includes poor sensitivity for detection of lymph node metastasis and poor evaluation of peritoneal carcinomatosis.[18] The use of tracers other than FDG (18 F flurodeoxy glucose) like fibroblast activation

protein inhibitors (FAPI) have shown rapid advancements for decision making and treatment planning of ovarian cancer.[19]

Table 1: Current imaging Modalities used for detection of Ovarian Cancer

Diagnostic Modality	Sensitivity	Specificity	Remarks
1. Imaging Modalities: • TVS	84%	96%	For detection of ovarian carcinomatosis5
• CT scan6,7	40.7 -92.16% 91%	57.14-89.1% 87%	
• MRI scan	84.6-90%	100%	MRI with gadolinium11
• PET scan			For recurrent cases14

Decoding the Invisible: Molecular and Computational Advances in Early Ovarian Cancer Detection:

Recent advances in **liquid biopsy and molecular diagnostics** are redefining the paradigm of early ovarian cancer detection beyond conventional CA-125 and transvaginal ultrasound. Among these, **circulating tumor DNA (ctDNA) analysis**, particularly **cfDNA fragmentomics integrated with serum protein markers (CA-125, HE4) and machine learning algorithms**, has demonstrated a substantial improvement in early-stage detection. A landmark multicentre study published in 2025 reported sensitivities of approximately **72% for stage I and 69% for stage II ovarian cancer at >99% specificity**, markedly outperforming CA-125 alone, while detecting nearly **90% of high-grade serous carcinomas**, underscoring the promise of integrated multi-analyte approaches[20].

Targeted ctDNA mutation assays, focusing on ubiquitous driver alterations such as **TP53 and BRCA1/2**, have shown high analytical specificity and are increasingly validated in minimal residual disease and recurrence monitoring. However, their sensitivity for primary screening in asymptomatic populations remains limited due to extremely low tumor fractions, necessitating further technical refinement and prospective evaluation.

Epigenetic biomarkers, particularly **cfDNA methylation signatures**, represent another promising strategy, as aberrant methylation is an early oncogenic event. Multi-gene methylation panels consistently outperform single-gene assays, achieving sensitivities in the **70–90% range** in exploratory and case-control studies. Nevertheless, most data remain retrospective, highlighting the critical need for large-scale prospective screening trials before clinical implementation.

Similarly, **non-coding RNAs**, including **microRNAs, long non-coding RNAs, and circular RNAs**, have demonstrated high diagnostic accuracy in pilot studies, with some panels achieving near-perfect discrimination in small cohorts. Despite their biological stability and ease of detection, lack of assay standardization and limited sample sizes currently preclude routine clinical use, emphasizing the requirement for robust validation in blinded cohorts.[21]

Exosome based assays, leveraging tumor-derived extracellular vesicles enriched with markers such as **EpCAM, CD24, and CA-125**, offer a multiomic snapshot of tumor biology. While early studies report high diagnostic accuracy, challenges related to isolation techniques, specificity, and reproducibility currently limit translational applicability.[22]

Parallel progress in **protein and multi-analyte panels**, increasingly analysed through **artificial intelligence and machine learning frameworks**, has improved early stage sensitivity by integrating proteomic, metabolomic, and genomic signals, reflecting a broader shift toward holistic biomarker strategies.

Advanced imaging techniques and analysis algorithms are also pushing earlier detection. Standard TVUS and MRI remain the workhorses, but new twists are emerging. Contrast-enhanced ultrasound (CEUS) and Doppler imaging are being refined to better characterize small ovarian lesions, though definitive trials are lacking. Micro-ultrasound (higher-frequency transducers) is under study for gynaecologic use. On MRI, diffusion-weighted imaging and perfusion imaging can sometimes pick up tumor characteristics before masses are obvious. Functional imaging (e.g. PET with novel tracers) is not yet used for screening, but may aid in problem-solving.

Importantly, hybrid and AI-enhanced imaging show promise. A 2025 European Journal of Gynecologic Oncology study developed a deep-learning radiomics nomogram combining ultrasound and MRI features: the model's AUC was 0.957 in distinguishing benign vs. malignant ovarian tumors.[23]**.** In the test cohort, sensitivity was 92.7% and specificity 98.6%, far outperforming ultrasound or MRI alone. This indicates that integrated multi-modality imaging + AI can greatly refine diagnostic accuracy. Similarly, Wang et al. (2025) reported that a ResNet50–VisionTransformer model on ultrasound images significantly improved classification: primary physicians' accuracy jumped from 76% to 91–96% when aided by AI.[24]

Overall, the field is moving decisively toward **integrated, AI-driven, multi-omics and imaging-based strategies.** While results are highly promising, most approaches remain investigational, and robust prospective trials are essential before these technologies can be adopted for population-level or high-risk ovarian cancer screening.

Table 2: New Frontiers in Early Ovarian Cancer Detection: A Comparative Overview

Modality	Principle	Advantages	Limitations / Current Status
ctDNA & Fragmentomics	Analysis of tumor derived cfDNA fragmentation patterns, copy number changes	Non-invasive; detects molecular changes before radiologic disease; high specificity	Expensive; requires ultra-deep sequencing and needs large prospective validation
Targeted ctDNA Mutation Panels	Detection of known driver mutations (TP53, BRCA1/2) in plasma	High specificity; biologically robust	Low sensitivity for early-stage disease; tumor fraction extremely low in screening population
DNA Methylation Biomarkers	Detection of aberrant promoter methylation in cfDNA	Early oncogenic event; stable biomarker; high discrimination	Mostly retrospective data; lack of prospective screening trials
MicroRNAs (miRNAs)	Circulating tumor-associated miRNA expression profiles	Stable in blood; easily measurable	Small cohorts; poor standardization; interstudy variability
Exosomes / Extracellular Vesicles	Detection of tumor-derived vesicles carrying proteins, RNA, DNA	Rich multi-omic content; stable	Isolation challenges; lack of standardized protocols; experimental
Multi-Analyte Panels (Proteomics / Metabolomics)	Integration of proteins, metabolites, cfDNA, RNA using AI	Captures tumor heterogeneity; synergistic performance	High computational demand; complex validation
AI-Enhanced Imaging (US + MRI)	Radiomics and deep learning on imaging data	Reduces operator dependency; scalable	Retrospective datasets; regulatory and validation challenges

However, there are major limitations: lack of external validation, standard reporting, and potential biases in training. In practice, no AI tool has yet received regulatory approval for standalone screening.

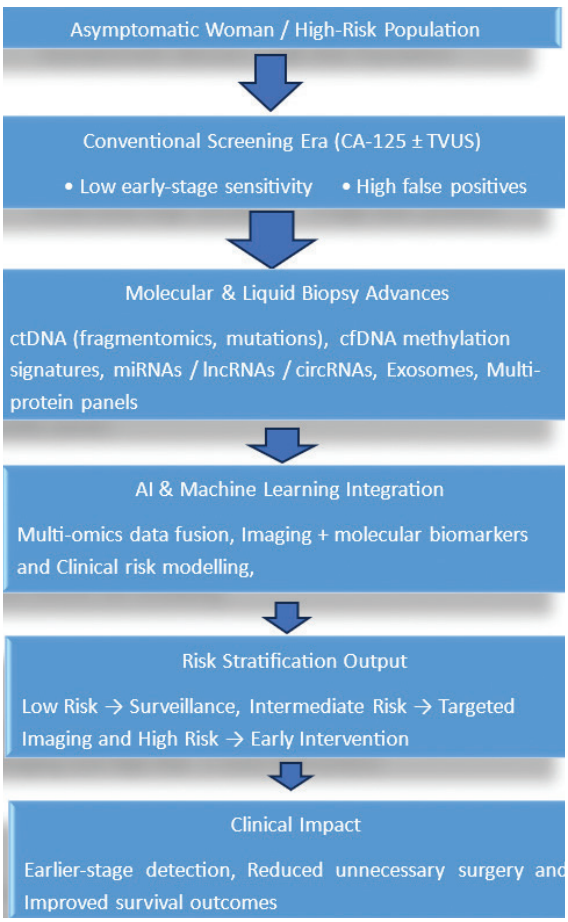

Fig 1: Conceptual overview of evolving strategies for early detection of ovarian cancer, highlighting the transition from conventional screening to integrated molecular, imaging, and AI-driven approaches.

Clinical Trials and Translational Research

Several recent trials and studies provide real world insight into early detection strategies. Aside from UKCTOCS/PLCO (past trials showing negative results), newer trials have explored refined approaches. The Normal-Risk Ovarian Screening Study (NROSS, JCO 2024) followed US women with annual CA-125 (using ROCA) and TVUS as needed. Over 21 years, it detected 34 ovarian cancers with a PPV of 50% well above the 10% target. Importantly, NROSS reported a significant stage shift: many screen-detected cancers were early-stage (and overall survival was better than expected).[25] These findings suggest that the two-step strategy could reduce late-stage diagnoses, though mortality impact is still under evaluation.

Other trials are underway. The United Kingdom has initiated the UK-CTRB3 trial of cfDNA screening in high-risk women (NCT05049470), and the planned U.S. WISE (Women's Early Detection of Ovarian Cancer) trial will test a multi-marker blood test in thousands of women. The PapSEEK approach (testing cervical or uterine fluid for tumor DNA) demonstrated 45% detection of ovarian cancer in a JAMA study.[26]

Translational research in this regard is also collecting serial blood from high-risk women for eventual retrospective marker analysis (e.g. the UKCTOCS biobank, and research initiatives by the Gynecologic Cancer InterGroup). Multi-cancer early detection (MCED) blood tests (like Galleri) now include ovarian cancer in their target tissue repertoire, raising the possibility that women might get an incidental early "signal" of ovarian cancer from a multi-cancer screen, although sensitivity for ovarian cancer in that context is still modest.

Barriers to Clinical Translation and Future Directions:

Despite progress, major challenges remain. Ovarian cancer is biologically heterogeneous (multiple histologic subtypes), which complicates screening. A single biomarker or algorithm may not capture all subtypes equally, for instance, mucinous or clear-cell tumors might shed less DNA or express different markers than high-grade serous tumors. This heterogeneity argues for multi-modal approaches but also makes validation harder. Additionally, the absence of a well-defined "preclinical" phase (as in cervical cancer with Pap smears) means that screening must catch asymptomatic invasive disease.

There are practical hurdles to any screening program. False positives can cause unnecessary anxiety and surgeries; any new test must have very high specificity. Large-scale trials (like UKCTOCS) are expensive and take years. Regulatory and implementation issues, such as standardizing AI algorithms, ensuring access to advanced diagnostics in low-resource settings, and training personnel; are non-trivial. Moreover, the vast majority of studies to date have been in Europe, North America or East Asia; their applicability to other regions (with different prevalence and resource levels) needs confirmation.

Nonetheless, the field is rapidly evolving. Technological advances (ultra-sensitive sequencing, cheaper computation, new imaging probes) and methodological best practices are moving us toward feasible early-detection solutions. Combining multiple biomarkers (genetic/epigenetic, proteomic, imaging features) through AI-driven integrative models appears particularly promising. For example, hybrid tests that analyze cfDNA patterns *and* protein levels have shown synergistic improvement in sensitivity for early-stage disease.[20]

In the coming years, international collaborations and harmonized studies will be key, with efforts focussing on: (1) collecting pre-diagnostic samples from large cohorts; (2) prospectively evaluating multi-analyte panels in women at high risk (e.g. BRCA carriers); (3) validating AI models on diverse populations and machines; and (4) ensuring equity in access, so that any successful screening tool benefits women globally.

Conclusion

Ovarian cancer's "silent" nature has long thwarted early detection, but recent innovations offer hope. Over the past five years, breakthroughs in liquid biopsy (e.g. cfDNA fragmentomics), multi-omic biomarkers (circRNAs/miRNAs), and AI-enhanced imaging have dramatically increased our ability to detect occult disease in principle. Statistically significant gains suggest that a practical early-detection test may finally be within reach. Ongoing clinical studies will determine whether these laboratory advances translate to reduced mortality. In the meantime, clinicians should stay informed about emerging diagnostics, as they may soon complement existing strategies. The global gynaecologic oncology community must be prepared to critically evaluate and adopt validated tools, with the ultimate goal of shifting ovarian cancer from a silent killer to a largely preventable disease through early intervention.

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Cutting edge Surgical strategies : From Cytoreduction to HIPEC in Ovarian Cancer Management

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Introduction

Optimal cytoreduction remains one of the cornerstones in the management of advanced ovarian cancer. The aim of cytoreductive surgery is complete gross tumor resection. This is because the amount of residual disease after cytoreductive surgery is a strong predictor of survival. The benefits of surgery include removal of poorly vascularized tumor where chemotherapeutic agents have poor access, as well as the removal of chemoresistant clones leaving behind smaller residual implants with a higher growth fraction which are more susceptible to chemotherapy.

Cytoreduction can be performed in primary, interval, and recurrent (secondary) settings. Optimal cytoreduction, as defined by the CC (Completeness of Cytoreduction) Score which assesses the extent of residual tumor after surgery is CC-0 (no visible residual disease) and CC-1 (residual tumor < 2.5 mm), with aim to achieve CC-0 wherever possible. Cytoreductive surgery which leaves behind any residual tumor of larger than 2.5 mm – CC-2 (residual tumor between 2.5 mm to 2.5 cm) or CC-3 (extensive residual disease greater than 2.5 cm) is defined as suboptimal cytoreduction.

Hyperthermic Intraperitoneal Chemotherapy (HIPEC) is an additional armamentarium with the surgeon in advanced ovarian cancer. The addition of HIPEC after optimal cytoreduction in interval setting has shown to significantly improve survival in randomized trials. The use of HIPEC in primary and secondary setting, however, remains investigational at present.

Primary Cytoreduction

Cytoreduction to no gross residual disease includes hysterectomy with bilateral salpingo-oophorectomy, peritonectomy, total omentectomy and excision of bulky pelvic and retroperitoneal lymph nodes. It may require 'radical' and 'ultra-radical' procedures including, rectosigmoid resection, small and/or large bowel resection-anastomosis, diaphragm peritonectomy or full thickness resection, splenectomy with or without distal pancreatectomy, cholecystectomy, and resection of parenchymal liver disease and porta hepatis disease; all of which can be performed with minimal additional morbidity. However, involvement of pancreatic head, confluent disease over most of small bowel and/or its mesentery, deep infiltration of porta hepatitis, and disease involving root of mesentery precludes a complete primary cytoreduction. Similarly peritoneal disease which require multiple bowel resections and anastomosis increase the risk of postoperative complications and decrease outcomes of primary cytoreductive surgery.

Cytoreduction involves peritonectomy, which can be selective parietal peritonectomy (SPP) that comprises of resection of macroscopically involved peritoneum, or a total parietal peritonectomy (TPP) performed for peritoneal carcinomatosis. Occult disease may be present in apparently normal looking peritoneum.[1] Multicenter studies may be needed to assess if a routine TPP would improve the survival outcomes with acceptable morbidity, compared to SPP.

The role of systematic lymphadenectomy, essentially the removal of clinically 'normal' nodes, in improving the survival outcomes in advanced ovarian cancer is controversial. While retrospective observational studies and meta-analyses including such trials have shown an improvement in OS[2,3], the two RCTs revealed no significant difference in OS between the lymphadenectomy and no-lymphadenectomy groups (OS: HR=1.02; 95% CI=0.85–1.22).[4,5] In fact, the LION trial[4] reported that in spite of detecting microscopic disease in 56% of clinically 'normal' nodes, systematic lymphadenectomy did not improve survival in advanced ovarian cancer.

The selection of patients for primary cytoreduction is crucial. It depends on the general condition and performance status of the patient, as well as the disease factors. Computed tomography (CT) imaging is the standard of care for pre-operative evaluation of the extent of disease in ovarian cancer. Contrast enhanced magnetic resonance imaging (MRI) with diffusion-weighted imaging (DWI) has shown to be superior to CT in detecting small peritoneal and bowel deposits. In a prospective comparative study with surgery as the reference standard, whole-body MRI using DWI was superior to CT and to PET-CT in the assessment of bowel serosal and mesenteric disease.[6] Fluorodeoxyglucose (FDG) PET-CT can detect lymph node and distant metastasis with high accuracy, and may be superior to CT in this regard.[7,8]

Radiological signs of unresectability include involvement of the bladder trigone, large diaphragm involvement, infiltration of the pancreatic head, mesenteric clumping or retraction and infiltration of the porta hepatis. Several models for prediction of resectability, including clinical and radiological criteria have been reported and validated by various authors including Suidan et al, Janco et al, Nelson

et al, Dowdy et al and Borley et al.[9-13] The peritoneal cancer index (PCI) is used to quantify the extent of peritoneal disease during surgery and current ESGO (European society of gynecologic oncology) guidelines recommend documenting it for all patients. The use of PCI applied to CT scan (CT-PCI) was considered by Diaz-Gil et al as a feasible and valid tool for evaluating 5-year survival.[14] Another study evaluated the importance of CT-PCI in the selection of patients for cytoreductive surgery, where patients with a score >15 were recommended neoadjuvant chemotherapy.[15]

Extensive bowel involvement – both serosal and mesenteric – may present a major limitation in optimal cytoreduction. Small peritoneal and bowel deposits (<5mm) are difficult to see on CT imaging. Hence diagnostic laparoscopy has been considered in the pre-operative assessment of ovarian cancer.[16] Studies incorporating CT-PCI and diagnostic laparoscopy have shown high sensitivity to detect peritoneal disease and to predict optimal or suboptimal cytoreduction in patients with advanced ovarian cancer.[17] The Fagotti score is a quantitative, laparoscopy based model for predicting the chance of optimal cytoreduction and includes 7 parameters: omental caking, peritoneal carcinomatosis, diaphragmatic carcinomatosis, mesenteric retraction, bowel and /or stomach infiltration and liver metastasis.[18]

Neo-adjuvant Chemotherapy and Interval Cytoreduction

Neo-adjuvant chemotherapy (NACT) is indicated in advanced ovarian cancer in the following conditions - poor performance status of the patient, when pre-operative evaluation precludes optimal cytoreduction, presence of pleural effusion, intraparenchymal liver metastasis, intraparenchymal lung metastasis, and presence of involved supraclavicular and/or inguinal lymph nodes and bulky suprarenal retroperitoneal lymph nodes. When NACT is planned, cytological and cell block evaluation of ascitic fluid or a tissue biopsy is performed prior to initiating chemotherapy. Wherever possible, an image guided biopsy from a representative lesion should be taken and sent for histopathological evaluation with immunohistochemistry.

Two randomized trials comparing primary and interval cytoreduction have shown similar progression-free survival (PFS) and overall survival (OS) in both arms.[19,20] However, these trials were criticized due to the quality of cytoreduction (40% optimal cytoreduction in primary debulking arm) , short operative times, low survival rates (12 months PFS and 24 months OS), patient heterogeneity (disease stage and performance status) and low accrual per center.

The recently published SCORPION trial used a standardized laparoscopic predictive index to randomize patients between primary and interval cytoreduction.[21] The trial was designed for a single institution with high accrual of patients per year and committed to maximal surgical effort. However, even this trial showed similar survival outcomes between the two arms, albeit with better OS rates (OS 41 months for primary and 43 months for interval p=0.56). The recently published TRUST trial - a randomized controlled trial (RCT) – is the first to have reported significantly better PFS and numerically longer OS with primary cytoreduction in appropriately selected patients, as compared to interval cytoreductive surgery.[22]

Secondary Cytoreduction

Three different RCTs have reported different outcomes with Secondary cytoreduction. DESKTOP III trial reported better overall survival rates with secondary cytoreduction followed by chemotherapy as compared to chemotherapy alone. The selection criteria was a positive AGO score (complete resection at initial surgery, ECOG status ≤ 1, and ascites ≤ 500 ml at recurrence) and optimal cytoreduction was achieved in 75% women.[23] The SOC-1 trial based on iMODEL criteria ≤ 4.7 (criteria including FIGO stage at primary diagnosis, residual disease after primary surgery, Platinum-free interval, ECOG status, CA-125 level at recurrence and presence of ascites at recurrence) for selection of suitable patients, also found better PFS with surgery in the recurrent setting.[24] The GOG 213 trial, however, did not report any survival benefit with secondary cytoreduction, but this trial did not define any selection criteria (investigator determined resectable disease), and also used Bevacizumab in both arms which probably affected the outcomes.[25]

BRCA mutated cases of ovarian cancer constitute a different subset of patients, being more chemo responsive, amenable to targeted therapy with PARP inhibitors, and showing better survival outcomes. Future trials on secondary cytoreduction should consider the BRCA status of patients to demonstrate its differential benefit, if any, in BRCA wild and BRCA mutated cases.

Cytoreductive Surgery with HIPEC

The randomized OVHIPEC trial in 2018 demonstrated an enhanced OS and DFS (Disease-free survival) after adding HIPEC for patients that underwent interval cytoreductive surgery for FIGO stage III epithelial ovarian cancer, without increasing the morbidity. After a median follow-up of 4.7 years, survival data for patients in the HIPEC arm were better than those in the control group: 15 versus 11 months, respectively, for DFS (HR = 0.65; P = 0.003) and 48 versus 34 months, respectively, for OS (HR = 0.64; P = 0.01)[26]. The Korean phase III trial evaluating HIPEC in the upfront and interval settings, reported on 184 patients who had CRS and HIPEC in the upfront setting. There was no difference in progression free survival (PFS) or overall survival (OS)

between the HIPEC and control arms. However, in the group undergoing interval cytoreduction, PFS was 15.4 months in the control group and 17.4 months in the HIPEC group (P = .04), and the OS was 48.2 months in the control group and 61.8 months in the HIPEC group (P = .04).[27]

The international OVHIPEC-2 trial is evaluating HIPEC with cisplatin during primary cytoreduction - Stage III ovarian cancer patients will be randomized immediately following optimal cytoreduction (≤ 2.5 mm residual) into HIPEC versus no HIPEC. Participants will then receive intravenous (IV) carboplatin and paclitaxel for 6 cycles, with option of bevacizumab [28]. The CHIPPI trial is another phase III randomized trial evaluating the impact of HIPEC in both primary and interval setting as well as the impact of HIPEC on the quality of life and the risk - benefit ratio.[29]

Two randomized trials have explored the role of HIPEC in recurrent ovarian cancer. A randomized Phase II trial showed that PFS in HIPEC patients was 12.3 months compared to 15.4 months in non-HIPEC patients while OS in HIPEC patients was 53.1 months compared to 69.2 months in non-HIPEC patients. In contrast to other prospective HIPEC trials, this study utilized carboplatin rather than cisplatin.[30] Another prospective, randomized Phase III trial in recurrent ovarian cancer reported a significant OS benefit in the HIPEC arm (26.7 vs 13.4 months), but the study did not report PFS, postoperative complication rates, or adjuvant chemotherapies. This trial has been heavily criticized for its study design.[31]

The recently published prospective CHIPOR study evaluated HIPEC with Cytoreduction versus Cytoreduction alone in platinum - sensitive relapse patients after their first relapse.[32] It reported that adding HIPEC to cytoreductive surgery after response to 6 cycles of platinum-based chemotherapy at first epithelial ovarian cancer recurrence, significantly improved overall survival. The HORSE trial is another RCT which recently reported the difference in survival rates with Cytoreduction plus HIPEC versus Cytoreduction alone (without neo-adjuvant chemotherapy) in platinum-sensitive first recurrence of ovarian cancer.[33] It, however, reported differently than the CHIPOR study – that the addition of HIPEC to complete or nearly complete primary Secondary cytoreduction did not confer a benefit in terms of PFS in patients with platinum-sensitive peritoneal recurrence.

A recent meta-analysis showed that the combination of HIPEC with interval CRS and neoadjuvant chemotherapy is a safe option that significantly improved 5-year OS and DFS. Its use in other settings should continue to be considered investigational.[34]

Data on efficacy of HIPEC in relation to BRCA mutational status in advanced ovarian cancer requires further development. Ghirardi et al found significantly better PFS and OS in BRCA mutated cases compared to BRCA wild cases without HIPEC, but these survival rates equalized between the two groups with administration of HIPEC, suggesting that HIPEC may be of benefit in BRCA wild type.[35] However, when we study the trials on intraperitoneal chemotherapy including GOG 172, women with mutated BRCA1 expression had markedly better survival rates when given intraperitoneal chemotherapy.[36,37]

There are various drugs and drug combinations reported in literature for HIPEC in advanced ovarian cancer.[38] The most commonly used drug is Cisplatin ranging in dose from 75 to 100 mg/m^2. Only cisplatin at a dose of 100mg/m2 has been included in the NCCN guidelines for HIPEC in Stage III ovarian cancer after neoadjuvant chemotherapy.[39] However, administration of 100 mg/m2 of Cisplatin requires the use of nephron-protective agents like sodium thiosulfate. Other drugs used in HIPEC are paclitaxel 175 mg/m2 alone or cisplatin plus paclitaxel. These regimens are suggested for patients with platinum-sensitive disease. Favorable outcomes have been also reported with administration of 35 mg/ m2 doxorubicin and 175 mg/m2 paclitaxel or 15 mg/m2 mitomycin for platinum- resistant disease.[40]

Conclusion

Cytoreduction should aim at no gross residual tumor (CC-0) in order to improve survival outcomes in advanced ovarian cancer. When the general condition of patient is good and optimal cytoreduction is possible in primary setting with acceptable morbidity, primary cytoreduction should be done followed by 6 cycles of adjuvant chemotherapy. When the general condition of the patient is poor, or when pre-operative radiological evaluation precludes optimal cytoreduction due to extensive disease, neo-adjuvant chemotherapy should be started (after tissue biopsy and histopathological confirmation of ovarian malignancy), and the patient assessed for interval cytoreduction after 3-4 cycles of NACT.

Secondary cytoreduction should be reserved for patients with a long disease-free or platinum-free interval with low volume, oligo-metastatic disease. Future trials on secondary cytoreduction should consider the BRCA status of patients to demonstrate its differential benefit, if any.

The addition of HIPEC after optimal cytoreduction in interval setting has shown to significantly improve survival in randomized trials, with acceptable morbidity. The use of HIPEC in primary and secondary setting, however, needs to be corroborated with Level 1 evidence and hence, remains investigational at present.

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Precision Medicine in Action: The Rise of PARP Inhibitors in Ovarian Cancer Therapy

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Introduction

Epithelial ovarian cancer (EOC) remains the leading cause of gynaecologic cancer death worldwide, largely because most women present with advanced-stage disease and relapse after an initial response to platinum-based chemotherapy.[1] High-grade serous ovarian carcinoma (HGSOC), the predominant histological subtype, is characterised by widespread genomic instability and frequent defects in homologous recombination repair (HRR), most notably through BRCA1/2 mutations.[2,3] For many years, platinum sensitivity was recognised as a clinical surrogate for underlying DNA repair deficiency, but this insight did not translate into targeted treatment beyond repeated cycles of platinum.

Poly(ADP-ribose) polymerase (PARP) inhibitors have fundamentally changed this landscape. By exploiting synthetic lethality in tumours with homologous recombination deficiency (HRD), PARP inhibitors can selectively kill cancer cells while sparing normal tissue. [4] Within just over a decade, they have evolved from experimental agents into a central component of standard-of-care management for newly diagnosed and recurrent ovarian cancer, particularly in women with BRCA-mutated or HRD-positive tumours.[5–9]

This review summarises the biological rationale for PARP inhibition, the major clinical trials defining their role, the central importance of biomarker-driven patient selection, safety and resistance issues, and practical considerations for implementing PARP inhibitors in routine practice, including in resource-constrained settings. The focus is on high-quality evidence from phase II–III trials and contemporary international guidelines.

1. Biological rationale: DNA repair, synthetic lethality and HRD

1.1 PARP function and synthetic lethality

DNA is constantly subjected to endogenous and exogenous damage, generating single-strand breaks (SSBs) and double-strand breaks (DSBs). PARP1 and PARP2 are nuclear enzymes that detect SSBs and catalyse the addition of ADP-ribose polymers onto target proteins, a signal that recruits base-excision repair machinery.[10] Inhibition of PARP leads to persistence of SSBs; during DNA replication, these lesions are converted into DSBs when replication forks encounter them.

In normal cells with intact homologous recombination repair, DSBs are accurately repaired using a sister chromatid template through a pathway that depends on BRCA1, BRCA2, RAD51 and other HR proteins.[11] In contrast, cells with HRD cannot efficiently repair DSBs and instead rely on error-prone mechanisms such as non-homologous end joining, leading to chromosomal instability and cell death. When PARP is inhibited in HR-deficient cells, the combined impact of unrepaired SSBs and HRD is lethal—a phenomenon known as synthetic lethality.[4,11]

Beyond catalytic inhibition, many PARP inhibitors also "trap" PARP–DNA complexes at sites of damage, physically blocking replication fork progression. The potency of PARP trapping varies among agents (talazoparib > niraparib ≳ olaparib ≳ rucaparib in preclinical studies) and may contribute to differences in both antitumour activity and toxicity.[12]

1.2 Homologous recombination deficiency beyond BRCA

Germline and somatic pathogenic variants in BRCA1/2 account for approximately 15–25% of HGSOC.[2,3] However, genomic analyses indicate that up to 50% of HGSOC harbour broader HRD due to alterations in other HRR genes (e.g. RAD51C/D, BRIP1, PALB2), promoter methylation of BRCA1, or other mechanisms that impair HR.[2,13,14] Tumours with this "BRCAness" phenotype show high levels of genomic scarring, including loss of heterozygosity and large-scale chromosomal aberrations, and exhibit enhanced sensitivity to both platinum and PARP inhibitors.[13,15]

Commercial HRD assays, such as the MyChoice® HRD test, integrate measures of genomic instability (loss of heterozygosity, telomeric allelic imbalance, large-scale state transitions) into a composite HRD score, combined with BRCA1/2 mutation status.[15] A predefined cut-off (e.g. score ≥42 or presence of a BRCA mutation) was used to define HRD-positive tumours in pivotal trials such as PAOLA-1 and PRIMA.[7,8,16] While these assays are imperfect surrogates of functional HRD and may be expensive or unavailable in many regions, they have become important tools for patient selection and reimbursement decisions.

2. Clinical evolution of PARP inhibitors in ovarian cancer

2.1 From relapse treatment to maintenance therapy

The first approvals of PARP inhibitors in ovarian cancer were for treatment of recurrent, heavily pretreated BRCA-mutated disease. For example, early single-arm trials of olaparib in germline BRCA-mutated, platinum-resistant ovarian cancer demonstrated objective response rates of around 30–40%.[17,18] Similar activity was shown with rucaparib and niraparib in later-line settings.[19,20] However, durable disease control was limited, and toxicity accumulated with prolonged continuous therapy.

Subsequently, attention shifted to using PARP inhibitors as **maintenance therapy**—that is, consolidating a response to platinum-based chemotherapy by continuing PARP inhibition as a lower-burden oral treatment. This strategy leverages the observation that platinum-sensitive tumours are often HR-deficient and may derive particular benefit from ongoing PARP blockade after chemotherapy has debulked the disease burden.

2.2 PARP inhibitors as maintenance in platinum-sensitive recurrent disease

Several phase III trials established PARP inhibitors as effective maintenance therapy following response to platinum in recurrent ovarian cancer.

NOVA (niraparib) randomised patients with platinum-sensitive recurrent EOC who had achieved a complete or partial response to platinum to niraparib or placebo.[21] Patients were stratified into a germline BRCA-mutated cohort and a non-germline BRCA cohort. PFS was significantly prolonged with niraparib in both groups: median PFS 21.0 vs 5.5 months in the germline BRCA cohort (hazard ratio [HR] 0.27), and 9.3 vs 3.9 months in the non-germline BRCA cohort (HR 0.45).[21] These results showed that PARP maintenance could benefit not only BRCA-mutated but also a broader population, albeit with a gradient of benefit according to underlying HRD.

SOLO2 (olaparib) evaluated olaparib tablets as maintenance in women with platinum-sensitive, relapsed HGSOC and germline BRCA mutations.[22] Olaparib significantly improved median PFS (19.1 vs 5.5 months; HR 0.30). Subsequent OS analyses showed a clinically meaningful survival advantage despite substantial cross-over to PARP inhibitors in the placebo arm.[23]

ARIEL3 (rucaparib) randomised patients with platinum-sensitive, recurrent high-grade ovarian carcinoma, who had responded to their most recent platinum regimen, to rucaparib or placebo.[24] The trial pre-specified three nested cohorts: BRCA-mutated, HRD-positive (including BRCA-mutated), and the overall intention-to-treat population. Rucaparib significantly improved PFS in all cohorts, with the largest benefit in BRCA-mutated tumours (median PFS 16.6 vs 5.4 months; HR 0.23), but a clinically relevant effect even in HRD-negative disease.[24]

Collectively, these studies firmly established PARP inhibitors as standard maintenance therapy following platinum-sensitive recurrence, particularly in patients with BRCA mutations or evidence of HRD.

2.3 Expansion into first-line maintenance

The most dramatic change in the treatment paradigm occurred when PARP inhibitors moved into the **first-line maintenance** setting for newly diagnosed advanced ovarian cancer.

SOLO1: changing the natural history of BRCA-mutated disease

SOLO1 enrolled women with newly diagnosed FIGO stage III–IV HGSOC or related histologies, harbouring germline or somatic BRCA1/2 mutations, who had achieved a complete or partial response to first-line platinum–taxane chemotherapy.[5] Patients were randomised 2:1 to olaparib (300 mg twice daily) or placebo for up to two years (longer allowed if there was residual disease).

At the primary analysis, olaparib reduced the risk of disease progression or death by 70% (HR 0.30; 95% CI 0.23–0.41).[5] At a median follow-up of 41 months, median PFS was not reached in the olaparib arm versus 13.8 months with placebo.[5] An updated analysis with longer follow-up reported a sustained benefit, with a substantial proportion of patients in the olaparib arm remaining recurrence-free several years after discontinuing treatment.[6] These results suggest that, for some women with BRCA-mutated disease, finite-duration first-line PARP inhibition may contribute to functional cure.

PRIMA: niraparib in higher-risk newly diagnosed disease

PRIMA (ENGOT-OV26/GOG-3012) enrolled patients with newly diagnosed, advanced high-grade ovarian cancer who were at higher risk of relapse (e.g. stage IV, or stage III with residual disease after primary surgery).[8] After responding to first-line platinum-based chemotherapy, participants were randomised to niraparib or placebo maintenance for up to three years.

Niraparib significantly improved PFS in the overall population (median 13.8 vs 8.2 months; HR 0.62).[8] The magnitude of benefit was greater in the HRD-positive subgroup (median 21.9 vs 10.4 months; HR 0.43) but was also seen, to a lesser extent, in HR-proficient tumours (median 8.1 vs 5.4 months; HR 0.68).[8] Importantly, later analyses incorporating an individualised starting dose (200 mg daily for patients with lower body weight or baseline thrombocytopenia) demonstrated improved

haematological tolerability without compromising efficacy.[25]

PAOLA-1: combining PARP inhibition with anti-angiogenic therapy

PAOLA-1 (ENGOT-ov25) evaluated the addition of olaparib to bevacizumab maintenance after first-line platinum–taxane plus bevacizumab in advanced ovarian cancer.[7] Unlike SOLO1 and PRIMA, patients were not selected by BRCA status, but tumour HRD testing was pre-planned. Bevacizumab was continued at the standard dose; patients received either olaparib or placebo in addition.

In the overall population, olaparib plus bevacizumab improved PFS compared with bevacizumab alone (median 22.1 vs 16.6 months; HR 0.59).[7] However, prespecified subgroup analyses revealed that benefit was almost entirely confined to HRD-positive tumours (including BRCA-mutated), where median PFS was 37.2 vs 17.7 months (HR 0.33).[7] In HRD-negative disease, there was no clinically meaningful improvement in PFS. These data establish olaparib plus bevacizumab as an important first-line maintenance option for women with HRD-positive disease who receive bevacizumab upfront.

Table 1. Selected phase III PARP inhibitor maintenance trials in ovarian cancer

Trial	Setting & population	PARP strategy	Key results (PFS)	Main message
SOLO1[5]	Newly diagnosed stage III–IV HGSOC with BRCA1/2 mutation, post-response to chemotherapy	Olaparib vs placebo, up to 2 years	HR 0.30; median PFS not reached vs 13.8 months	First-line olaparib maintenance dramatically prolongs remission and may alter long-term prognosis in BRCA-mutated disease.
PRIMA[8]	Newly diagnosed high-risk advanced EOC, irrespective of biomarker status	Niraparib vs placebo, up to 3 years	HR 0.62 (overall); HR 0.43 in HRD+, HR 0.68 in HRD–	Niraparib improves PFS across biomarker groups, with greatest benefit in HRD-positive tumours.
PAOLA-1[7]	Newly diagnosed advanced EOC after chemo + bevacizumab	Olaparib + bevacizumab vs bevacizumab	HR 0.59 overall; HR 0.33 in HRD+, no benefit in HRD–	Combination of olaparib and bevacizumab is a key option for HRD-positive disease when bevacizumab is used upfront.
NOVA[21]	Platinum-sensitive recurrent EOC, post-response	Niraparib vs placebo	HR 0.27 (gBRCA); HR 0.45 (non-gBRCA)	PARP maintenance benefits both BRCA-mutated and non-BRCA populations in recurrent setting.
SOLO2[22]	Platinum-sensitive recurrent HGSOC with gBRCA mutation	Olaparib vs placebo	HR 0.30; median PFS 19.1 vs 5.5 months	Strong PFS benefit and later OS advantage in BRCA-mutated relapse.
ARIEL3[24]	Platinum-sensitive recurrent high-grade ovarian carcinoma	Rucaparib vs placebo	HR 0.23 (BRCA); HR 0.32 (HRD+); HR 0.36 (ITT)	Rucaparib maintenance improves PFS across biomarker-defined cohorts.

HGSOC = high-grade serous ovarian carcinoma; EOC = epithelial ovarian cancer; HR = hazard ratio; HRD = homologous recombination deficiency; ITT = intention-to-treat.

3. Biomarker-guided patient selection

3.1 BRCA testing: germline and somatic

Given the magnitude of benefit seen in BRCA-mutated disease, universal **germline BRCA1/2 testing** is now recommended for all women with non-mucinous epithelial ovarian, fallopian tube or primary peritoneal carcinoma.[1,26,27] Identification of a germline mutation has implications for treatment selection, prognosis and familial risk management.

Somatic BRCA mutations, present only within the tumour, also predict high sensitivity to PARP inhibitors and should be assessed using tumour sequencing when feasible.[3,28] Current guidelines encourage both germline and somatic BRCA testing to capture the full spectrum of BRCA-driven HRD.[26,27]

3.2 HRD testing and clinical surrogates

Where available, HRD assays such as MyChoice® are useful to refine patient selection beyond BRCA status.[7,8,15,16] In PAOLA-1, only HRD-positive tumours derived meaningful benefit from adding olaparib to bevacizumab; in PRIMA, HRD-positive tumours experienced the largest PFS improvement with niraparib.[7,8] These findings support HRD testing as a decision-making tool, particularly when access to PARP inhibitors is limited or when bevacizumab is being considered.

However, HRD testing is not universally accessible. In such

settings, clinical surrogates remain important. Strong platinum sensitivity (e.g. prolonged interval to relapse, repeated responses to platinum) and a family history suggestive of inherited susceptibility can act as practical proxies for underlying HRD.[2,4,11] When resources are constrained, prioritising PARP inhibitors for patients with known BRCA mutations and those with clear platinum-sensitive disease may be a rational approach.

Table 2. Practical biomarker-based approach to first-line PARP inhibitor maintenance

Biomarker profile	Preferred strategies (where available)	Comments
BRCA1/2-mutated (germline or somatic), bevacizumab not used	Olaparib maintenance for up to 2 years (SOLO1)	Highest level of evidence; large and durable PFS benefit with emerging OS advantage.
BRCA1/2-mutated, bevacizumab used upfront	Olaparib + bevacizumab (PAOLA-1) or olaparib alone	Choice depends on clinical factors, cost and tolerance of bevacizumab.
HRD-positive, BRCA-wild type	Niraparib (PRIMA) or olaparib + bevacizumab (PAOLA-1, if bevacizumab used)	Substantial PFS benefit; HRD testing strongly recommended where possible.
HR-proficient / HRD-negative	Consider niraparib (PRIMA) in selected high-risk patients vs no PARP	Benefit is modest; shared decision-making and cost–effectiveness are crucial.

4. Safety profile and toxicity management

4.1 Common adverse events

PARP inhibitors are generally well tolerated, but class-specific toxicities are frequent and require proactive management.[17–21,24,29] Common adverse events include:

- Haematological toxicity: anaemia, thrombocytopenia, neutropenia
- Gastrointestinal symptoms: nausea, vomiting, dyspepsia, constipation or diarrhoea
- Constitutional symptoms: fatigue, asthenia, headache
- Others: mild creatinine elevation (due to transporter inhibition), hypertension (particularly with niraparib), transient liver enzyme elevations

Niraparib is particularly associated with thrombocytopenia, especially when initiated at a fixed high dose in patients with low body weight or baseline platelet counts. The adoption of an individualised starting dose has reduced the incidence of grade ≥3 thrombocytopenia.[25] Olaparib and rucaparib more commonly cause anaemia and mild gastrointestinal toxicity; rucaparib is also associated with transient transaminase increases.[24,29]

Most toxicities occur early and can be managed with supportive care, temporary interruption and dose reduction according to standard guidelines. Regular full blood counts, blood pressure monitoring (for niraparib) and periodic assessment of renal and hepatic function are recommended during treatment.

4.2 Serious but rare adverse events

A small but clinically important risk of therapy-related myelodysplastic syndrome (MDS) and acute myeloid leukaemia (AML) has been reported with PARP inhibitors, particularly in heavily pretreated patients with prior exposure to multiple lines of platinum and alkylating agents.[11,19,29] The absolute incidence is low (generally <2%), but patients should be counselled about this risk, and persistent cytopenias warrant prompt evaluation.

Non-haematological serious adverse events are uncommon but include rare pneumonitis and hypersensitivity reactions. Long-term safety data from first-line trials such as SOLO1, PRIMA and PAOLA-1 have thus far been reassuring, with no new safety signals emerging on extended follow-up.[6–8]

Table 3. Typical class-related adverse events of PARP inhibitors

Toxicity	Olaparib	Niraparib	Rucaparib	Management principles
Anaemia	Common	Common	Common	Monitor full blood counts; consider iron/B12/folate assessment; dose interrupt/reduce if grade ≥3.
Thrombocytopenia	Less frequent	Common, especially at high starting dose	Moderate	Individualised starting dose for niraparib; platelet transfusions rarely required; stepwise dose reduction.
Neutropenia	Common	Common	Common	Monitor counts; prophylactic G-CSF not routinely required but may be used in high-risk patients.

Nausea, vomiting	Common	Common	Common	Prophylactic or as-needed antiemetics; take with food; consider switch of timing (evening dosing).
Fatigue	Common	Common	Common	Reassure; manage anaemia, thyroid dysfunction or sleep issues; dose modifications if severe.
Hypertension	Rare	Relatively frequent	Uncommon	Monitor blood pressure regularly; initiate or adjust antihypertensives; consider dose modification.
Elevated ALT/AST	Mild, transient	Occasional	More frequent	Monitor liver enzymes; interrupt and re-challenge if grade ≥3.

ALT = alanine aminotransferase; AST = aspartate aminotransferase; G-CSF = granulocyte colony-stimulating factor.

5. Mechanisms of resistance and evolving strategies

Despite impressive initial responses, many patients eventually relapse on PARP inhibitors. Mechanisms of resistance are diverse and illustrate the dynamic nature of DNA repair networks.[30–32]

Key resistance mechanisms include:

- BRCA reversion mutations: secondary mutations that restore the open reading frame and partially restore BRCA function, re-establishing HR competence.
- Upregulation of drug efflux pumps: increased expression of ABCB1 can reduce intracellular concentrations of PARP inhibitors.
- Restoration of end resection pathways: loss of 53BP1 or components of the shieldin complex allows DNA end resection and HR repair even in the absence of BRCA.[31]
- Replication fork protection: changes in proteins that protect stalled replication forks, reducing the accumulation of DSBs.

Understanding these mechanisms has stimulated trials of rational combination therapies designed to either prevent resistance or overcome it once established. Strategies under investigation include combinations of PARP inhibitors with:

- Anti-angiogenic agents (e.g. bevacizumab, as in PAOLA-1)
- Immune checkpoint inhibitors, based on the hypothesis that HRD increases neoantigen load and STING pathway activation
- ATR, CHK1, WEE1 or DNA-PK inhibitors, aiming to intensify DNA damage response disruption
- POLθ (DNA polymerase theta) inhibitors to exploit alternative repair dependencies in HRD tumours
- Most of these combinations remain experimental and are best offered within clinical trials.

6. Implementing PARP inhibitors in routine and resource-limited practice

6.1 Guideline recommendations

International guidelines, including those from ASCO and ESMO, now recognise PARP inhibitors as a standard component of therapy for newly diagnosed and recurrent ovarian cancer.[26,27] Key recommendations include:

- Universal germline BRCA testing at diagnosis for women with non-mucinous EOC.
- Tumour BRCA and HRD testing where available, particularly when bevacizumab is used and when decisions about first-line maintenance are being made.
- First-line maintenance for patients with newly diagnosed advanced disease who respond to platinum, using olaparib (± bevacizumab) or niraparib, with choice guided by BRCA/HRD status, bevacizumab use, comorbidities and access.
- Maintenance in platinum-sensitive recurrence for PARP-naïve patients, especially those with BRCA mutations or HRD-positive tumours.
- Cautious use or avoidance of PARP inhibitors in heavily pretreated patients, in light of emerging overall survival and safety concerns in that setting.

6.2 Prioritisation and access in low- and middle-income countries

In many low- and middle-income countries (LMICs), access to both molecular testing and PARP inhibitors is limited by cost, infrastructure and reimbursement barriers. For clinicians practising in such settings, pragmatic strategies are needed to ensure that the greatest benefit is delivered to the largest number of patients.

Priority actions may include:

- Ensuring germline BRCA testing is available and affordable, given its dual therapeutic and familial implications.

- Using clinical features such as strong platinum sensitivity and young age at diagnosis to triage patients for tumour testing when resources are limited.
- Prioritising PARP inhibitors for BRCA-mutated and HRD-positive patients, in whom the absolute benefit is largest.
- Where HRD testing is not available, considering first-line olaparib maintenance for BRCA-mutated disease and cautiously using niraparib in selected high-risk, clearly platinum-sensitive patients after detailed discussion of benefits, risks and costs.
- Working with policy-makers and payers to integrate cost-effective PARP inhibitor strategies into national cancer control plans, supported by local real-world data.

Building multidisciplinary teams that include medical oncologists, pathologists, genetic counsellors and pharmacists is essential to implement precision medicine effectively.

Summary and conclusion

The introduction of PARP inhibitors into the management of ovarian cancer is one of the most compelling success stories of precision oncology. By exploiting synthetic lethality in tumours with BRCA mutations and broader HRD, PARP inhibitors have transformed the treatment paradigm from empiric cytotoxic chemotherapy to biomarker-driven maintenance strategies.

First-line trials such as SOLO1, PRIMA and PAOLA-1 show that appropriately selected patients can experience markedly prolonged remissions, and in some cases long-term disease control that persists years after stopping therapy.[5–8] In platinum-sensitive recurrence, trials like NOVA, SOLO2 and ARIEL3 confirm that consolidating platinum response with PARP maintenance is superior to observation.[21,22,24]

At the same time, the experience with late-line use and long-term follow-up has highlighted important caveats. The benefit of PARP inhibition is not uniform across all biomarker groups; HR-proficient tumours derive more modest gains. Potential long-term risks such as therapy-related MDS/AML, and emerging overall survival data in heavily pretreated settings, underscore the need for careful patient selection and adherence to evidence-based indications.[11,19,29]

Going forward, the challenge is to refine and broaden the precision medicine framework that underpins PARP inhibitor use: improving HRD testing, understanding and overcoming resistance, designing rational combinations, and ensuring equitable access across diverse health systems. If these challenges can be met, the "rise of PARP inhibitors" will not simply be a transient therapeutic trend but a durable advance that permanently alters the natural history of ovarian cancer for many women worldwide.

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Transforming OB-GYN Care: Key Insights from the Latest Clinical Trials: Landmark Studies in Ovarian Cancer

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Introduction

Epithelial ovarian cancer, predominantly high-grade serous ovarian cancer (HGSOC), remains the most lethal malignancy of the female reproductive tract with 5 year survival in advanced stages varying between 20-40%. Although ovarian cancer accounts for approximately 23% of gynecologic cancers, it is responsible for 47% of all deaths from female genital tract malignancies.

Characterized by a distinctive natural history of initial chemosensitivity followed by inevitable recurrence and the progressive acquisition of chemotherapy resistance, the disease has challenged oncologists for decades. Traditionally management of ovarian cancer has focussed on extensive cytoreductive surgery combined with platinum-taxane chemotherapy which is usually given intravenously with or without intraperitoneal chemotherapy.

However all these efforts yielded only incremental improvements in overall survival(OS). The trajectory of the disease was often cyclical, with shortening intervals of remission, culminating in platinum-resistant disease where therapeutic options were limited and palliative in nature.

However, the last decade has witnessed a paradigm shift driven by the elucidation of the molecular markers of epithelial ovarian cancer. The discovery that approximately 50% of HGSOC tumors exhibit Homologous Recombination Deficiency (HRD)—driven by germline or somatic *BRCA1/2* mutations, as well as epigenetic silencing of *RAD51C* and other mechanisms opened the door to synthetic lethality and the era of Poly (ADP-ribose) polymerase (PARP) inhibitors.

There are also lot of upcoming clinical trials on hyperthermic intraperitoneal chemotherapy (HIPEC) in advanced or recurrent ovarian cancer in which heated chemotherapy is delivered directly into abdomen after surgery so that combination of heat and concentrated chemotherapy kills microscopic cancer cancers after the surgery and before adhesion formation. This article will focus on few landmark trials which have shaped the treatment of epithelial ovarian cancer.

Neoadjuvant chemotherapy versus primary debulking surgery

For most patients presenting with suspected advanced stage malignant ovarian, fallopian tube or primary peritoneal cancer, initial surgery includes comprehensive staging and debulking. Primary debulking surgery (PDS) may not be appropriate for patients with a poor performance status, significant medical co- morbidities, or who have disease unlikely to be optimally cytoreduced (residual disease <1 cm) i.e., visceral metastases, large volume pleural effusions or evidence of extraperitoneal disease. In patients with apparent Stage IIIC and IV disease who are not considered to be good surgical candidates, 3–4 cycles of neoadjuvant chemotherapy (NACT) may be given initially after histological confirmation of the diagnosis

with core biopsies, followed by interval debulking surgery (IDS) and additional adjuvant chemotherapy. NACT-IDS has lower perioperative complications, less severe bleeding, and higher rates of complete cytoreduction, especially for those initially deemed unresectable.

Recent metaanalysis comparing 5 major randomized phase III trials (RCTs) namely EORTC 55971, CHORUS, JCOG0602, SCORPION and multicentre TRUST trial (ENGOT-ov33/AGO-OVAR OP7) showed that in FIGO stage III–IV, NACT-IDS achieves survival endpoints similar to PDS, while increasing the likelihood of complete macroscopic resection and reducing severe perioperative morbidity. As per the authors upfront surgery in advanced ovarian cancer management should likely be reserved for patients with feasible complete resection and presumed low morbidity.

The forthcoming SUNNY trial, an initiative of SGOG and international collaborators of Korean Gynecologic Oncology Group and Japanese Gynecologic Oncology Group, similarly tests PDS superiority over NACT-IDS in stage IIIC–IVB ovarian cancer with patients being stratified by the combined Peritoneal Carcinoma Index (cPCI) scoring based tumor burden (low, middle and high).

Other surgical trials in advanced ovarian cancer

Minimally invasive cytoreductive surgery (laparoscopic or robotic) have been shown to be safe , technically feasible and can achieve optimal cytoreduction in both early and advanced ovarian cancer as shown in recent studies and metanalysis. However case selection and prior surgeon experience are important for optimal results . Ongoing trials like LANCE are expected to provide robust evidence in this context. Patients requiring multivisceral resections will usually require conversion to open surgeries. Role of systematic lymphadenectomy in ovarian cancer is controversial. For patients with presumed early stage

disease, a randomized trial showed that systematic aortic and pelvic lymphadenectomy improved detection of metastatic nodes and help in prognostication but was not associated with improved progression free survival (PFS) or overall survival (OS) . In patients with stage IIB-IV ovarian cancer , recent large randomised Lymphadenectomy in Ovarian Neoplasm (LION) trial showed that the removal of clinically negative lymph nodes during cytoreductive surgery in advanced ovarian cancer does not increase the PFS or OS and was associated with increased rates of serious postoperative complications and 60 day mortality.

Chemotherapy in advanced ovarian cancer

Patients with stage 1C, stage 2 and advanced disease who have had primary cytoreduction should receive chemotherapy after surgery. The accepted standard is six cycles of platinum- based combination chemotherapy, with carboplatin and a taxane (paclitaxel or docetaxel) as shown in multiple studies. Dose dense regimens have also shown to improve OS and PFS in Japanese patients (JGOG 3016). In elderly patients dose may be reduced.

Intraperitoneal chemotherapy

Although intraperitoneal chemotherapy has been shown to be associated with improved PFS and OS in selected patients with optimally debulked Stage III ovarian cancer, it is not widely used because of concerns regarding increased toxicity and catheter related problems.

Hyperthermic intraperitoneal chemotherapy (HIPEC) in ovarian cancer

Hyperthermic intraperitoneal chemotherapy (HIPEC) is a technique in which chemotherapy is delivered in a heated solution throughout the peritoneal space after surgery. In this technique , various protocols have perfused chemotherapy for 60 or 90 minutes and solution is heated to 41-43° C. Potential advantages include increased penetration of chemotherapy due to heat , increased DNA damage and increasing sensitivity of cancer cells to chemotherapy by inhibiting DNA repair mechanism and making the tumor more BRCAness-like . Also the chemotherapeutic agent can be exposed to the entire visceral and parietal peritoneum before adhesions occur after surgery. In recent decade , few randomised trials and numerous non randomised trials have been conducted on HIPEC. However major/severe complications have been shown in 9-40% of patients including fistulas, abscesses, infections, bowel perforations , ileus, renal insufficiency/ failure, pleural effusion, pneumothorax, myocardial infraction.

Recent randomised OVHIPEC 1 trial by Van Driel et al confirms that adding HIPEC to post NACT IDS surgery significantly improves PFS (14.2 vs 10.7 months) and OS (median not reached vs 45.7 months) for Stage III ovarian cancer patients and did not result in higher rates of adverse effects. Unfortunately, the study did not have an arm with intraperitoneal cisplatin alone without HIPEC; therefore, it is not possible to know whether the improved survival was due to the addition of intraperitoneal cisplatin alone or HIPEC.

In 2022, Lim et al. reported that there was no survival benefit of HIPEC during upfront surgery in the KOV-HIPEC-01 trial, but as in the OVHIPEC-01 trial, HIPEC increased PFS and OS when interval cytoreductive surgery was performed after neoadjuvant chemotherapy.

In recurrent ovarian cancer , CHIPOR and HORSE studies were conducted . The HORSE trial evaluated HIPEC in the first-recurred platinum-sensitive recurrent ovarian cancer during secondary cytoreductive surgery but found no significant benefit in either PFS or OS. However, the CHIPOR trial demonstrated a significant survival benefit (median OS: 54.3 vs. 45.8 months; HR=0.73, p=0.024) by administering 6 cycles of platinum-based chemotherapy to patients with platinum-sensitive recurrent ovarian cancer, followed by consolidation HIPEC after cytoreductive surgery.

HIPEC might offer clinical benefits in cases where recent chemotherapy exposure has occurred, and the tumor is resectable. Currently, NCCN guidelines supports the use of HIPEC at the time of IDS while the European Society of Gynecologic Oncology (ESGO) guidelines did not reach a consensus regarding the role of HIPEC at the time of IDS and recommend against HIPEC at the time of secondary cytoreduction.

Trials like **RECOVER (KOV-HIPEC-02R)** are underway to better define HIPEC's role in platinum-resistant recurrence. In primary stage III ovarian cancer HIPEC after upfront PDS , the **OVHIPEC-02** trial is currently underway. The role of HIPEC during interval cytoreductive surgery after neoadjuvant chemotherapy in stage III and IV patients with maintenance therapy with poly(ADP-ribose) polymerase inhibitors or bevacizumab is being evaluated in the ongoing **KOV-04, FOCUS**.

Surgery in recurrent ovarian cancer

Surgery is most effective when performed for platinum sensitive recurrence.

Predictive AGO score (complete resection during primary surgery, ECOG performance status of 0, and ascites ≤ 500 mL) was determined in the DESKTOP I trial which was further validated in DESKTOP II trial with 76% complete resection rates in patients with a positive AGO score. To date, three randomized trials GOG-0213, DESKTOP III , SOC 1 have been conducted on secondary cytoreductive surgery for recurrent cancer.

DESKTOP III and **SOC-1** (iModel) confirm that for selected, platinum-sensitive recurrent ovarian cancer patients, secondary cytoreductive surgery aiming for complete

tumor removal significantly OS and PFS compared to chemotherapy alone. In contrast, GOG-0213 trial did not show an overall survival benefit and highlighted the importance of strict patient selection using evidence-based selection criteria including the AGO and iMODEL scores and importance of complete resection. Trials using newer approaches like HIPEC are currently underway with HORSE and CHIPOR trial showing mixed results **.**

Targeted therapy in advanced ovarian cancer

PARP inhibitors in ovarian cancer

PARP inhibitors (PARPi) are targeted drugs that work via principle of "synthetic lethality"**.** They work by blocking PARP preventing DNA single-strand break repair and turning them into lethal double-strand breaks which cancer cells can't fix, hence significantly extending remission, especially as maintenance therapy after platinum based chemotherapy.

In the newly diagnosed ovarian cancer , PARPi provide the greatest clinical benefit in patients with a BRCA 1and /or BRCA 2 mutation (BRCAm) or whose tumours test positive for homologous recombination deficiency. Key trials like SOLO- 1 (Olaparib for BRCAm) and NOVA (niraparib for platinum sensitive ovarian cancer) showed huge PFS and OS benefit as front line maintenance therapy. In the recurrent settings , the FDA has approved PARPi only for BRCA mutated cancers.

Numerous ongoing trials are exploring combinations to enhance PARPi efficacy and overcome resistance. Combinations include: PARPi and Anti-Angiogenic Agents (bevacizumab) as studied in PAOLA-1 trial in HRD-positive patients. Combination of PARPi and Immunotherapy (niraparib with pembrolizumab or Olaparib with durvalumab) is being evaluated in TOPACIO and MEDIOLA trial in platinum-sensitive recurrent ovarian cancer patients. Research into combining PARPi with cell cycle checkpoint inhibitors (inhibitors of ATR or WEE1 kinases) is ongoing to explore potential synergies and reverse resistance. New trials, such as the academic-led IPIROC trial funded by the ICMR, are investigating intermittent or individualized dosing strategies to manage toxicity and maintain cost-effectiveness of PARPi. The DUO O trial showed statistically significant and clinically meaningful PFS benefits in both t-BRCA mutated and non BRCA mutated groups on addition of durvalumab to chemo+/- bevacizumab.

All PARPi are associated with mainly low grade adverse effects such as nausea, fatigue, and myelosuppression (anemia can be caused by all, neutropenia and thrombocytopenia mainly by niraparib), which can mostly be managed with dose reductions and interruptions. However there is a higher risk of secondary cancers (like myelodysplastic syndrome/acute myeloid leukaemia) with long-term exposure.

Bevacizumab in ovarian cancer

Bevacizumab targets tumor blood vessel growth (anti-VEGF) and has been shown to improve PFS in first-line and recurrent settings, especially with continuous maintenance therapy with some OS benefits. In first line settings , trials like GOG 0218 and ICON7 showed bevacizumab added to chemotherapy in doses of 7.5mg/kg to 15mg/kg significantly improved PFS in advanced ovarian cancer, particularly for high-risk patients. In recurrent ovarian cancer , studies like AURELIA and OCEANS showed strong PFS benefits in platinum-sensitive and resistant recurrent cancer, with continuous bevacizumab therapy until progression. It is currently being evaluated with other targeted therapy like PARPi. Bevacizumab also has some adverse effects like hypertension, GI bleeding/perforation, and wound healing issues.

Immunotherapy in ovarian cancer

Recent studies on ovarian cancer immunotherapy focus on combination therapies (checkpoint inhibitors + PARP inhibitors/chemo), new targets (TIGIT, epigenetic modulators), personalized approaches (biomarkers like *PPP2R1A* mutations), and advanced cell therapies (CAR-T, off-the-shelf CAR-NKTs), aiming to overcome challenges like immune resistance by modifying the tumor microenvironment and identifying responders, with growing evidence showing promise in recurrent cases and specific subtypes.

To conclude, the evolution of epithelial ovarian cancer management is inseparable from the evidence generated by the well designed clinical trials. Ongoing and future trials exploring immunotherapy combinations, novel targeted agents, biomarker-driven treatment selection, and multimodal strategies promise to further refine disease management

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Understanding Hereditary Risk: BRCA Mutations and Preventive Strategies in Ovarian Cancer- Updates from the UK FOCSS study on surveillance and the PROSE trial on risk-reducing salpingo-oophorectomy

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Introduction

Approximately 20% of Epithelial ovarian cancers (OC) occur in women with germline pathogenic variants in the ovarian cancer susceptibility genes. BRCA1/2 pathogenic variants are the most common among them. BRCA 1/2 carriers have 44% and 17% lifetime OC risks, respectively.[1] Consequently, they are advised to undergo risk- reducing bilateral salpingo- oophorectomy (RRSO) to prevent ovarian cancer; from age 35 (BRCA1- heterozygotes) or 40 years (BRCA2- heterozygotes) onwards as these women have a life time risk of 10% for developing ovarian cancer which is in contrast to only 1.5% risk in general population.[2-4] RRSO confers an associated ovarian cancer risk reduction of 80–90% and a breast cancer risk reduction estimated at 50%, particularly in BRCA2 carriers.[5] While some research is exploring the efficacy of early salpingectomy and delayed oophorectomy, RRSO remains the standard of care for BRCA carriers.

Despite the effectiveness and marked cancer reduction of RRSO, between 20–40% of patients with BRCA1/2-heterozygotes delay or decline RRSO. Reasons for delaying/declining RRSO include: ongoing breast cancer treatment, addressing breast cancer risks first, completing families, waiting until natural menopause, the existence of comorbidities which make RRSO hazardous, fear of surgery, lack of available time, or simply not wanting surgery. Delaying/declining surgery leaves these women at risk of OC, so an effective OC surveillance programme would be an important option. To explore the surveillance options in this particular group of women, multiple strategies were explored. In this review, we shall discuss the evidences behind the prevention of OC and the available surveillance strategies available for these high-risk women.

UKFOCSS study

The United Kingdom Familial Ovarian Cancer Screening Study group (Phase 1) did a prospective cohort study on ovarian cancer screening using annual CA125 and annual TVS among high-risk women who are BRCA1/2 carriers (6). They found that this annual screening had a sensitivity of 81-87%, Positive and negative predictive values of 25% and 99.9%. The incident cancers detected within one year of last screening were 30% in the early stage and 70% in the advanced stage. Although phase 1 study demonstrated a high sensitivity (> 80%),69% of detected cancers were stage III to IV. Also, the annual screening interval has been associated with a poor 10-year survival rate of 36% in BRCA1/2 carriers.[6] This left with the idea of having intensified surveillance protocol in these high-risk women. Here comes the role of Risk of Ovarian Cancer Algorithm (ROCA) test. As the single value of CA 125 with the cut off of 35 IU/L along with transvaginal ultrasound had sensitivity of 40-50% and specificity of 99% for detection of early-stage ovarian cancer, researchers evaluated if serial CA 125 measurements help in early diagnosis of cancer. This led to the development of ROCA test. The ROCA test calculates the probability of a woman having epithelial OC or fallopian tube cancer (FTC) by analysing changes in her CA-125 levels over time. This algorithm-based approach stratifies women into risk categories to guide appropriate clinical management. Abnormal ROCA test results prompt early CA 125 repeat tests and transvaginal ultrasound scan (TVS).[7] Surgical intervention is recommended for those with sufficiently elevated ROCA results or concerning scans. While it remains speculative that ROCA results translate into improved survival, it is suggested that this form of surveillance may be a useful short- term strategy in BRCA1/2- heterozygotes who are not yet ready for RRSO. To evaluate the diagnostic performance of ROCA test among high-risk women, UKFOCSS phase 2 study was initiated.

UKFOCSS Phase 2 Study

This large UK multicenter study evaluated whether intensive screening using serum CA-125 interpreted through the Risk of Ovarian Cancer Algorithm (ROCA) combined with transvaginal sonography (TVS) could effectively detect ovarian or fallopian tube cancer in women at high familial or genetic risk who were not ready for risk-reducing salpingo-oophorectomy (RRSO). A total of 4,348 high-risk women underwent ROCA testing every four months and TVS either annually (if ROCA was normal) or within two months if ROCA is abnormal. Over a median follow-up of 4.8 years and 13,728 women-years of screening, 19 invasive cancers were diagnosed within one year of a prior screen—13 screen-detected and six occult at RRSO—with no symptomatic interval cancers. This model of screening demonstrated a high sensitivity of 94.7%, a

PPV of 10.8%, and an NPV of 100%, indicating excellent detection capability but a relatively low yield relative to the number of tests performed.[8]

A key finding of this Phase 2 study was a significant stage shift toward earlier-stage disease during the screening period: 52.6% of cancers detected within a year of screening were Stage I–II, compared with only 5.6% of cancers diagnosed after screening ended. Additionally, almost all cancers detected during active screening achieved zero residual disease at surgery, suggesting less surgical complexity. These results demonstrate that ROCA-based screening can identify cancers earlier and avoid advanced-stage presentation in high-risk women who delay or decline RRSO. However, whether this earlier detection translates into a survival benefit remains unproven, and RRSO continues to be the only intervention with established mortality reduction.[8]

Avoiding Late Daignosis of Ovarian Cancer study (ALDO)

Based on these encouraging results of phase 2 UKFOCSS, the Avoiding Late Diagnosis of Ovarian Cancer (ALDO) pilot project for BRCA1/2 carriers denying RRSO was initiated, with the ultimate objective of establishing a robust and cost-effective OC surveillance programme for such women. ROCA test was done among 875 high risk women which showed sensitivity of 87.5%, positive predictive value of 75% and negative predictive value of 99.9%.[9] Economic analysis also found ROCA to be a cost-effective tool in the OC screening among high-risk women compared with no screening. Below, shows the work flow when ROCA test is used as a screening tool.[9]

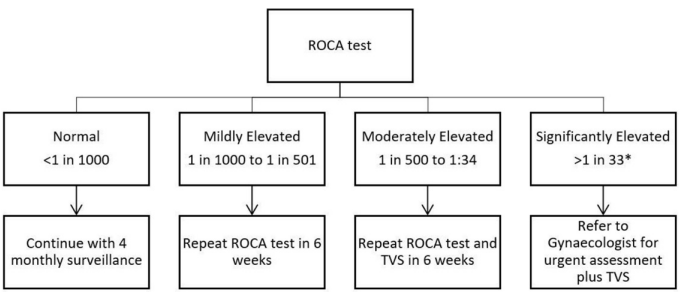

Fig.1: Flowchart depicting the workflow of ROCA test.[9]

Risk reducing salpingo-oophorectomy

Domchek et al in the PROSE (Prevention and Observation of Surgical Endpoint) study which was a prospective, multicenteric cohort study done among 2482 women who harboured BRCA1 or BRCA2 mutations from the PROSE consortium to assess the relationship of risk-reducing salpingo-oophorectomy with ovarian and breast cancer outcomes.[5] The results of this study showed that compared with women who did not undergo risk-reducing salpingo-oophorectomy, women who underwent salpingo-oophorectomy had 83% lower risk of ovarian cancer, ([HR], 0.14; 95% confidence interval [CI], 0.04-0.59) and a lower risk of first diagnosis of breast cancer in BRCA1 mutation carriers (HR, 0.63 [95% CI, 0.41-0.96]) and BRCA2 mutation carriers (HR, 0.36 [95% CI, 0.16-0.82]). The mortality risk was also drastically reduced in women who underwent risk-reducing salpingo-oophorectomy, compared with women who did not and found 60% reduction in all-cause mortality HR, 0.40 [95% CI, 0.26-0.61]),56% reduction in breast cancer–specific mortality (HR, 0.44 [95% CI, 0.26-0.76]), and 79% reduction in ovarian cancer–specific mortality (HR, 0.21 [95% CI, 0.06-0.80]).[5] This very well undermines the importance of risk reducing salpingo-oophorectomy in these high-risk women.

Which option is better among these high-risk women, RRSO or ROCA?

GOG 199

We have another study, GOG 199 which looked at these two options. GOG 199 was a prospective, international, two-cohort, nonrandomized study of women at genetic risk of ovarian cancer, who chose either to undergo RRSO or screening using ROCA test. 2,605 participants were enrolled: 1,030 (40%) into the surgical cohort and 1,575 (60%) into the screening cohort.[10] The objectives of the study were to compare the ovarian and breast cancer incidence in the two study groups and also to assess feasibility and performance of the ROCA test. All patients were followed up for 5 years. The results showed that in the ROCA arm, 11 incident ovarian/tubal cancers were detected. This shows that screening did not prevent ovarian cancer and cancers still occurred despite intensive surveillance.[10] However, the point to note was ROCA was able to detect some cancers earlier, but no survival advantage was demonstrated. In the RRSO arm, among ~1,000 women who underwent RRSO at enrollment, 2.6% were found to have occult neoplasia (inclusive of STIC, serous intraepithelial lesions, or invasive tubal/ovarian/peritoneal cancer). Occult cancer rates were higher in BRCA1 carriers (approx. 4–5%), supporting early prophylactic surgery. Only 1 primary peritoneal carcinoma occurred in the RRSO group during follow-up—indicating very strong protection against ovarian/fallopian/peritoneal cancer. RRSO also contributed to lower subsequent breast cancer incidence (HR ≈ 0.86), although this was not statistically significant in GOG-199 due to limited follow-up. RRSO is highly effective, both in detecting occult early cancers at surgery and in dramatically reducing future ovarian/tubal/peritoneal cancer incidence. Thus, this study supports RRSO as the preferred risk-reduction strategy for BRCA1/2 carriers, while ROCA-based screening is considered a secondary option only for women delaying surgery.[10]

A recent paper published by Hassen et al showed that RRSO is not associated to long term health outcomes.[11] The authors showed that RRSO was associated with

a reduced risk of second non-breast cancer in the combined BRCA1 and BRCA2 sample (HR 0·59, 95% CI 0·37–0·94), not associated with increased risk of cardiovascular diseases (HR 0·73, 95% CI 0·53–1·01), ischaemic heart disease (1·04, 0·48–2·26), cerebrovascular disease (0·32, 0·11–0·90), non-breast cancer specific mortality (0·72, 0·45–1·16), contralateral breast cancer (1·18, 0·64–2·16), or depression (0·94, 0·62–1·42).[11]

Is there a role of chemoprevention in high-risk women?

Although prophylactic surgery is the most effective means to prevent ovarian cancer in high-risk women, for women who have not completed childbearing, medical prevention may provide an active path to cancer prevention until they are ready to undergo RRSO. An ideal chemopreventive medication should be efficacious, risk-free, easy to administer, and cost-effective. There are two types of chemoprevention: blocking and suppressing agents. Blocking agents act on the initial phase of carcinogenesis while suppressing agents delay the progression of premalignant cells to an invasive tumour. Several drugs have been proposed to prevent OC, but oral contraceptives alone have robust data in support. Studies have shown that oral contraceptive pills provide 50% reduction in ovarian cancer risk without increase in the breast cancer risk (summary relative risk (SRR)=0.50; 95% (CI), 0.33-0.75).[12-14] The authors also observed a significant 36% risk reduction of ovarian cancer risk for each additional 10 years of OC use (SRR: 0.64; 95% CI, 0.53-0.78; P trend<0.01). Clinicians should balance the usage of OCP by weighing the benefits against the risks of undesirable side effects like secondary cancer risk, thromboembolism etc. Literature suggests that, compared to women without a personal history of use of hormonal contraceptives assumption, patients with at least once prescription of OCP had a significantly increased incidence of breast cancer with an OR -1.33, 95% CI 1.26–1.41 $p < 0.001$. In a nested case–control study that included almost 10,000 women aged under 50 years old and with a diagnosis of breast cancer, those prescribed any form of hormonal contraceptives were shown to have an increased risk of breast cancer. The average time between the last prescription and the breast cancer diagnosis is about 3 years. The results were similar regardless of the type of OCP used. Women who use the OCP have a time-dependent increase in cervical cancer risk of about 10% for use during fewer than 5 years, 60% in 5–9 years, and doubling with ten or more years of use. The gynaecologist and the oncologist should balance the data on the augmented risk of breast cancer and cervical cancer with the documented beneficial effects on OC and other cancers like endometrial and colon cancer, reduced by 30% and 15–20%, respectively.[12-14]

What are the other options in pipeline?

Early salpingectomy with delayed oophorectomy may be a novel risk-reducing strategy with benefits of delaying menopause which can be an alternative to RRSO. The TUBA study by SteenBeek et al compared menopause-related quality of life after risk-reducing salpingectomy with delayed oophorectomy with RRSO in carriers of the BRCA1/2 pathogenic variant and found that patients have better menopause-related quality of life after risk reducing salpingectomy than after RRSO, regardless of hormone replacement therapy.[15] However, we should wait for the results of the three ongoing trials (PROTECTOR, SORROCK, TUBA WISP II) in early salpingectomy with delayed oophorectomy which aim to address its effectiveness in the prevention of ovarian cancer among high-risk women.[16]

Conclusion

Risk-reducing salpingo-oophorectomy (RRSO) remains the gold standard preventive strategy for women at high hereditary risk of ovarian cancer, offering the most significant reduction in ovarian, fallopian tube, and peritoneal cancer incidence as well as overall mortality. For women who wish to delay definitive surgery to complete childbearing or avoid premature menopause, serial screening with CA-125 interpreted through the Risk of Ovarian Cancer Algorithm (ROCA) provides the most effective surveillance option currently available, with better performance than fixed-threshold CA-125 or ultrasound alone.

In addition, chemoprevention—particularly the use of oral contraceptives—may be considered in women without a prior history of breast cancer, as evidence supports a meaningful reduction in ovarian cancer risk without increasing breast cancer risk in this subgroup. Ultimately, preventive strategies should be individualised, balancing cancer risk, reproductive goals, comorbidities, and patient preferences.

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Calendar for AOGD Monthly Clinical Meeting 2025-2026

30th January 2026	Dr RML Hospital
27th February 2026	UCMS & GTB Hospital
27th March 2026	LHMC & SSK Hospital
24th April 2026	Hamdard Institute of Medical Sciences and Research

Breaking New Ground in OB-GYN with - The Latest Evidence-Based Guideline: Global Perspectives: ESMO–ESGO–ASCO Guidelines on Ovarian Cancer (2023)

An Evidence-Based Summary of International Consensus on Diagnosis, Staging, Treatment, and Follow-up

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Introduction

Ovarian cancer remains one of the most lethal malignancies affecting women, largely because it is diagnosed at an advanced stage in the majority of patients.[1] The absence of effective population-based screening tools and the non-specific nature of early symptoms contribute significantly to diagnostic delay. Over the past decade, however, major advances in surgical techniques, systemic therapy, maintenance strategies, and genetic testing have substantially altered the therapeutic landscape.

In response to this rapidly evolving evidence base, several international organisations periodically update their clinical practice guidelines. In 2023, three leading bodies—the European Society for Medical Oncology (ESMO), the European Society of Gynaecological Oncology (ESGO), and the American Society of Clinical Oncology (ASCO)—released updated recommendations for the management of ovarian cancer. While developed independently, these guidelines demonstrate increasing convergence in key principles. This review synthesises areas of consensus, highlights relevant differences, and provides a pragmatic summary tailored for day-to-day clinical practice.

1 Epidemiology and Risk Factors

Ovarian cancer is the eighth most common cancer in women worldwide and remains a leading cause of death among gynaecological cancers[1]. Most cases are epithelial cancers, especially high-grade serous carcinoma. Many women are diagnosed at Stage III or IV because the symptoms such as bloating, abdominal pain, or early fullness — are common in normal life, hence seeking medical advice is delayed

Genetic factors play a major role

Mutations in BRCA1/BRCA2, and genes involved in homologous recombination repair, increase lifetime risk[2]. ESMO and ASCO stress that every woman diagnosed with epithelial ovarian cancer should undergo genetic testing for BRCA mutations and receive counselling[3].

Other risk factors include:

- Increasing age
- Family history
- Endometriosis (especially for clear cell and endometrioid types)[4]
- Hormonal factors such as low parity
- Lifestyle factors (obesity, smoking for mucinous type)

The guidelines also agree that oral contraceptives reduce the risk, especially after long-term use[5].

2 Principles of Diagnosis

2.1 Clinical Evaluation

Most women present with **non-specific symptoms**, so a combination of pelvic examination, ultrasound, and tumour markers is recommended. No guideline recommends population screening.

2.2 Transvaginal Ultrasound (TVUS)

TVUS remains the **first-line imaging test**. Guidelines support using structured scoring systems such as **IOTA Simple Rules** for better accuracy[6].

Suspicious features include:

- Solid components
- Papillary projections
- High vascularity
- Ascites
- Irregular walls

2.3 Tumour Markers

- CA-125: Useful but non-specific.
- HE4: Helpful in specific situations.
- ROMA score: Can aid in triaging premenopausal women.

The guidelines emphasise using tumour markers **to support diagnosis**, not as standalone tests.

2.4 CT, MRI, and PET-CT

For suspected ovarian cancer:

- CT scan of chest, abdomen, pelvis is the preferred staging tool[7].

- MRI is helpful in characterising indeterminate adnexal masses.
- PET-CT is not mandated routinely, but may help in recurrent disease.

2.5 Role of Biopsy

Biopsy is generally **avoided in operable disease** because of the risk of tumour spillage.

However, **ASCO and ESMO recommend biopsy** when:

- Disease is unresectable at presentation
- Neoadjuvant chemotherapy (NACT) is being considered
- Histology is unclear
- A non-ovarian primary needs to be ruled out[8]

3. Surgical Staging and Management

3.1 Importance of Complete Surgical Staging

Accurate staging is essential, especially in early disease. ESGO recommends that surgeries should ideally be done in **high-volume centres** by trained gynaecologic oncologists[9].

Standard staging includes:

- Total abdominal hysterectomy
- Bilateral salpingo-oophorectomy
- Omentectomy
- Peritoneal biopsies
- Pelvic and para-aortic lymph node sampling as indicated
- Collection of peritoneal washings

3.2 Early-Stage Disease (Stage I–II)

Fertility-Sparing Surgery

All guidelines allow fertility-sparing surgery in selected young women with:

- Stage IA or IC1 disease
- Grade 1 or 2 tumours
- Non-clear cell histology[10]

The uterus and one ovary can be preserved with close follow-up.

Adjuvant Chemotherapy

Chemotherapy is recommended for:

- Stage IC disease
- High-grade tumours
- Clear cell histology
- Stage II disease[11]

The preferred regimen is **carboplatin + paclitaxel** for 3–6 cycles.

3.3 Advanced-Stage Disease (Stage III–IV)

Primary Debulking Surgery (PDS)

All guidelines agree that **complete cytoreduction with no visible disease** is the strongest prognostic factor[12].

Neoadjuvant Chemotherapy

NACT followed by interval debulking surgery is recommended when:

- Primary surgery is unlikely to achieve complete cytoreduction
- The patient is medically unfit for major surgery
- Disease is widespread (e.g., diaphragmatic, mesenteric involvement)[13]

Both ESMO and ASCO state that NACT should only follow **histological confirmation**.

4. Systemic Therapy for Newly Diagnosed Disease

4.1 First-line Chemotherapy

Across ESMO, ESGO, and ASCO, there is strong agreement that the **standard first-line regimen** remains:

Carboplatin + Paclitaxel every 3 weeks for 6 cycles[14]. This is recommended for both early high-risk disease and all advanced-stage cancers.

Weekly (dose-dense) paclitaxel

The Japanese JGOG trial showed benefit, but Western studies did not confirm it consistently. The guidelines state that dose-dense therapy **may be considered selectively**, but is not routinely required[15].

Intraperitoneal (IP) chemotherapy

All three guidelines acknowledge that IP therapy can improve survival in optimally debulked Stage III disease. However, the use has decreased because:

- It requires specialised expertise
- It is associated with more toxicity
- More effective maintenance treatments (PARP inhibitors) are now available[16]

Thus, IP chemotherapy is listed as **optional**.

4.2 Addition of Bevacizumab

Bevacizumab, an anti-angiogenic agent, may be added to chemotherapy and continued as maintenance.

Guidelines support its use in:

- Stage III with residual disease

- Stage IV disease
- Patients with high-risk features (ascites, bulky disease)[17]

Typical dose: **15 mg/kg every 3 weeks**, continued for up to 15 months.

Bevacizumab improves **progression-free survival (PFS)** but shows modest or selective improvement in overall survival.

4.3 PARP Inhibitors in First-Line Maintenance

The biggest change in ovarian cancer management over the last few years has come from **PARP inhibitors**. ESMO–ESGO–ASCO guidelines all emphasise this strongly.

Who should receive PARP inhibitors?

Women who respond (complete or partial) to platinum-based chemotherapy should be considered for maintenance if:

- They have a BRCA1/2 mutation (germline or somatic)
- They have HRD-positive tumours
- They have high-grade serous or high-grade endometrioid carcinoma[18]

Available options

Drug	Key Recommendation	Notes
Olaparib	Strongly recommended for BRCA-mutated patients	SOLO-1 trial showed major PFS benefit[19]
Niraparib	Can be used regardless of HRD/BRCA status	Benefit strongest in HRD+ tumours[20]
Olaparib + Bevacizumab	For HRD+ disease	Based on PAOLA-1 trial[21]

Duration

- Olaparib: up to 2 years
- Niraparib: up to 3 years
- Olaparib + bevacizumab: 15 months bevacizumab + 2 years olaparib

All guidelines stress careful **dose adjustments** for anaemia, thrombocytopenia, and fatigue.

5. Management of Recurrent Ovarian Cancer

Recurrent disease is grouped according to **platinum sensitivity**.

5.1 Platinum-Sensitive Recurrence

Patients who relapse **more than 6 months** after completing platinum therapy generally benefit from another platinum-based combination.

Common regimens:

- Carboplatin + paclitaxel
- Carboplatin + gemcitabine
- Carboplatin + liposomal doxorubicin[22]

Bevacizumab may be added.

Maintenance therapy

For platinum-sensitive recurrence:

- Olaparib (BRCA-positive)[23]
- Niraparib (regardless of mutation)
- Bevacizumab for selected patients

PARP inhibitors have become a standard part of recurrent disease management unless there are contraindications.

5.2 Platinum-Resistant Recurrence

Defined as recurrence **within 6 months** of completing platinum therapy.

Recommended options include:

- Weekly paclitaxel
- Liposomal doxorubicin
- Topotecan
- Gemcitabine[24]

Bevacizumab can be added to some regimens to improve response.

PARP inhibitor use

PARP inhibitors are **not routinely recommended** in platinum-resistant recurrence unless:

- Patient has not previously received a PARP inhibitor
- BRCA mutation is present
- Benefit is expected to outweigh toxicity issues[25]

5.3 Role of Secondary Cytoreductive Surgery

The three guidelines agree on a selective approach.

Surgery **may** be offered in recurrence if:

- Disease is limited
- Complete resection is likely
- Patient is fit
- Surgery is performed in expert centres[26]

The DESKTOP III trial supports this approach. The GOG-0213 trial showed no survival benefit, so patient selection remains crucial.

6. Follow-Up and Survivorship

Guidelines highlight the importance of **structured follow-up** after treatment.

Routine follow-up schedule

- Every 3–4 months for the first 2 years
- Every 6 months for the next 3 years
- Annually thereafter[27]

Key elements

- Detailed symptom review
- Physical and pelvic examination
- CA-125 levels only if elevated earlier
- Imaging only when clinically indicated

All guidelines warn against **overuse of CA-125**, because early detection of biochemical recurrence does **not** improve survival.

7. Special Populations

7.1 Elderly Patients

ESMO–ESGO–ASCO recommend individualised treatment based on:

- Frailty
- Comorbidities
- Expected tolerance to chemotherapy[28]

Dose modifications may be needed.

7.2 Low-Grade Serous Carcinoma

Because this tumour responds poorly to chemotherapy:

- Hormonal therapy (letrozole)
- MEK inhibitors (trametinib)[29]

are supported.

7.3 Non-Epithelial Ovarian Tumours

These require separate protocols:

- Germ cell tumours: BEP chemotherapy
- Sex cord–stromal tumours: surgery + hormonal therapy[30]

8. Tables

Table 1: Areas of Strong Agreement Among ESMO–ESGO–ASCO (2023)

Domain	Consensus Points
Genetic testing	BRCA testing for all women with epithelial ovarian cancer
Imaging	CT chest–abdomen–pelvis for staging
First-line therapy	Carboplatin + paclitaxel
Maintenance	PARP inhibitors for BRCA/HRD+ disease
Surgery	Maximal cytoreduction in expert centres
Follow-up	Symptom-based, avoid routine imaging

Summary & Conclusion

Ovarian cancer remains a complex disease, but treatment has improved significantly in recent years. The 2023 guidelines from ESMO, ESGO, and ASCO show a remarkable level of agreement on the diagnosis, staging, and management of the disease.

The core principles that emerge across all three guidelines are:

- Universal BRCA and HRD testing
- Accurate staging and preference for complete cytoreduction
- Carboplatin–paclitaxel as the backbone of treatment
- Important role of bevacizumab in selected patients
- Major survival gains from PARP inhibitor maintenance
- Careful selection for secondary cytoreduction
- Follow-up focused on symptoms, not routine imaging

These guidelines provide clinicians with a clear pathway and help standardise care across regions. With evolving research on targeted therapies and personalised medicine, future updates will further refine management strategies.

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Forthcoming Events

- 14th -18th January – 68th AICOG Conference at Yashobhumi, Dwarka, New Delhi.
- 14th March 2026 - "Decoding the Fetus Basics of Fetal Health & Genetics Through Real-Life Cases" will be organized by the Department of Obstetrics & Gynaecology, VMMC & Safdarjung Hospital, by the Fetal Medicine & Genetics Subcommittee in association with the Society of Fetal Medicine (SFM) from 9:00 AM to 4:00 PM.

Next Generation innovations in women's healthcare with- Managing the Challenge of Recurrence: Innovations in Recurrent Ovarian Cancer

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Ovarian Cancer is the third most common cancer among women in India. Each year 47,333 cases are added to the disease burden. It is a deadly cancer. 32,978 women succumb to the disease in India annually.[1]

Ovarian cancer mostly presents in advanced stages (60-70%).[2] The clinical presentation is usually vague and varied, thus, posing a diagnostic dilemma. Lack of effective screening method till date, further delays the diagnosis. The Modified Goff Symptom Index helps in the diagnosis of ovarian cancer by identifying some persistent common symptoms like abdominal/ pelvic pain, bloating/ increased abdominal size, difficulty eating / feeling full and urinary urgency/ frequency, occurring over 12 times/ month for less than 1 year duration. Hence, whenever the diagnosis of Ca Ovary is suspected, CA 125 and other relevant tumour markers, ultrasound by an expert sonologist and further imaging according to the clinical findings should be advocated.

Epithelial ovarian cancer contributes to 90% of all the total ovarian neoplasms, with High Grade Serous (HGSC) being the most common (70%).[3] Most HGSC are highly sensitive to platinum based chemotherapy (60-80%). The other less common ovarian cancers (LCOC) like endometrioid, low grade serous, clear cell and mucinous cancers are less chemosensitive. 50% of all HGSC are Homologous Recombination Deficiency (HRD) positive and 13-15 % are germline BRCA 1 and 2 positive.[4]

Patients with high grade advanced ovarian cancers have a relapse rate of upto 70 % within 3 years. The relapse can be platinum sensitive, resistant or refractory. Platinum sensitive relapse presents > 6months after completing the platinum based chemotherapy regimen (TFIp > 6 months). If the disease relapses less than or equal to 6 months after treatment then it is labeled as platinum resistance (TFIp </= 6 months). Platinum refractory disease fails to respond to platinum based chemotherapy or relapses within 4 to 6 weeks of the last chemotherapy dose. With no molecular biomarkers available currently to detect platinum based chemotherapy response, hence, these definitions are prior therapy oriented.

Evidence is lacking regarding the advantage of regular follow up but it increases the possibility of early detection of recurrence and successful surgical cytoreduction. CA 125 is the cornerstone for detection of recurrent epithelial ovarian cancer. It supplements the clinical findings and guides further workup including imaging, histopathology etc. But treatment based solely on rising CA 125, did not show any survival benefit in previous randomized control trials (RCTs).

The management of recurrent ovarian cancers (OCs) is complex and should be individualized after multidisciplinary team discussion. It involves surgery, chemotherapy and targeted therapies. Treatment of ovarian cancer recurrence does not guarantee prevention against future relapses. Recurrent ovarian cancer requires long term repetitive treatment like chronic diseases. Only patients presenting with platinum sensitive recurrent disease are candidates to be considered for repeat cytoreductive surgery. Surgery can be either therapeutic or palliative.

Decision for repeat surgical procedure is based upon the combination of various parameters. Trials like the German DESKTOP series, the Chinese SOC-1 and the American GOG0213 have evaluated the role of surgery in the recurrent setting.

Complete cytoreduction (R0) with no residual disease after surgery was found as the only predictor for survival benefit in all these trials. In fact the presence of residual disease after surgery was found to be associated with worse survival outcomes than chemotherapy without surgery.

As per the DESKTOP series, AGO score was validated as a positive predictor of completeness of surgery and it included good performance status, complete resection at primary surgery and absence of large volume ascites (>500ml). Overall Survival (OS) and Progression Free Survival (PFS) benefits were noted exclusively in patients with positive AGO score and R0 resection.

In the multicentre, open label phase 3 trial, SOC-1, women with platinum sensitive relapse of ovarian cancer were randomly assigned to either the surgery group (n-182) or no surgery group (n-175). iMODEL, which is based on the logistic regression of six variables including FIGO stage, presence of residual disease following primary surgery, PFS, ECOG performance status, CA 125 levels and the presence of ascites at recurrence along with Positron Emission Tomography – Computed Tomography (PET-CT) was used to decide the possibility of complete cytoreduction. It

showed same survival benefits as noted in the DESKTOP trials. It also evaluated the impact of number of relapse sites on survival outcomes. OS benefit with surgery was only seen in patients with less than 20 relapse lesions.

In the GOG 0213 trial, in which complete cytoreduction was predicted based on surgeon's discretion, PFS benefit was seen only in patients with complete gross resection versus those without any surgery.

Hence, repeat cytoreductive surgery should be considered in all patients whom a high possibility of R0 resection was anticipated. Even in patients with second or third recurrences surgery should be considered only if this criteria is fulfilled.[5]

Oligometastatic disease (OMD), with <5 sites, can be treated with surgery (if resectible), thermal ablation, radiofrequency ablation and radiotherapy after MDT review. Site of OMD being the most important factor influencing management and prognosis.

Role of Hyperthermic Intraperitoneal Chemotherapy (HIPEC), in which heated chemotherapeutic agent is instilled into the abdominal cavity to penetrate and kill the cancer cells, after complete cytoreduction is still under evaluation in recurrent ovarian cancer. HORSE and CHIPOR trials are landmark trials in the recurrent setting. Neither showed PFS benefit. In CHIPOR trial OS benefit was noted and OS data of HORSE trial is not mature yet.[6]

Even in patients undergoing surgery with or without HIPEC, adjuvant platinum based chemotherapy must be administered.

Palliative surgical intervention is done in cases presenting with malignant bowel obstruction (MBO) due to disseminated peritoneal recurrent disease. Endoscopic interventions including gastrostomy tube and colorectal stent placement are surgical alternatives for MBO.

Neoadjuvant Chemotherapy (NACT) before surgery is yet to be approved in recurrent settings and should not be offered outside of clinical trials.

Platinum sensitive relapses, who are not candidates for repeat surgery, should be rechallenged with platinum based combination chemotherapy for four to six cycles. Carboplatin based combination therapy has shown better survival outcomes over single agent carboplatin monotherapy in RCTs. Monotherapy is preferred only if there is a contraindication to combination therapy.

In platinum resistant and refractory cases, single non platinum agents like weekly paclitaxel, doxorubicin, topotecan, gemcitabine and oral metronomic cyclophosphamide are the commonly used agents. Patient preference and toxicity profile are the guiding factors. In such cases treatment may be continued till there is clinical benefit and no serious side effects.[3]

Targeted therapy in recurrent ovarian cancer has revolutionized the current treatment scenario but still many clinical trials are needed in this setting to standardize treatment protocols.

Antiangiogenic agents like Bevacizumab, Nintedanib, Pazopanib, Cediranib and Trebananib have been evaluated in the treatment of recurrent ovarian cancer. Bevacizumab is a humanized monoclonal antibody against Vascular Endothelial Growth Factor (VEGF). It is the only anti angiogenic agent approved for the treatment of ovarian cancer.

In Platinum sensitive relapse, role of bevacizumab was evaluated by the OCEANS and GOG0213 trials. Bevacizumab has been used in platinum sensitive recurrent disease (TFIp >6 months) in combination with platinum based chemotherapy followed by as maintenance therapy. In patients previously treated with bevacizumab, bevacizumab rechallenge can be given. Maintenance treatment with bevacizumab should be continued till the disease progresses or unacceptable side effects.

AURELIA is the first trial to assess the combination of bevacizumab with chemotherapy in platinum resistant ovarian cancer. It demonstrated improved PFS and Quality of life scores. The common side effects of this drug include high blood pressure, skin changes, nose bleeds and gastrointestinal (GI) symptoms like nausea, diarrhea etc. However, it can also cause serious complications like stroke and GI perforation.

PARP inhibitors (PARPi) like olaparib, niraparib, rucaparib are approved for maintenance therapy in patients with platinum sensitive relapses, supported by trials like NOVA, SOLO2 and ARIEL3. Treatment with PARPis as maintenance treatment can be continued till disease progression or unacceptable side effects, whichever comes earlier. However, certain revisions have been made in the recent years with respect to PARPi in the management of ovarian cancers. Data from ARIEL4, SOLO3 and QUADRA studies have led to the withdrawl of these drugs as single agents in recurrent ovarian cancer in patients previously treated with second/ third lines of chemotherapy. The toxicities of PARPis are usually managed by dose alterations and treatment individualisations. The most common dose limiting toxicities of PARP inhibitors are hematological which are well managed with supportive care and dose reductions. The grave adverse effects can include myelodysplastic syndromes which require discontinuations.[3]

Among the most groundbreaking advances is immunotherapy, which harnesses the power of the body's own immune system to recognize and destroy cancer cells. This innovative approach has ushered in a new era in oncology—one marked by hope, precision, and in some cases, durable cures. Unlike chemotherapy, which targets rapidly dividing cells (often harming healthy cells too),

immune check-point inhibitors (ICIs) aims to enhance the body's natural defenses with more specificity and fewer systemic side effects.[7]

Based upon the Garnet study and Le DT et al., Dostarlimab and Pembrolizumab are approved for MMR deficient recurrent, both platinum sensitive and recurrent cancers.

The combinations of PARP inhibitors, anti-angiogenic agents and ICIs is quite promising; but the need of the hour is more evidence in this area with respect to treatment schedule, duration and the management of toxicities. AVANOVA 2 study in platinum sensitive recurrent ovarian cancer supports the combination of niraparib and bevacizumab as apposed to niraparib alone.

Studies like MEDIOLA, Lee et al., and TOPACIO have evaluated the role of Immunotherapy with PARPi. ANITA study is an ongoing study for the same, however, till date enough evidence to support these combination targeted therapies is still lacking.

Antibody drug Conjugate (ADCs) are a class of targeted therapies to selectively deliver cytotoxic drugs to cancer cells with the help of tumor antigen specific antibody as a carrier agent for drug delivery (figure 1). Normally systemic chemotherapeutic drugs have small therapeutic index leading to narrow therapeutic window. Delivery of chemotherapy drugs via ADC leads to better drug delivery with wide therapeutic index leading to limited systemic toxicity (figure 2).

Fam- trastuzumab deruxtecan- nxki, approved for both platinum sensitive and recurrent HER2 positive ovarian cancer based on the DESTINY-PanTumor02 Phase 2 trial.

Mirvetuximab soravtansine- gynx is approved for folate receptor alpha (FRα) expressing platinum sensitive and resistant recurrent disease, alone or in combination with bevacizumab depending upon the percentage of FRα positive tumor cells. Secord AA et al., Gilbert L et al., and MIRASOL trial are the basis of these recommendations.

Despite of the varied advances in systemic treatment and ongoing research on Targeted therapy, surgery still remains the cornerstone when feasible and indicated depending on patient and tumour factors. Considering the multidisciplinary management recurrent ovarian cancer patients need to be evaluated in cancer centres with experienced gynaecological oncologists.

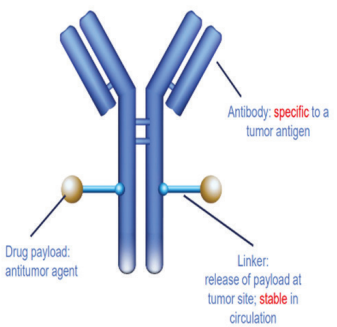

Figure 1. Components of ADC

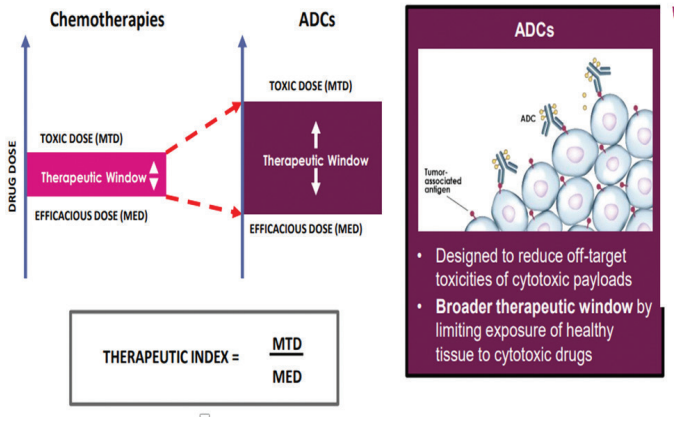

Figure 2. Therapeutic window shift with ADC
MTD- Maximum Toxic Dose
MED- Minimum Effective Dose

Reference

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6. Lim, M.C. (2025) 'Chipor, horse, and beyond: Unraveling the role of Hyperthermic Intraperitoneal Chemotherapy (HIPEC) in ovarian cancer', Journal of Gynecologic Oncology, 36(1). doi:10.3802/jgo.2025.36.e73.
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Quiz - Early Ovarian Cancer

Niharika Dhiman, Preeti Yadav*
Professor, *Postgraduate, Department of Obstetrics and Gynaecology
Maulana Azad Medical College & associated Hospitals, New Delhi

1. All the factors increase relative risk of ovarian cancer except
   a. early menarche
   b. late menopause
   c. history of hysterectomy or tubal ligation
   d. nulliparity
2. Strongest predictor of overall survival in ovarian cancer is
   a. performance status
   b. Ca125 levels
   c. stage of the disease
   d. complete tumor resection in either primary or interval cytoreduction
3. The B rules of IOTA include all the following except:
   a. unilocular tumor
   b. presence of acoustic shadow
   c. no blood flow
   d. papillary projection
4. Choose the false statement regarding ovarian cancer prognosis
   a. Histologic grade is a predictor of occult metastasis
   b. positive cytology in early-stage disease
   c. capsular rupture in early-stage disease
   d. dense adhesions have no prognostic value
5. True statement regarding germ cell tumor includes all except
   a. juvenile GCT is more aggressive than adult one
   b. absence of call exner bodies is a predictor of early recurrence
   c. bilateral in 2% cases
   d. none of the above
6. Markers of Germ Cell Tumor include:
   a. inhibin B b. estrogen
   c. AMH d. CD99
   e. all of the above
7. Most common malignant ovarian sex cord stromal tumor is
   a. GCT b. sertoli leydig tumor
   c. thecoma fibroma d. fibroma
8. Prophylactic bilateral salpingoophrectomy reduces RR of BRCA related gynecological cancer by
   a. 96% b. 86%
   c. 76% d. 66%
9. Most common mode of spread in malignant ovarian tumor is
   a. trans coelomic b. lymphatic
   c. hematogenous d. direct
10. Risk reducing prophylactic surgery in a female with BRCA 1&2 mutations include
    a. removal of both ovaries only
    b. removal of both fallopian tubes only
    c. removal of both tubes and ovaries
    d. removal of both tubes and ovaries and total peritonectomy
11. Ovarian cancers occuring due to germline mutations in BRCA 1&2?
    a. 5-10% b. 10-15%
    c. 15-20% d. 20-25%
12. A woman's risk at birth of having ovarian cancer in lifetime is
    a. 1% b. 2%
    c. 3% d. 4%
13. All of the following increase the risk of ovarian cancer except:
    a. childhood obesity/high BMI
    b. infertility
    c. nulliparity
    d. infertility drugs
14. "Early satiety" in early ovarian cancer is best explained by
    a. Hyperacidity b. mass effect
    c. ovarian torsion d. both a and b
15. Five years use of OCPs causes what % risk reduction in ovarian cancer?
    a. 20% b. 30%
    c. 50% d. 70%
16. Placental alkaline phosphate is increased in
    a. dysgerminoma
    b. immature teratoma
    c. endodermal sinus tumor
    d. all of the above
17. Which clinical feature strongly suggests COWDEN syndrome in a young woman with early ovarian cancer?
    a. Family history of colon cancer
    b. Mucocutaneous papillomas and trichilemmomas
    c. Early menarche
    d. HPV infection
18. Most important prognostic factor in immature teratoma is
    a. age b. grade
    c. nodal involvement d. tumor markers

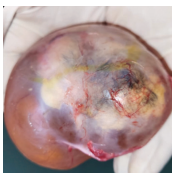
19. O-RADS primarily helps by:
    a. Diagnosing genetics
    b. Standardizing USG risk categories and management recommendations
    c. Replaces histopathology
    d. Staging early ovarian cancer

20. ROMA includes:
    a. Ca 125+ HE4 + menopausal status
    b. Ca 125 + AFP + LDH
    c. Ca 19.9 + HE4
    d. Ca 125 + ultrasound score

21. Grading of ovarian immature teratoma is based upon
    a. LVSI component
    b. AFP
    c. neuroepithelial component
    d. glial implants

22. Ovarian fibromas may resemble which other tumour on gross cut surface due to similar whorled appearance?
    a. Mature teratoma
    b. Brenner tumor
    c. Uterine leiomyoma
    d. Sertoli-Leydig cell tumor

23. Most common complication associated with the tumor shown below is -
    a. Malignant transformation
    b. Haemorrhage
    c. Torsion
    d. Rupture



24. Select the true statement
    a. Hereditary ovarian cancers occur 15-20 years later than the sporadic cancers
    b. 7% ovarian tumors in premenopausal women are malignant
    c. 80% ovarian tumors in postmenopausal women are malignant
    d. Almost all epithelial ovarian cancers are genetic

25. If a 30-year-old female having BRCA 1 mutation wants to preserve her reproductive function, what would be your next advice?
    a. Get BSO done and go for donor ova
    b. TVS and CA125 at 6 monthly interval, complete family and then go for BSO
    c. Cryopreserve ova and get BSO
    d. cryopreserve ova, get Hysterectomy with BSO and go for surrogacy

26. A 31-year-old female has BRCA1 mutation. How frequently should she be offered breast examination and mammography?
    a. Annual MRI mammogram with USG
    b. Annual mammogram
    c. any of the above
    d. Annual mammogram and annual MRI mammogram with contrast alternating every 6 months

27. All of the statements are true for a 35/F with LYNCH syndrome (HNPCC) except
    a. Annual colonoscopy
    b. Timing of development of cancer in the family is important
    c. 5 yearly EB to be done
    d. Hysterectomy with BSO after completing her family at 40 years.

ANSWER KEY

1-C, 2-D, 3-D, 4-D, 5-A, 6-E, 7-A, 8-A, 9-A, 10-C, 11-C, 12-A, 13-D, 14-B, 15-C, 16-A, 17-B, 18-B, 19-B, 20-A, 21-C, 22-C, 23-C, 24-B, 25-B, 26-D, 27-C,

AOGD Clinical Meet from Sir Ganga Ram Hospital held on 26th December 2025

Case Study: Management of infected Bladder Flap Hematoma following repeat Caesarean Section

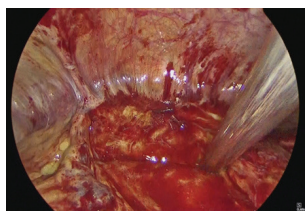
Ashmita Jawa*, Renuka Brijwal*
Kanwal Gujral, Chandra Mansukhani****
*Associate Consultants, **Senior Consultants, Institute of Obstetrics & Gynecology, Sir Gangaram Hospital, Delhi

Introduction: Rising global caesarean section rates and advanced imaging have increased detection of bladder flap hematomas. With an incidence of 0.5–1% of cases, this often-misdiagnosed complication involves collection of blood in the vesico-uterine space due to uterine incision bleeding, presenting a diagnostic challenge compared to more common infections like endometritis/ wound infections.

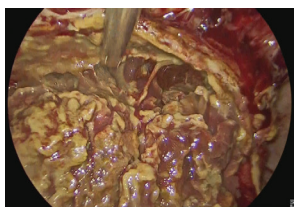
Case Presentation: Mrs. X, 37-year-old, P3L2, underwent elective LSCS in view of previous 2LSCS at private hospital. She had intraoperative postpartum hemorrhage, managed conservatively. Subsequently, she developed oliguria, hematuria and fever- referred to higher center. She was admitted in ICU with sepsis, DIC, and acute kidney injury. Her inflammatory markers were significantly elevated, and USG revealed a 9.5*9 cm hemorrhagic collection along anterior aspect of LUS, posterior to bladder. Conservative management done involving multisiciplinary team (nephrologist). Patient's clinical condition & lab profile improved; and she was discharged on day 11. Follow-up USG after two weeks showed persistent hematoma. NCCT revealed pelvic collection of 12*10 cm, with internal air foci suggestive superimposed infection. Patient underwent laparoscopy at SGRH involving gynecologist, surgeon & urologist. Surgical findings revealed a large loculated collection containing 800cc of gangrenous tissue with organized clots with a 3x3cm rent over posterior bladder wall. Bladder injury repaired by urologist, and omental live graft placed between bladder and uterus. Postop uneventful. Cystogram on POD14 reported normal.

Discussion: The clinical manifestation of BFH is often atypical, leading to delayed identification. Patients may present with suprapubic discomfort, low-grade fever, hematuria, or a significant drop in haemoglobin and even hypovolemic shock in severe cases. The development of BFH is often linked to surgical technique, particularly during closure of visceral peritoneum or inadequate hemostasis of vesico-uterine vessels. Risk factors include emergency surgery and prior adhesions from previous C-sections, as in this case. Research by Maldjan et al. highlighted that MRI performed for persistent fever post-CS revealed BFH in 64% of cases, proving its role as a silent driver of postoperative morbidity. Radiological assessment is the cornerstone of diagnosis. Ultrasonography is the first-line tool, typically showing a heterogeneous collection between the bladder and anterior uterine wall. CT/ MRI scans provide superior delineation of the hematoma's extent, urinary tract injuries (if any), and for better surgical planning. Scientific literature lacks a defined universal protocol for BFH, & management is decided by hematoma size and patient's clinical condition: conservative management is suited for hematomas <4cm or stable patients where serial imaging is suggestive of decrease in collection. Surgical intervention is required for large, infected, or symptomatic collections ranging from USG-guided drainage, laparoscopy, or re-laparotomy.

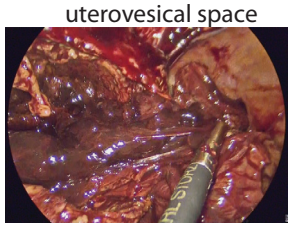
Conclusion: Bladder flap hematoma should be considered amongst primary differentials for any puerperant presenting with unexplained fever, suprapubic pain, or hematuria. Early detection and individualized management are vital for bladder flap hematomas. While conservative care may suffice with close follow up, large infected cases involving bladder require would need early surgical intervention to ensure optimal outcomes.



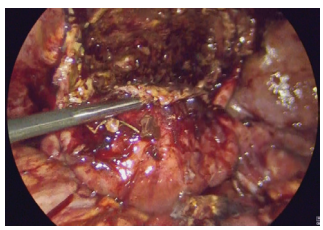
Adhesion band obliterating uterovesical space



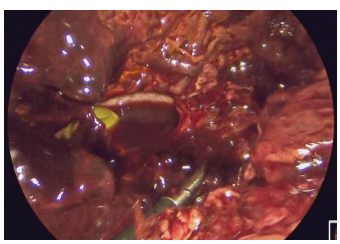
Bladder fat

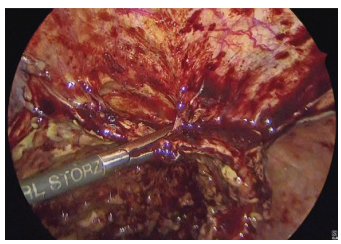


Clots in vesicouterine space

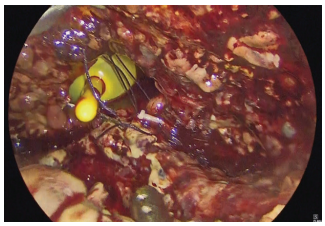


Uterus wrt bladder

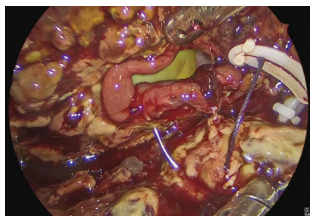




Bladder mobilisation from ant abd wall

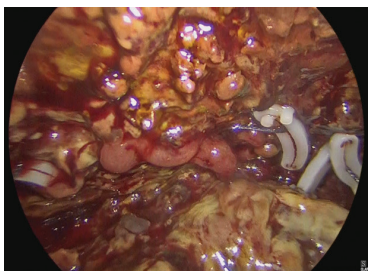


Repair of bladder rent



Repair of bladder rent

Repair of bladder rent



Final Repair of bladder injury

The Mosaic Miracle: A Healthy Live Birth After Dual PGT Screening

Kajal Baleja, Neeti Tiwari
Senior IVF consultant
Centre of IVF, Sir Ganga Ram Hospital (SGRH), Delhi

Introduction: This case presentation illustrates the successful management of a complex genetic scenario involving secondary infertility and a history of genetic disorders. The report highlights the clinical utility of dual Preimplantation Genetic Testing (PGT-M and PGT-A) and the decision making process regarding the transfer of a mosaic embryo.

Case Presentation : A 37-year-old female, and her 39 year old husband presented with secondary infertility since 6 months. Their obstetric history was significant for a previous natural conception resulting in a male child affected by Fragile X Syndrome, characterized by cognitive difficulties. Genetic testing confirmed the son was positive for Fragile X methylation, and the mother was identified as a carrier with an expansion of the trinucleotide repeat (>200) in the FMR1 gene. Basic infertility investigation revealed an AMH:0.61ng/ml, Normozoospermic semen analysis and bilateral tubal blockage.

Clinical Management: Given the advanced maternal age, tubal factor infertility and the history of Fragile X, the couple was advised for IVF with dual screening: PGT-M (for the monogenic disorder) and PGT-A (for aneuploidy). A Duostim protocol was utilized, resulting in five blastocysts that were biopsied and vitrified.

The PGT-M results indicated that while two embryos were "at-risk" for Fragile X, three were "lowrisk" (unaffected). However, PGT-A analysis of the unaffected embryos revealed a diagnostic dilemma: the only viable option was a Day 6 blastocyst identified as "Low Mosaic Trisomy 21", rest two embryos had complex aneuploidy.

The Mosaic Dilemma and Outcome : The couple underwent extensive genetic counseling regarding the transfer of a mosaic embryo. Risks discussed included lower implantation rates, higher miscarriage risks, limited long-term data on congenital anomalies, diagnostic uncertainty and need for invasive prenatal testing preferably amniocentesis. Current guidelines from the Preimplantation Genetic Diagnosis International Society (PGDIS) and ESHRE suggest that while euploid embryos are preferred, mosaic embryos may be considered when no euploid embryos are available, provided the patient understands the risks.

The couple consented to the transfer. A frozen embryo transfer of the low-level mosaic embryo was performed. The patient conceived, and at 16 weeks gestation, an invasive prenatal diagnosis (Amniocentesis with FISH and CMA) was performed. The results were negative for Trisomy 21,13,18 confirming a healthy genetic profile. In November 2025, the patient delivered a healthy male child via cesarean section.

Discussion and Institutional Data: Mosaic embryos contain distinct cell lines (euploid and aneuploid). Literature reviews, such as Greco et al. (2015), confirm that healthy live births are possible from mosaic transfers. Low level mosaicism reported on embryo testing does not always reflect true mosaicism of the entire embryo. In many cases the mosaicism may be confined to the trophoblastic cells rather than the inner cell mass that forms the fetus. Additionally, embryos have the ability to undergo spontaneous correction through selective loss or repair of abnormal cells. As a result, transfer of low level mosaic embryo, can still lead to development of a health and chromosomally normal fetus.

Conclusion: This case reinforces that mosaic embryos should not be automatically discarded. With rigorous risk stratification, mandatory genetic counseling, and subsequent invasive prenatal testing, mosaic embryo transfer can serve as a viable second-line option to achieve a healthy live birth.

CASE SERIES: ADENOMYOMECTOMY AND ITS IMPACT ON FERTILITY

Punita Bhardwaj
Senior consultant, Department of Obstetrics and Gynaecology, Sir Gangaram Hospital

Background: Adenomyosis is defined by the presence of endometrial glands and stroma within the myometrium, with a reported prevalence ranging from 8.8% to 61.5%. It is increasingly diagnosed in women of reproductive age and is associated with subfertility and adverse pregnancy outcomes. The disease alters the uterine hormonal, cellular, and immunological environment, resulting in impaired

decidualization and abnormal embryonic development. Defective spiral artery remodeling within the junctional zone leads to impaired deep placentation, placental hypoperfusion, and suboptimal placental development. These pathophysiological changes contribute to reduced implantation rates, lower clinical pregnancy and live birth rates, and increased risks of miscarriage, preterm delivery, pre-eclampsia, postpartum hemorrhage, and small-for-gestational-age infants.

Aim: To evaluate the impact of laparoscopic adenomyomectomy on pain, menorrhagia, recurrence, long-term symptom control, and pregnancy outcomes.

Methods: This ambispective study was conducted over a 10-year period (January 2015–December 2025) at Sir Ganga Ram Hospital, New Delhi, in accordance with institutional ethical standards. Sixty-two women with symptomatic adenomyosis who had failed medical therapy for at least six months were included. Indications for surgery included severe dysmenorrhea (VAS score), menorrhagia (pads used per day), recurrent pregnancy loss, failed IVF, incomplete childbearing, and unwillingness or unfitness for hysterectomy. Women older than 42 years were excluded. All procedures were performed by a single surgeon experienced in advanced laparoscopy. No preoperative medical therapy was used. Surgical technique was individualized based on ultrasonography and/or MRI findings, with maximal excision of adenomyotic tissue while preserving uterine architecture and ensuring adequate uterine reconstruction to maintain scar integrity for future pregnancy. Follow-up was conducted at 1 week, 1 month, 3 months, 6 months, 1 year, and 2 years postoperatively, with additional telephonic follow-up at 6 and 10 years using a structured proforma. Variables analyzed included age, symptoms, associated pathology, recurrence, and reproductive outcomes.

Results: All 62 patients presented with severe dysmenorrhea, and 42 had significant menorrhagia. Coexisting endometriosis was observed in 32 patients, while fibroids were present in 22 patients. Postoperatively, there was a significant reduction in dysmenorrhea, with marked improvement in VAS scores during early follow-up. A gradual increase in pain scores was noted after three years. Introduction of postoperative medical therapy, including LNG-IUS, oral contraceptives, or dienogest during later follow-up (4–6 years), resulted in symptomatic improvement. Recurrence occurred in approximately 27% of patients, usually after two years. Higher recurrence rates were observed in women with coexisting endometriosis, elevated CA-125 levels (>200 U/ml), and younger age (<39 years), though these trends were not statistically significant. Among women desiring pregnancy, the clinical pregnancy rate was 66%, with time to conception ranging from 1.5 months to 3 years after surgery.

Discussion: Adenomyosis frequently coexists with endometriosis and fibroids, and there is no universally accepted management strategy. Medical therapy may offer temporary symptom relief but often compromises fertility outcomes. Laparoscopic adenomyomectomy allows removal of diseased tissue while preserving the uterus, though maintaining normal myometrium and scar integrity remains technically challenging. In this study, favorable reproductive outcomes were observed in selected patients, with age at surgery emerging as the only important determinant of pregnancy. Pregnancy outcomes varied by disease subtype and extent, with better results in focal adenomyosis compared to diffuse disease. Published literature reports pregnancy rates of 32%–50% following conservative surgery, with focal disease associated with live birth rates up to 70%. Diffuse adenomyosis is associated with poorer reproductive outcomes, with clinical pregnancy rates around 36% and live birth rates as low as 18%. The risk of uterine rupture following adenomyomectomy was less than 6% in diffuse disease, and all pregnancies were delivered by cesarean section.

Conclusion: Laparoscopic adenomyomectomy is a valuable fertility-preserving option for selected women with symptomatic adenomyosis who desire pregnancy. Successful outcomes depend on careful patient selection, disease extent, surgical expertise, and awareness of potential pregnancy-related complications. Further high-quality, standardized studies are required to define optimal fertility-preserving management strategies and to minimize risks such as uterine rupture and placenta accreta spectrum in future pregnancies.

AOGD Subcommittees Chairperson Election (2026-28)
Call for nominations

Nominations for the **Chairperson Medico-legal subcommittee of AOGD** is extended till 15 January 2026 as no nominations have been received so far. Nominations for other subcommittees are closed

Last date for submission of nominations is **15/01/2026**

- ✓ Applications by desirous candidates should be submitted on the prescribed form available on AOGD website (www.aogd.org) / bulletin / office, with due entry in the office register in a sealed envelope & through email aogdlhmc2025@gmail.com
- ✓ Nominations as per the eligibility criteria should reach AOGD secretariat: Department of Obst. & Gynae LHMC & SSK Hospital, New Delhi- 110001 (Phone no. 9717392924) by **15/01/2026.**

Dr. Ratna Biswas (Secretary AOGD , 9971372695)

Important announcement : The chairpersons after being nominated have the responsibility to call for application for members of their respective subcommittee for up to a maximum of 10 members.

Eligibility Criteria for AOGD Sub-committee chairperson

1. The chairperson of a sub-committee should have been a member of the sub-committee in question for at least one term, with one term being equivalent to two years, prior to his/her appointment as chairperson of that sub-committee.
2. He/she should have been a member of the AOGD for fifteen years.
3. He/she should have experience in the field related to the subcommittee.
4. He/she should have completed at least fifteen years from the date of his/her registration as a medical practitioner. Further, he/she should have held a senior / faculty position for not less than that of associate professor, senior consultant or an equivalent there of in his/her respective organization, for a period of at least five years .
5. No person should hold chairperson ship of the same subcommittee for two consecutive terms with each term comprising of two years. Further, a person who has been chairperson of one subcommittee cannot be nominated as chairperson of another subcommittee unless separated by a duration equivalent to two terms of the subcommittee.
6. The Executive Committee may lay down additional criteria for the eligibility and pre-requisites for appointment as chairperson of each sub-committee from time to time.
7. An eligible member must send an application for nomination as chairperson of a sub-committee stating therein his/her previous experience in the field related to the sub-committee and future vision for furthering the goals of the AOGD through such sub-committee. One person shall not apply for chairpersonship of more than one sub- committee at a time. The application shall be scrutinized by the Executive Committee of AOGD for nomination as chairperson.
8. In the event of more than one application being received for appointment as chairperson of a subcommittee, and in the absence of unanimous decision of the Executive committee in this regard, the Executive Committee shall decide the nomination by cast of secret ballot.
9. The tenure of the chairperson of subcommittee shall be for a period of two years.

The Association of Obstetricians & Gynaecologists of Delhi

Nomination Form

Name:_____

Designation/Affilation_____

AOGD Membership no:_____

Official Address:_____

Residential Address:_____

Phone:_____Email:_____

Bio Sketch (Relevant to the Eligibility Criteria in 250words)

Post Applied for

Sub-committee Chairperson
2026-28

Subcommittee Name

Proposed by – Name AOGD Membership no. Signature

1.

Seconded by

1.

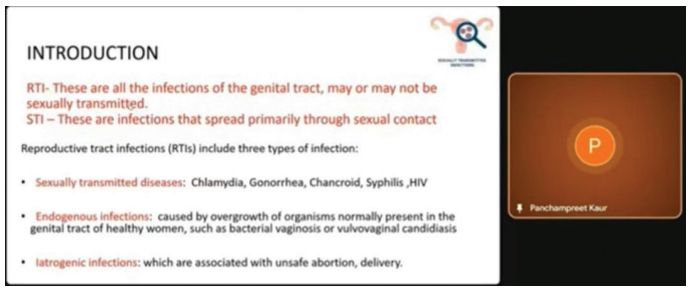
2.

Nominations should reach at AOGD Office
For any Query please call Mrs. Sarita : 9211656757, 9717392924

Events Held 2025

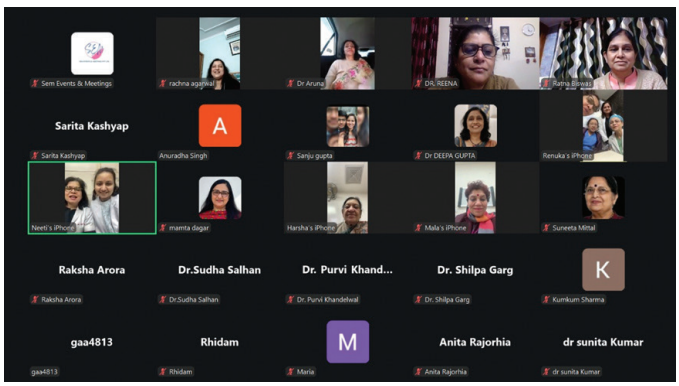
CME on "Elimination of Vertical Transmission of HIV & Syphilis (EVTHS)" conducted by Department of Obst & Gynae, ESIC Medical College in association with Safe Motherhood Committee on 13th December, 2025

Mission Adolescent Health conducted by DGF and Adolescent Subcommittee AOGD on 15 th December, 2025



CME on " Enhancing Maternal and Fetal Health" conducted by Fetal Medicine and Genetics subcommittee on 17th December, at Eros Hotel, Nehru Place.

The AOGD Monthly Clinical Meeting (virtual) conducted by the Department of Obst. & Gynae, Sir Ganga Ram Hospital on 26th December, 2025



Association of Obstetricians & Gynaecologists of Delhi

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Date of Birth: Date.....**Month** ..... **Year**.....

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Proposed by .....

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Cheque/Demand Draft should be drawn in favour of**: Association of Obstetricians and Gynaecologists of Delhi**

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Account no: 5786412323
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Branch: LHMC & SSK Hospital
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MICR code: 110016067

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12418708@cbin

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For New Annual Membership*	: Rs. 2,000 + Rs. 360 (18% GST applicable) = Rs. 2,360
For Old Renewal Membership+	: Rs. 1,200 + Rs. 216 (18% GST applicable) = Rs. 1,416

Encl.: Attach Two Photocopies of All Degrees, DMC Certificate and Two Photographs (Self attested)

*** Annual Membership is for the calendar year January to December.**

*** In case of renewal, mention old membership number.**

Note: 18% GST will be applicable as FOGSI requires it.

Send Complete Membership Form Along With Cheque / DD and Photocopy of required documents to the secretariat.
For online transaction send scan copy of all documents with payment slip on given mail id

Secretariat
Department of Obstetrics and Gynaecology
Lady Hardinge Medical College & SSK Hospital, New Delhi-110001
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68th All India Congress of Obstetrics & Gynaecology

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Advocate Innovate Challenge Optimise Globalise

Conference Theme

68th AICOG 2026 DELHI

All India Congress of Obstetrics & Gynaecology

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All India Congress of Obstetrics & Gynaecology

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