AOGD BULLETIN

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Safeguarding women and their Doctors

Issue Theme:
Ovarian Cancer- Catch it early

AOGD SECRETARIAT

Department of Obstetrics and Gynecology
Maulana Azad Medical College & Lok Nayak Hospital
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Editor
Dr. Madhavi M Gupta
Ph. No. 9968604351; Email: aogdeditor22@gmail.com

Foreword

It gives me immense pleasure to write the foreword to this issue of the AOGD Bulletin focussed on Ovarian Cancer, a notorious and most fatal cancer in women. The relevance of the topic cannot be overstated.

Detecting the condition early is important for optimal management and enabling the woman to live longer with good quality of life. Unlike cervical cancer screening, there is no screening protocol for ovarian cancer in the general population hence, the disease is diagnosed in the advanced stage in more than half the women. A lot of work focussing on biomarkers that can identify asymptomatic disease is in progress to improve early detection.

The therapy is decided by the response to first-line platinum therapy and platinum resistance needs alternative management strategies ranging from anti-angiogenic factors to immunotherapy which sound promising in various trials.

The role of PET/CT in ovarian cancer is specific and the indiscriminate use of this imaging modality may only cause exposure to radiation.The rationale use of PET/CT should guide management as required.

The theme for AOGD 2022-23 is 'Safeguarding Women and their Doctors'. Formation of "Self Help Groups" will boost the morale and provide support to the doctors in times of need.

My Best wishes to the AOGD team at Maulana Azad Medical College for a fruitful year ahead.

Dr. V.L. Bhargava
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From the AOGD Office

Dr. Asmita M. Rathore

Dr. Y. M. Mala

Dr. Deepti Goswami

Dear AOGD members

Warm Greetings!

It has been three months since we have had the opportunity to serve the AOGD- the vibrant, ever-growing family of obstetricians & gynaecologists. Our endeavour is to maintain its functioning to the highest standards and do value addition during our tenure. AOGD Risk Management Support (ARMS) Group is one such novel idea conceptualized to extend support to a colleague in need. Mounting expectations from doctors and the changing doctor-patient relationship may challenge even the most experienced among us. When required, an AOGD member can reach out to "ARMS"for advice and support. The details are there inside the bulletin.

In today's scenario, as knowledge is advancing, so are avenues for learning. The COVID pandemic took us towards online deliberations. Post-COVID, while offline events have taken off with great gusto, online events are here to stay. Both formats are being used liberally by the AOGD to exchange ideas, stimulate discussion, and update knowledge for day-to-day practice. AOGD is well supported in these academic endeavours by its active subcommittees and together we are able to put together a rainbow of events- CMEs, webinars, symposiums, case discussions -for our members through online as well as offline mode.

The highlight of the month of June was the hugely successful FOGSI conference, organized in physical mode, which was very well attended and appreciated. We thank our members for their full support in making it a memorable event. We now have set the ball rolling for the mega event - **44th Annual Conference of AOGD-to be held on November 12th and 13th, 2022**. This would be preceded by an array of focused workshops by the various sub committees. After a gap of two years, the conferenceis going to be in physical mode this time. So do take note and block the dates!

Dr. Madhavi and her editorial team have put together this bulletin with carefully curated content on the theme of "ovarian cancers" to provide the monthly quota of learning apart from the information about the forthcoming events and general updates.

Enjoy reading!

Dr. Asmita M Rathore, President
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From the Editor's Desk

Dr. Madhavi M. Gupta
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Hello Friends,

Greetings and welcome to the rains !

We are happy to bring to you the AOGD Bulletin for the month of July 2022.

This month the Game Changer section brings to you the O-RADS US Risk Stratification and Management System. Risk stratification is the first step towards optimal management. Ovarian cancer is known for late diagnosis and its subsequent unwelcome outcome. We compare different systems for stratification of ovarian masses.

The problem in ovarian cancer starts right from delayed diagnosis to the unpredictable response to platinum therapy and which higher imaging modality to be used when and why so. The challenge of a robust screening method in ovarian cancer is still out there. Lacking this, most cases are diagnosed late and the disease keeps coming back. New research focussing on early detection is in the pipeline. Platinum resistance and variable response to first-line platinum therapy requires alternative management strategies. Imaging in ovarian cancer is an integral part of diagnostic work-up. Judicious use of PET/CT is very important to minimise exposure to radiation and practice evidence based management.

All this has been covered very well by the authors and being the most recent in this area makes it interesting and informative. I sincerely thank them for their contribution.

The second article under the "Safeguarding the Doctors" is about Self-Help Groups. Problems and situations are better managed when we work as a team. The author takes us through the entire process of forming such local groups and also the practical problems encountered. I am sure that this will help all of you in your efforts to form such groups in your areas.

Your views and comments are welcome and these are important to improve with every issue.

Yours in health

Dr. Madhavi M Gupta
Editor

"And when it rains on your parade, look up rather than down.
Without the rain, there would be no rainbow."
– Gilbert K Chesterton

AOGD Risk Management Support [ARMS] Group

One of the ways to ensure the stress-free work environment and optimal patient care is mutual support among professional colleagues. We propose to form an advisory group of senior AOGD members that can be contacted if one of us is caught in a complex clinical dilemma / dealing with aggressive clients or is apprehensive about how to document or effectively troubleshoot a potential problem. This group will provide the timely advice and will be led by-

Convener- **Dr. Vijay Zutshi** - 9818319110

Co convener- **Dr. Aruna Nigam** - 9868656051

We invite suggestions from all members regarding functioning of this cell which will guide us forming the SOPs. Any member interested in being part of Advisory group may contact the convener.

Pl mail to aogdmamc2022@gmail.com

Game changer:
Risk Stratification for Ovarian-Adnexal Masses- O-RADS US Risk Stratification and Management System

Madhavi M Gupta*, Reena Rani**
*Director-Professor, **Assistant-Professor, Department of Obstetrics & Gynaecology, MAMC & Lok Nayak Hospital, New Delhi

Abstract of the research articles are available free at the journal websites and on Pubmed (http://www.ncbi.nlm.nih. gov/PubMed)

Andreotti RF, Timmerman D, Strachowski LM, et al. O-RADS US Risk Stratification and Management System: A Consensus Guideline from the ACR Ovarian-Adnexal Reporting and Data System Committee. Radiology. 2020;294(1):168-185.

This consensus guideline has been formulated with the aim of optimal patient management based on accurate assessment of ovarian and adnexal masses on ultrasound (US) imaging. The level of expertise varies and this guideline establishes standardized and evidence-based risk-assessment algorithms to improve risk stratification.

It was developed by an international multidisciplinary committee sponsored by the American College of Radiology and applies the standardized reporting tool for US based on the 2018 published lexicon of the O-RADS US working group.

Ultrasound (US) is an initial imaging investigation of choice for identifying and characterising adnexal masses, which is essential for optimal patient management. Unnecessary surgical procedures for benign lesions can be avoided by improving preoperative assessment of these lesions. Many structured reporting systems which use sonography to characterize adnexal masses have been developed so far. The International Ovarian Tumor Analysis (IOTA) group proposed the use of US simple rules (B & M features) for the diagnosis of ovarian malignancy. Gynecology Imaging Reporting and Data System (GI-RADS) is another standardized system for reporting adnexal masses as benign or malignant. However, these systems are unable to classify all adnexal masses and around 20% are categorized as inconclusive.

Risk Stratification Methodology

A retrospective analysis of prospectively collected data for the multicentre IOTA phase 1-3 was performed. This data came from women with an adnexal lesion across 24 centres in 10 countries between 1999 and 2012. A standardized US examination using IOTA terms and definitions was performed for all patients and the treating doctor decided on the surgical procedure. After excluding 9 women, the data set comprised of 5905 patients the largest with histologic findings available as a reference standard.

Based on expert opinion of the committee members, lexicon features were combined to represent clinically relevant groups of tumors and were placed in the different pre specified risk categories based on their corresponding prevalence of malignancy as found in the IOTA database. This classification that includes a clinical management scheme agreed on by the gynecologists, gynecologic oncologists, and radiologists in the O-RADS US working group formed the basis for the O-RADS US stratification system.

The O-RADS US working group defined six categories for risk classification. These include O-RADS 0, an incomplete evaluation; O-RADS 1, the physiologic category (normal premenopausal ovary); O-RADS 2, the almost certainly benign category (<1% risk of malignancy); O-RADS 3, lesions with low risk of malignancy (1% to <10%); O-RADS 4, lesions with intermediate risk of malignancy (10% to <50%); and O-RADS 5, lesions with high risk of malignancy (≥50%).

In summary, the Ovarian-Adnexal Reporting

and Data System (O-RADS) US risk stratification and management system (2018) for evaluation of ovarian and other adnexal masses is based on a standardized lexicon, incorporates all classes of risk, and offers an associated management strategy for each risk category. It offers a means to provide consistent interpretations and decrease ambiguity in US reports in assigning risk of malignancy with higher accuracy,and guiding in the management of average-risk patients without acute symptoms who demonstrate adnexal lesions.

Comparison of O-RADS, GI-RADS, and IOTA simple rules regarding malignancy rate, validity, and reliability for diagnosis of adnexal masses

Basha MAA, Metwally MI, Gamil SA, et al. Comparison of O-RADS, GI-RADS, and IOTA simple rules regarding malignancy rate, validity, and reliability for diagnosis of adnexal masses. EurRadiol. 2021;31(2):674-684. doi:10.1007/s00330-020-07143-7

This study aimed to compare the O-RADS with two other well-established US classification systems for diagnosis of adnexal masses (AM).

This was a multicentre retrospective study from May 2016 to December 2019. Adnexal masses were independently categorised by five experienced radiologists using the three risk stratification systems- O-RADS, gynecologic imaging reporting and data system (GI-RADS), and international ovarian tumor analysis (IOTA) simple rules. For calculating the validity of three US classification systems for diagnosis of AM, histopathology and adequate follow-up were used as reference standards.

The study included 609 women with 647 AM, 178 malignant and 469 benign. Malignancy rates were comparable to recommended rates by previous literature in O-RADS and IOTA, but higher in GI-RADS. O-RADS had significantly higher sensitivity for malignancy than GI-RADS and IOTA (96.8% vs 92.7% and 92.1%; $p = 0.003$ and 0.0007, respectively), but non-significant slightly lower specificity (92.8% vs 93.6% and 93.2%, respectively; $p > 0.05$). The inter-reviewer agreement (IRA) was higher with O-RADS than with GI-RADS and IOTA ($\kappa = 0.77$, 0.69, and 0.63, respectively).

The authors concluded that O-RADS compares favorably with GI-RADS and IOTA. O-RADS had higher sensitivity than GI-RADS and IOTA simple rules with relatively similar specificity and reliability.

Ovarian Cancer: Screening & Prevention: The Journey so Far & The Road Ahead

Bindiya Gupta*, Astha Srivastava**
Professor*, Assistant Professor **, Obstetrics and Gynecology, UCMS and GTB Hospital, New Delhi

1. Introduction

Ovarian cancer (OC) is the third most common gynaecological malignancy and the most lethal worldwide. According to GLOBOCAN 2020, approximately 314 000 new ovarian cancer cases and 207 000 deaths occurred worldwide. Most patients (60%) are diagnosed with advanced disease[1] which is associated with significant mortality. Five-year survival rates for FIGO stage I disease are 90%, stage II 65%, stage III 34%, and stage IV 15%.[1] This has spurred efforts to reduce mortality through screening.

Screening is looking for early signs of a particular disease in apparently 'healthy' people who do not have 'any symptoms'. A good screening test should be inexpensive, easy to administer, valid, cause minimal discomfort and should be consistently reliable. The screening program should be designed for the population section which has the highest prevalence of the disease to ascertain a satisfactory positive predictive value. Finally, the screening test should definitely show improvement in morbidity and mortality in that particular population section. Besides screening, various surgical and chemoprevention strategies have been studied and recommended in both average and high risk population.

2. Risk assessment for Ca Ovary

The average lifetime risk of an individual developing ovarian cancer in general population is 1.3-2%.[2] In high-risk population the lifetime OC risk is 10% or more. However, there is wide variation in an individual's OC risk due to lifestyle, reproductive and genetic factors.

2.1 Lifestyle and reproductive factors: These include[2]:

- Obesity- Risk of OC increases with increased BMI (BMI> 40: 22% increase in risk)
- Use of talc OR 1.31
- Black tea consumption OR 1.56
- Cigarette smoking increased incidence of mucinous cancers OR 1.31

2.2 Gynaecological risk factors

- Endometriosis (OR-1.46)
- Hormone replacement therapy (RR-1.37)

2.3 Genetic factors:

Moderate to high penetrance genes: account for 5-15% of ovarian malignancy

- BRCA1 - 44%
- BRCA2-17%
- MLH1, MSH2- 10-15%
- RAD51C, RAD51D - 11-12%
  BR1P1 - 5.8%, PALB2 - 5%

Low penetrance: account for 1.2-1.4 % of ovarian cancers

Unidentified low risk loci - 60% of unaccounted inherited risk.

2.4 Protective factors for ovarian cancer:

- Long term use of low dose aspirin OR 0.56
- Use of OCP (≥10yrs) OR 0.43
- Increasing parity
- Breastfeeding
- Tubal ligation OR 0.87
- Prophylactic salpingectomy OR 0.35

Risk stratification should be done by combining genetic, reproductive and lifestyle factors to better understand an individual's risk. Various familial risk tools have been proposed and some of them are shown in Table -1.

Table-1: Familial risk assessment tools for ovarian cancer

U.S. Preventive Services Task Force
• Ontario Family History Assessment Tool
• Manchester Scoring System
• Referral Screening Tool
• Pedigree Assessment Tool
• 7-Question Family History Screening Tool (FHS-7)
• International Breast Cancer Intervention Study instrument (Tyrer-Cuzick)
• Brief versions of BRCAPRO
Women with a positive screening result should receive genetic counseling, with further BRCA testing if warranted. Women without a family history associated with an increased risk for mutations should not receive routine risk assessment, genetic counseling or BRCA testing.

National Comprehensive Cancer Network

The NCCN provides specific criteria for genetic counseling and testing of BRCA, as well as additional genetic mutations associated with ovarian cancer risk: CDH1, STK11/LKB1, and Lynch syndrome (hereditary nonpolyposis colorectal cancer [HNPCC]) genes.

The criteria for affected individuals include having at least one of the following risk factors:

- Known genetic mutation within the family or from a population at increased risk
- Breast cancer before age 50
- Triple negative (estrogen receptor, progesterone receptor, HER2-) breast cancer
- Two primary breast cancer tumors
- Breast cancer and a close relative with breast cancer before age 50, or ovarian cancer at any age, or two or more close relatives with breast cancer or pancreatic cancer at any age
- A family member with a combination of breast cancer and either pancreatic cancer, prostate cancer, sarcoma, adrenocortical carcinoma, brain tumors, endometrial cancer, leukemia/lymphoma, thyroid cancer, hamartomatous polyps of the GI tract, or diffuse gastric cancer
- Ovarian cancer

The criteria for unaffected individuals include a family history of at least one of the following:

- Known genetic mutation within the family or from a population at increased risk
- One individual with two or more primary breast cancer tumors
- Two or more individuals on the same side of the family with breast cancer
- Ovarian cancer
- First- or second-degree relative with breast cancer before age 45
- A family member with a combination of breast cancer and either pancreatic cancer, prostate cancer, sarcoma, adrenocortical carcinoma, brain tumors, endometrial cancer, leukemia/lymphoma, thyroid cancer, hamartomatous polyps of the GI tract, or diffuse gastric cancer
- Male breast cancer

Women who meet the assessment criteria should receive genetic counseling, with further *BRCA* testing if warranted. Multi-gene testing may be considered in women who have tested negative (indeterminate) for a single syndrome, but whose personal or family history remains suggestive of an inherited susceptibility.

3. Screening methods

3.1 Goff Symptom index: Epithelial ovarian cancer in early stages usually presents with non specific and vague gastrointestinal, abdominal, and urinary symptoms. The Goff symptom index suggests that occurrence of any of the eight symptoms including pelvic/abdominal pain, urinary urgency/frequency, increased abdominal size/bloating, and difficulty eating/feeling full more than 12 times a month for less than one year may be considered positive for ovarian cancer.
In the confirmatory sample sensitivity was 56.7% for early-stage disease; 79.5% for advanced-stage disease. Specificity was 90% for women age >50 years.

3.2 Pelvic examination: The USPTF have stated that there is insufficient evidence to assess the balance of benefits and harms of performing screening pelvic examinations in asymptomatic, non-pregnant adult women for detection of ovarian cancer.

3.3 Transvaginal ultrasound (TVS)
TVS permits direct visualization of the adnexa and detection of disease directly through morphological changes or through characteristics associated with increased OC risk such as increase in ovarian volume.

Limitations of TVS

- Many aggressive tumours metastasize before reaching sonographically detected size
- Subjective nature of assessment & interobserver variations
- Difficult visualization of ovaries (obese, hysterectomized, tubal ligated)
- Poor visualization of fallopian tubes & tumor <1cm

Techniques aimed at improving image resolution such as doppler flow, microbubble contrast enhanced ultrasonography, and photo-acoustic imaging may allow detection of smaller, earlier cancers in the future.[5]

3.4 Tumor markers and longitudinal algorithms

CA125 remains the most effective biomarker of high grade serous OC. The application of CA125 in screening has evolved from use of cut-offs, such as >35 IU to change over time using longitudinal algorithms, such as the risk of ovarian cancer algorithm (ROCA).[6] CA125 change as measured by ROCA has been shown to detect a greater proportion of cancers.

Additional combinations of biomarkers have been suggested to improve sensitivity. Of these, HE4 (Human Epididymis 4) has been the most promising, although its performance, when used alone, is inferior to CA125. Potential strategies of combining a wide range of blood biomarkers have therefore been considered, using CA125 in addition to HE4, transthyretin, CA15-3, CA72.4 ,

TP53 , glycodelin, mesothelin, MMP7, CYFRA 21-1, VTCN1, Protein Z, Fibronectin, and C-reactive protein.[2]

4. Screening strategies and guidelines

The search for an ideal screening test for ovarian cancer has been going on for quite some time now. Transvaginal ultrasound, CA-125, and bimanual pelvic examination have been used in various screening studies to evaluate their role as screening tests but have not found much supportive evidence.

4.1 Screening trials in general population

Among the three good quality studies identified by USPSTF, the largest and the most recent was the UK Collaborative Trial of Ovarian Cancer Screening (UKCTOCS). The UKCTOCS was a randomized clinical trial of 202638 postmenopausal women aged 50–74 years not known to be at high risk of ovarian cancer.[6] In this trial, women were randomly assigned to two annual screening groups— multimodal screening (MMS; longitudinal CA125 and second line TVS) and ultrasound screening (USS; TVS first and second-line test), and a no screening group. After a median follow-up of 11.1 years, there was no significant difference in mortality due to ovarian cancer among the control group and the two intervention groups (0.35% in the control group, 0.32% in the TVS group, and 0.32% in the CA-125 ROCA group). Long term follow up of UKCTOCS (median 16·3 years after randomisation), showed that neither MMS or USS, significantly reduced deaths from ovarian and tubal cancer. There was a 47·2% higher incidence of stage I cancer and 24·5% lower incidence of stage IV cancer, resulting in an overall 39·2% higher incidence of stage I or II cancer and 10·2% lower incidence of stage III or IV cancer in the MMS group than in the no screening group.[7]

In the United States Prostate, Lung, Colorectal, and Ovarian cancer (PLCO) trial, no difference was found in the ovarian cancer mortality (including primary peritoneal cancer) with 0.34% in the screening group and 0.29% in the usual care group (RR 1.18 [95% CI, 0.82–1.71]) at a median follow-up for 12.4 years.[8] In this trial, 68,557 women aged 55–74 years who had at least one ovary at baseline were randomized to either annual screening (both CA-125 and TVS for first four rounds of screening, then two rounds of CA-125 testing only) or usual care after ruling out previous diagnosis of lung, colorectal, or ovarian cancer.

Surgery to investigate positive screening test results among women who ultimately did not have ovarian cancer occurred in 0.2% of participants in the UK Pilot CA-125 group, 0.97% of participants in the UKCTOCS CA-125 ROCA group, 3.25% of participants in the UKCTOCS ultrasound group, and 3.17% of participants in the PLCO CA-125 plus ultrasound group. Up to 15% of these women had major surgical complications. [9]

In the Japanese Shizuka Cohort Screening Study which randomized 82,487 women, at a mean follow-up of 9.2 years, the proportion of women with stage I ovarian cancer was higher in the screened group (63%) than in the control group (38%) but did not reach statistical significance ($p < 0.2285$). No mortality results have been published from this trial. [10] The University of Kentucky Study was a single arm prospective study in which 25,327 women underwent TVS screening. Sensitivity for detection of primary ovarian cancer was 81%. Five-year survival rates were higher in screened women who developed OC compared to unscreened women treated for ovarian cancer using the same institutional protocols. (74.8% ±6.6% vs 53.7% ±2.3% $P < 0.001$).[11]

4.2 Trials in high risk population

Trials in high risk population	Screening Strategies	Outcomes
UK Familial Ovarian Cancer Screening study UK FOCSS Phase 1[12]	Annual combined screen of transvaginal Ultrasound and CA125	Ineffective in detecting early stage disease
UK Familial Ovarian Cancer Screening study UK FOCSS Phase 2 [13]	4 monthly serum CA125 interpreted with ROCA and annual transvaginal ultrasound Eligibility criteria:>10% lifetime risk of ovarian cancer, age>35 yrs, declined RRBSO	1.Significant increase in low volume disease (Stage I-IIIa Vs IV) (63% vs 6% P = 0.0004) 2. Non-significant zero residual disease after debulking 3. Significant decrease in use of neo-adjuvant chemotherapy (5% vs 44%; p =0.008)
US Cancer Genetics Network and Gynaecologic Oncology Group trials [14]	3 monthly multi-modality screening (CA125 interpreted using ROCA)	Significant increase in Stage I/II (50% vs. 10% P =0.016) compared to historical BRCA1 controls

There are two ongoing trials in high-risk

populations. In the UK, a pilot NHS study, 'Avoiding Late Diagnosis of Ovarian Cancer (ALDO)' is underway in BRCA mutations carriers who decline RRSO and is using a multimodal screening strategy with CA125 interpreted using ROCA.[15] In the United States, a randomised trial is underway with high-risk women undergoing 6-monthly screening and intermediate-risk women undergoing annual screening. Women are being randomized to CA 125 and HE4 at every screen or CA 125 as first line test followed by HE4 as second-line test. The longitudinal PEB algorithm is being used to interpret the blood biomarkers and those with high levels undergo TVS.

4.3 Screening guidelines

4.3.1. In average risk population United States Preventive Services Task Force (USPSTF) has recommended against screening for ovarian cancer in asymptomatic women (level D) who are not at high risk for the disease.[4] The USPSTF identified limited evidence on the psychological harms of screening for ovarian cancer from the UKCTOCS and QUEST trials.[6,7,16] Society of Gynecologic Oncologists (SGO) also does not recommend screening for ovarian cancer in average-risk women.[17] Memorial Sloan Kettering (MSKCC) in its screening guidelines recommends that women with increased risk for ovarian cancer due to reasons other than genetic mutations may be offered screening within the framework of research studies to evaluate the efficacy of this approach after thorough counseling.

Prophylactic bilateral salpingectomy (PBS) should be performed in women undergoing hysterectomy for benign indication as a preventive strategy for ovarian cancer. In an evidence based analysis of 5 studies, PBS lowers the risk of ovarian cancer by 29.2%-64% without any significant impact on quality of life or ovarian function.[18] The pathologic specimen processing in low risk-women should include representative sections of the tube, any suspicious lesions, and entire sectioning of the fimbriae.[17]

4.3.2 In women with genetic mutations

For women with genetic mutations, ovarian cancer screening using a combination of CA-125 and TVS should be done. Screening in women with BRCA1 mutations or the mismatch repair gene (MLH1, MSH2, and MSH6) defect should begin between 30 and 35 years of age. For women with BRCA2 mutations, screening is initiated between 35 and 40 years of age. Screening is done by 6 monthly TVS & CA125 starting at 30-35 yrs until definitive risk reduction surgery.

The National Comprehensive Cancer Network (NCCN), UPSTF guidelines and ACOG guidelines, recommend risk-reducing salpingo-oophorectomy (RRSO) in women with BRCA1/2 mutations after 35 years of age once childbearing is complete.[19,20,21] Hysterectomy should be offered in women with Lynch syndrome. NCCN guidelines also give an option of an individualized age based on earliest age of ovarian cancer diagnosed in the family. The women considering RRSO should be made aware of the increased risks associated with premature menopause like osteoporosis and cardiovascular disease and potential effects of possible cognitive changes and vasomotor symptoms on quality of life. In absence of contraindications, premenopausal women undergoing RRSO should be offered hormone therapy until menopause, except for women with personal history of breast cancer.

SGO guidelines recommend that RRSO is the best strategy; however, if the woman is not willing due to adverse effects of premature menopause, option of risk reducing salpingectomy after childbearing is completed, followed by delayed oophorectomy may be offered after thorough counselling.[17] In pathological evaluation of the specimen the Sectioning and Extensively Examining the FIMbriated End (SEE-FIM) protocol should be followed to identify the precursor lesions i.e. Serous tubal intraepithelial carcinoma (STIC).[22]

5. Futuristic Roadmap

There remains an urgent need for strategies to detect ovarian cancer earlier in order to reduce mortality. Both in the low-risk and in the high-risk population, there is evidence that a multimodal strategy based on longitudinal CA125 profile and second line TVS can lead to earlier diagnosis.

However, no screening strategy has been shown to definitively decrease OC mortality. A key limitation of current screening strategies is the lack of tests that are able to detect pre malignant and early stage disease. Innovative strategies being investigated include longitudinal biomarker algorithms, detection of tumour DNA in cervical cytology or uterine lavage specimens and blood, detection of cell free DNA and circulating tumor cells and improved targeted imaging of the adnexa.

Increased understanding of the environmental, reproductive, and genetic risk factors for OC is improving risk stratification which is key to defining the target population for screening or primary prevention. Existing OC screening trials have used age and family history of ovarian cancer to identify target populations for screening. In addition, high risk trials have also used mutation status.

The current focus is to incorporate additional SNPs, epidemiological, lifestyle and reproductive factors to individualise OC risk prediction. CanRisk (BODICEA V) is one such recently released ovarian and breast cancer risk assessment tool that can assist clinicians during a consultation.[23] Alongside this, there are studies such as 'FORECEE' exploring molecular markers and methylation profiles in cervical cytology cells for risk prediction of ovarian and other (breast, cervical, and endometrial) women's cancers.[24]

Currently, no agent is proven by interventional trials to possess chemo preventive properties against OC. Chemoprevention strategies using oral contraceptives, non-steroidal anti-inflammatory drugs, retinoids, angiopreventive agents, poly(adp-ribose) polymerase inhibitors, and tyrosine kinase inhibitors have shown promise for OC chemoprevention.

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Alternative management strategies in ovarian cancer

Shalini Rajaram*, Parmita Tiwari**
*Professor & Program Coordinator MCh Gynecologic Oncology, **MCh Trainee, Dept. of Obstetrics & Gynecology
AIIMS Rishikesh

Introduction

Ovarian cancer is the eighth most common cancer in women worldwide and a leading cause of gynaecological cancer-related death in women globally.[1] According to GLOBOCAN data, 3,13,959 new cases of ovarian cancer were diagnosed in 2020 and 2,07,252 women died due to the disease.[1] Ovarian cancer is more common in high-income countries, although its incidence is rising in lower-income countries as well. In 2020, 45,701 Indian women were diagnosed with ovarian cancer and 32,077 died.[1] By the year 2040, global incidence will rise by 37% to a total of 4,28,966 cases, with an even larger increase in the number of deaths.[1]

Due to ambiguous symptoms and lack of screening methods most women (75%) are diagnosed at an advanced stage.[2] Most of these patients will experience a recurrence with emergence of chemotherapy-resistant disease and exhaustion of available treatment options. This explains low five-year survival rates (35%) for advanced stage disease.[2]

The concept of platinum free interval (PFI) was first developed in the early 1990s.[3] Definition of PFI was specified at the fourth Ovarian Cancer Consensus Conference, based upon the time interval between the last platinum dose and relapse of the disease.[4] Patients were categorized into four subgroups as platinum refractory disease (PFI <1 month), platinum resistant disease (PFI 1 to 6 months), partially platinum sensitive (PFI 6 to 12 months) and fully platinum sensitive (PFI >12 months). The development of platinum resistance is a complex phenomenon influenced by tumour microenvironment and a variety of intracellular alterations. Possible mechanisms for development of platinum resistance, include decreased intracellular drug accumulation, increased ability to repair drug induced DNA adducts, and defective apoptosis pathway.[3] Cancer stem cell repopulation and heterogeneity of the cancer genome also plays a role.

The relevance of PFI in the era of molecular targeted therapy and immunotherapy has been questioned on several occasions. It was proposed to be replaced by the broader term "treatment-free interval" (TFI) at the fifth OCCC in Tokyo.[5] The role of targeted therapies and immunotherapies in the management of this recalcitrant disease is currently being evaluated. Aside from survival rates, patient-reported outcomes and health-related quality of life continue to be important goals in management of these patients.

Antiangiogenic Therapy

Angiogenesis is one of the hallmarks of cancer development. Antiangiogenic therapy is a type of targeted therapy that acts against tumour vasculature. Bevacizumab, is a humanized monoclonal antibody that acts against vascular endothelial growth factor A (VEGF). It is the most meticulously studied targeted agent in the treatment of ovarian cancer. GOG-218 and ICON-7 are the two phase III trials that established its role in the first-line treatment of platinum-sensitive ovarian cancer.[6,7]

In both of these trials, bevacizumab was added to the standard regime (6 cycles of platinum and taxane-based chemotherapy). In GOG-218 trial, bevacizumab was given up to 22 cycles at a dose of 15 mg/kg, and in ICON 7 trial, 18 cycles of bevacizumab were given at a dose of 7.5 mg/kg. Despite of different treatment durations and dosing schedules, both of these trials showed an increase in PFS (progression free survival). In GOG-218, the median PFS in bevacizumab group was seen in frontline group and maintenance was increased to 14.1 months compared to 10.3 months in the standard treatment arm (HR0.72; 95% CI, 0.63–0.82).[6] In the ICON 7 trial, PFS at 36 months was 20.3 months with standard

therapy, as compared with 21.8 months with standard therapy plus bevacizumab (HR, 0.81; 95% CI, 0.70–0.94; *P* = .004).[7] Both studies have found that patients with high-risk disease and poor prognostic characteristics benefited the most from bevacizumab treatment. Based upon the results of these studies in June 2018 United States Food and Drug Agency (FDA) approved use of bevacizumab in frontline therapy for epithelial ovarian cancer.

The AURELIA trial, a phase III randomised study, in which 361 platinum-resistant and platinum-refractory recurrent ovarian cancer patients were randomized to either single chemotherapy agents (topotecan, pegylated liposomal doxorubicin and paclitaxel) alone or in combination with bevacizumab.[8] The bevacizumab combination therapy resulted in an objective response rate (ORR) of 27.3% versus 11.8% for chemotherapy alone (P = 0.001). Bevacizumab combination resulted in almost doubling of the PFS (6.7 months versus 3.4 months) (HR 0.48; P <0.001) without any significant improvement in median overall survival (OS) (16.6 months versus 13.3 months) (HR 0.85, 95% CI 0.66–1.08).

Tyrosine kinase inhibitors

Pazopanib an oral multi-target tyrosine kinase inhibitor, has also been evaluated for management of platinum-resistant recurrent ovarian cancer in few phase II studies.[9,10] MITO-11 was an open-label, randomised phase II trial, which was conducted at eleven hospitals in Italy to assess the effect of adding pazopanib to weekly paclitaxel in treatment of women with platinum-resistant or platinum-refractory advanced ovarian malignancy.[10] Results showed addition of pazopanib to paclitaxel improved median PFS (6.35 vs 3.49 months); (HR =0·42, 95% CI 0·25–0·69, p=0.0002). The grade 3–4 adverse events were more common in the Pazopanib group including neutropenia (30%), fatigue (11%), leucopenia (11%), hypertension (8%), raised liver enzymes (8%), and anaemia (5%). The NCCN recommendations for recurrent ovarian cancer presently list pazopanib as a category 2B recommendation.

PARP Inhibitors (Poly Adenosine Diphosphate Ribose Polymerase inhibitors)

PARP inhibitors act on the principle of tumor-specific synthetic lethality, which means that their efficacy enhances when a preexisting BRCA1/2 mutation is present. They have been approved for multiple indications in management of ovarian cancer. In 2014, FDA approved the first PARP inhibitor, olaparib, in the treatment of epithelial ovarian cancer patients with germ line BRCA mutations who had received three or more prior lines of chemotherapy.[11,12] In 2016, Rucaparib was approved by FDA for treatment of germline/somatic BRCA mutated recurrent ovarian cancer.[11,12] In 2017, niraparib and, later, olaparib were approved as maintenance therapy for women who had a complete or partial response to platinum-based chemotherapy.[11,12] It has been confirmed from the recent studies that their efficacy is enhanced not only in germline/somatic BRCA mutated epithelial ovarian cancer but also in which homologous recombinant deficiency is caused by some other underlying etiologies. These drugs are used in oral tablets or capsule form.

Four trials have investigated role of PARP inhibitors in the upfront (frontline maintenance) settings; SOLO-1, PRIMA trial, PAOLA-1 trial and VELIA trial.[13,14,15,16] The SOLO-1 trial evaluated efficacy of maintenance therapy with olaparib in comparison to placebo in patients with newly diagnosed advanced ovarian cancer with a BRCA1/2 mutation[13]. A total of 391 patients were included into study, 260 in olaparib group and 131 in placebo group. Olaparib in a dose of 300 mg BID was used in this study. Treatment with olaparib monotherapy improved PFS in the olaparb group with a 70% lower risk of progression or death (HR 0.30; 95% CI, 0.23 to 0.41) compared to placebo. Patients who had previously received bevacizumab were excluded from the study. A subgroup analysis revealed that the PFS advantage was significant regardless of the type of BRCA mutation (BRCA 1 or 2).

PRIMA trial was conducted to assess efficacy of niraparib in patients with newly diagnosed

advanced ovarian cancer after a response to first-line platinum-based chemotherapy, regardless of BRCA mutation status.[14] Results showed significant improvement in the PFS with niraparib maintenance therapy compared to placebo (13.8 months versus 8.2 months; HR, 0.62; 95% CI, 0.50 to 0.76; P <0.001), regardless of the presence or absence of homologous-recombination deficiency.

PAOLA-1 trial, a randomized, double-blind, international phase 3 trial was conducted to assess effect of combining maintenance olaparib and bevacizumab in patients diagnosed with advanced, high-grade ovarian cancer and who had complete/ partial response to first-line standard platinum- based chemotherapy given with bevacizumab.[15] Patients were randomly assigned to receive olaparib tablets (300 mg twice daily) or placebo for up to 24 months; all patients received bevacizumab at a dose of 15 mg per kilogram body weight every 3 weeks for a total of 15 months. Results showed that addition of maintenance olaparib provided a significant progression-free survival benefit (22.1 months versus 16.6 months) (HR 0.59; 95% CI 0.49 to 0.72; P<0.001), effect was substantial in patients with HRD-positive tumors, including those without a *BRCA* mutation. In both trial groups, 31% of patients experienced serious adverse events. The adverse events were in alignment with the known safety profiles of bevacizumab and olaparib. Anemia was the most frequent serious adverse event that occurred more frequently with olaparib plus bevacizumab than with placebo plus bevacizumab (6% versus 1% in the placebo group). Hypertension was the most frequent serious adverse event that occurred more frequently with placebo plus bevacizumab than with olaparib plus bevacizumab (13% in placebo group versus 9% olaparib group). Usually, dose modification rather than discontinuation was used to treat adverse events. Anemia and nausea were the most frequent side effects that led to drug discontinuation in olaparib group.

The VELIA (GOG-3005) trial, a phase III, placebo-controlled trial, included patients with previously untreated advanced epithelial ovarian cancer.[16] This trial had a similar design like GOG-218 and ICON 7 trial. Veliparib was administered concomitantly with first line chemotherapy and was continued as subsequent maintenance therapy. Compared to carboplatin plus paclitaxel induction therapy alone, a regimen of carboplatin, paclitaxel, and veliparib induction therapy followed by veliparib maintenance therapy resulted in significantly prolonged progression-free survival across all study populations. Due to lack of "veliparib maintenance-only" group significance of veliparib induction therapy without veliparib maintenance was less obvious. At present veliparib is not approved by FDA.

In all four trials, the proportion of patients with adverse events leading to treatment discontinuation was at least threefold higher in the PARP inhibitor-containing arm than the control arm and was highest in PAOLA-1 study. In PRIMA/ENGOT-OV26 trial of niraparib, there was a substantially higher incidence of thrombocytopenia. The ARIEL 2, Study 10, SOLO3 trial and QUADRA trial evaluated the role of PARP inhibitors in treatment of recurrent disease (Table 1). [17,18,19,20]

Table1: Clinical trials of PARP Inhibitors in recurrent ovarian cancer

S. N.	Trial	Phase	Drug	No. of patients	Indication	Results
1.	ARIEL 2 Trial[17]	II	Rucaparib (600 mg BID)	206	Deleterious germline OR somatic BRCAm and ≥ 2 prior systemic therapies	ORR:54% DOR:9.2 months amPFS:11.1 months
2.	Study 10 Trial[18]	I/II	Rucaparib (600 mg BID)	42	Deleterious germline OR somatic BRCAm and ≥ 2 prior systemic therapies	ORR: 59.5% mPFS:7.8 months
3.	SOLO 3 Trial[19]	III	Olaparib (300 mg BID) Vs physician's choice chemotherapy	266	Deleterious germline BRCA mutation, ≥ 3 prior systemic therapies	ORR: 72% vs 51% mPFS: 13.4 vs 9.2 months
4.	QUADRA Trial[20]	II	Niraparib (300mg daily)	463	Recurrent ovarian cancer treated with ≥ 3 prior chemotherapy regimens and cancer is associated with HRD positivity	ORR:27.7% DOR:9.2months mOS:17.2 months

BRCAm: BRCA mutation, ORR: overall response rate, DOR: duration of response, mPFS: median progression-free survival, mOS: median overall survival

Immune checkpoint inhibitors

Multiple mechanisms are involved for cancer evasion from immune surveillance, including disruption of antigen presentation, immunosuppressive cells infiltration, and over-expression of co-inhibitory molecules such as programmed death-ligand 1 (PD-L1) or up-regulation of CTLA-4, a co-inhibitory regulator of central T cell activation[3]. Immune checkpoint inhibitors have been one of the most thoroughly studied immunotherapeutic approach in recent decades.

A phase II study, KEYNOTE-100 trial, evaluated role of pembrolizumab in advanced recurrent ovarian cancer.[21] Single-agent pembrolizumab showed modest activity, over all response rate 8% and median PFS 2.1 months. Those with higher PD-L1 expression, combined positive score, CPS ≥10 had a higher overall response rate (17.1%) compared to those with CPS <1 (5%). Based upon the results of a phase II study, KEYNOTE-158 trial pembrolizumab got FDA approval for treatment of patients with DNA mismatch repair (dMMR) or high microsatellite instability (MSI-H), previously treated, advanced non-colorectal cancers.[22] Out of 233 enrolled patients, 15 (6.4%) had ovarian malignancy. Study showed an objective response rate of 34.3% (95% CI, 28.3% to 40.8%) and median progression-free survival of 4.1 months (95% CI, 2.4 to 4.9 months).

The therapeutic efficacy of other checkpoint inhibitors has been modest at best, as reported in several studies. In a phase II trial including 20 patients with platinum resistant ovarian cancer, Nivolumab, a PD-1 inhibitor, showed an overall response rate of 15% and a median PFS of 3.5 months.[23] Avelumab, an anti–programmed death-ligand 1 was evaluated in a phase Ib study, JAVELIN Solid Tumor Trial, to assess its efficacy and safety in recurrent or refractory ovarian cancer.[24] Out of 125 women treated with three prior lines of therapy, objective response was seen in 12 patients (9.6%) (95% CI, 5.1%-16.2%). One year PFS was 10.2% (95% CI, 5.4%-16.7%) and median OS was 11.2 months (95% CI, 8.7-15.4 months). Total 16.8% patients suffered from immune-related adverse reaction of any grade.

Novel agent combinations therapies

Several trials are looking into ways to improve chemotherapy efficacy and overcome drug resistance by combining standard chemotherapy with various other novel agents. The combination of PARP inhibitors with VEGFR inhibitors (cediranib and olaparib), which has been evaluated in platinum-sensitive disease, was later being evaluated in platinum-resistant disease (NRG-GY005 study).[25] Chemotherapy combinations, PARP inhibitors, other immunotherapy agents, anti-angiogenic therapies, and epigenetic therapy are being investigated as "immunologic priming" strategies for transforming "cold tumours" into "hot tumours".[3,25] Despite the inconclusive results of the avelumab/PLD combination in the JAVELIN Ovarian 200 trial (phase III), other immunotherapy and chemotherapy combinations are being investigated (OCTOPUS trial and MITO 27 study).[3] Preclinical models show synergy between PARP inhibitors and anti-PD-1 agents, regardless of BRCA mutation status or PD-L1 expression. The KEYNOTE-162 study (niraparib and pembrolizumab combination) looked at this synergy in patients with recurrent platinum-resistant ovarian cancer.[26]

Other newer agents

Folate receptor alpha (FR) is a transmembrane glycoprotein that mediates folate transport into cells. It exhibits selective expression as it is overexpressed in most epithelial ovarian cancers but not in normal ovarian epithelial cells[3]. This makes it a good target for antibody-drug conjugates (ADCs) that deliver cytotoxic payloads to cancer cells.[27] Mirvetuximab soravtansine is being evaluated in various trials either alone or in combination with other drugs such as bevacizumab, anti-PD-1 antibody and PARP inhibitors (FORWARD I & II).[3]

Tissue factor (TF), which is normally involved as a cofactor in the coagulation process, can be abnormally expressed on the surface of cancer cells in a variety of tumours, represents a potential new target for anticancer therapy.[25,27] Tisotumab vedotin is one such TF-targeted ADC being studied in some phase I-II trials. Drugs targeting protein kinase-mediated pathways responsible for cancer recurrence and dissemination are also being studied

(Adavosertib, Alpelisib, Ralimetinib mesylate, Prexasertib, Berzosertib).[25,27] The Edmonston lineage measles virus (MV-Edm) derivatives are currently being tested in clinical trials and have been genetically engineered to express the human carcinoembryonic antigen (MV-CEA virus) or the human sodium iodide symporter (MV-NIS virus). Few phase I and II studies are currently underway to explore the effect of MV-NIS in ovarian cancer.[3,25]

Conclusion

Despite significant advances in the treatment of advanced ovarian cancer, the treatment of patients with refractory/resistant disease remains a challenge. Improved understanding of the molecular mechanisms of ovarian cancer is required for the development of new therapies. Due to cancer genome heterogeneity and marked adaptability, overcoming resistance to therapy necessitate a variety of combination approaches. Immunotherapy and targeted therapies can be an effective option for the personalized treatment to increase the efficacy and reduce the adverse effects. Ongoing trials involving novel agents and recombination fusion proteins should add to our arsenal against this lethal disease.

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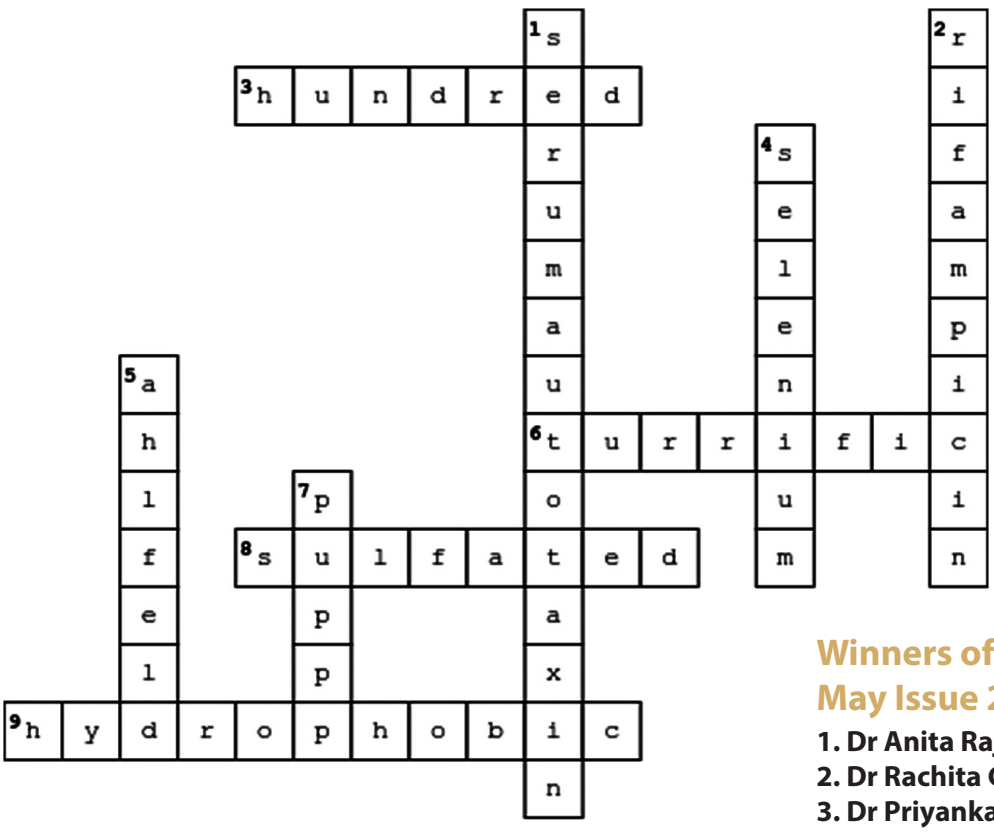
Answer key of Quiz of June 2022



Winners of the monthly quiz, May Issue 2022

1. Dr Anita Rajoria
2. Dr Rachita Garg
3. Dr Priyanka Lader

PET/CT in Ovarian Cancer

Rudrika Chandra*, PrateekKaushik, MadhaviTripathi***,SeemaSinghal******

*Senior Resident (Acad) M.Ch Gynae Oncology,, **Senior Resident Department of Nuclear Medicine & PET, ***Additional Professor, Department of Nuclear Medicine & PET, ****Additional Professor Department of Obstetrics and Gynaecology, All India Institute of Medical Sciences, New Delhi

Introduction

Ovarian cancer accounted for 3,13,959 new cases and 2,07,252 deaths worldwide in 2020 as per GLOBOCAN 2020.[1,2] Ovarian tumours are divided into epithelial tumours, accounting for almost 90% cases, germ cell tumours (3-5%), and sex cord-stromal tumours (2-5%).[3] Epithelial ovarian cancer (EOC) is diagnosed in advanced stages in two third of cases, at a median age of 63 years with a 5 year relative survival of 40-50%.[4] Germ cell ovarian tumours and sex cord stromal tumours are usually diagnosed in early stage with a better prognosis compared to EOC.

Principle of F-18 fluorodeoxyglucose PET:

F-18 labelled fluorodeoxyglucose (FDG) is a glucose analogue. After intravenous injection, it is transported into intracellular compartment via membrane glucose transporters (GLUT). Once inside the cell, it enters the glycolytic pathway and is phosphorylated by hexokinase to FDG-6-phosphate. However, unlike glucose, it is not metabolised further and is therefore trapped inside the cell (metabolic trapping). The degree of FDG uptake in a tissue depends on the degree of its glucose metabolism. Malignant cells have a high metabolic rate and depend heavily on glycolysis for energy production (Warburg effect) with upregulation of GLUT transporters and hexokinase activity and a downregulation of glucose-6-phosphatase activity; therefore, they show a high degree of FDG uptake compared to normal tissue.

Evaluation of adnexal masses with PET/CT

Pelvic ultrasonographic examination for morphological assessment of adnexal mass is the investigation of choice for evaluation. MRI is used as a trouble-shooter investigation for indeterminate masses and is not recommended routinely.

Studies have explored the utility of PET/CT to differentiate: -

1. *Malignant ovarian tumours from benign ovarian tumours:*

   Malignant ovarian tumours have been shown to have an average SUV max of 7.6 which is unrelated to the grade or histology.[5] Clear cell ovarian tumours and mucinous ovarian tumours have a lower FDG uptake compared to serous or endometrioid histologies.[6] Thus, high SUV max value on PET/CT is highly specific for malignant ovarian tumours barring a few exceptions like clear cell and mucinous carcinomas. The presence of FDG uptake in the adnexa of a postmenopausal woman should raise the concern for ovarian cancer (Figure 1).

2. *Borderline ovarian tumours (BOT) from malignant ovarian tumours:*

   A study has shown SUV max cut off of 3.7 to distinguish BOT from stage I ovarian cancer with a sensitivity of 83.3%, specificity of 85.7% and AUC 0.893.[7]

FDG PET has low diagnostic value in differentiating benign from borderline tumors and there is no established SUV cut-off value to differentiate benign from malignant tumors. While there is evidence on the utility of PET/CT in adnexal evaluation, the cost effectiveness is unproven and pelvic USG still remains the most commonly used imaging modality for this indication.

PET/CT for staging of ovarian cancer

PET/CT is an effective imaging modality for staging EOC, with a sensitivity of 75.5–83.3%, specificity of 68.4–99.4%, positive predictive value of 87.5–95.3%, and negative predictive value of 96.5–98.6%.[8]

Preoperative staging by PET/CT shows 70-80% concordance with surgical staging but should be interpreted with caution as possibility of false negative and false positive findings should be borne in mind (Table A: Inherent errors of FDG PET/CT imaging). It is highly specific in detecting lymph node metastasis (including extra-abdominal nodes like cardiophrenic and supraclavicular lymph nodes) and extra abdominal spread of disease leading to upstaging in 30-40% cases and can detect unsuspected synchronous malignancies. PET can also detect normal-sized metastatic lymph nodes which may be missed on CT[9] Although both FDG PET/CT and contrast enhanced computerised tomography (CECT) are useful in detecting peritoneal spread, PET/CT is superior in detecting peritoneal spread in subdiaphragmatic peritoneal surfaces and bowel mesentery (Figure 2).[10] Although PET/CT staging is superior for N and M staging of ovarian cancer, its role is limited for T staging.

Table A: Inherent errors of PET/CT imaging

Potential False positive	Potential False negative
Physiologically increased FDG uptake 1. Ovaries: during ovulation 2. Endometrium: during menstruation	Tumour histology: 1. Mucinous 2. Clear cell 3. Low grade 4. Necrotic tumors
Benign lesions: 1. Uterine fibroids 2. Endometriomas	Tumour size: 1. Small volume peritoneal disease (<5mm) 2. Small lymph nodes
Urine has increased FDG uptake: 1. Focal ureteric activity or bladder activity 2. Vesicovaginal fistula can limit disease evaluation	Masking of disease by adjacent structures: 1. Physiological bowel activity may mask peritoneal disease, serosal disease and small lymph nodes 2. Peri-vesical disease masked by urine with high uptake in bladder

Role in ovarian cancer treatment planning: Primary cytoreductive surgery or Neoadjuvant chemotherapy

CECT abdomen, pelvis is the most commonly used imaging modality for metastatic workup of advanced ovarian cancer and for further treatment planning. Various studies have reported an accuracy of 70–90% for detection of disease at all stages with CECT imaging. CECT has been evaluated to predict surgical peritoneal carcinomatosis index (PCI) with a sensitivity of 67% - 84% for detection of peritoneal implants in abdominopelvic region, 56% - 67% for detection of small intestinal deposits and specificity of 100% for all abdominal regions[11] Thus, there is a moderately good correlation between radiological PCI score and surgical PCI score (sensitivity 76%, specificity 69%).[12]

For complex cases, multimodality imaging like FDG PET/CT may be required for further examination and problem solving. Studies comparing CT, PET and PET/CT with intraoperative findings have found the respective sensitivity of 46-63%, 80-84% & 85-89% and specificity of 89-95%, 77-88% & 85-90%[13] 504 patients with 5,939 PET/CT examinations were enrolled in the registry, resulting in evaluable data from 3,724 patients receiving 4,754 scans. The impact of PET/CT on patient management was assessed across 22 tumor types, for different indications (diagnosis, staging, suspected recurrence. FDG PET/CT was the most accurate of these imaging modalities.

The detection of mediastinal nodes on PET/CT has been found to be associated with a higher chance of suboptimal cytoreduction thereby indicate the aggressive tumour biology[14] inability to undergo general anaesthesia, recurrent ovarian cancer, and borderline or nonepithelial malignancy. Whole-body PET/CT was performed after intravenous (18. PET/CT features predictive of suboptimal cytoreduction include: [15–16]

1. Extra-abdominal spread (including mediastinal nodes)
2. Sub-diaphragmatic deposits
3. Ascites

4. Pleural exudates
5. Peritoneal carcinomatosis
6. Large bowel mesenteric implants
7. Small bowel mesenteric implants
8. Hepatic hilar infiltration
9. Root of mesentery involvement

Role in ovarian cancer treatment prognosis and response evaluation

Patients with a low primary tumor SUV max have longer overall survival rate and disease free survival rate than patients with a high primary tumor SUVmax.[17] In addition, semiquantitative metabolic parameters like pretreatment metabolic tumor volume (MTV) and total lesion glycolysis (TLG) measured from PET/CT are inversely associated with progression free interval.[18] Patients whose PET scans convert from positive to negative after treatment, more commonly have complete pathologic responses and typically better disease-free survival and overall survival than patients whose scans remain positive (Figure 2). PET/CT has been studied as a tool to predict the histopathological response among patients with advanced EOC undergoing NACT by comparing the SUV parameters in the Pre-NACT and Post-NACT PET/CT imaging.[19,20] After chemotherapy, waiting a minimum of 10 days before performing 18F-FDG PET is advised. This time permits bypassing of the chemotherapeutic effect and of transient fluctuations in 18F-FDG uptake that may occur early after treatment.

FDG PET/CT is useful to differentiate responders from non-responders following neoadjuvant treatment[9] Martoni et al. performed PET/CT at baseline and after three and six courses of neoadjuvant chemotherapy with carboplatin-paclitaxel in 42 advanced ovarian cancer patients. Patients who showed normalization of SUVmax after three courses of treatment had a higher likelihood of complete pathological response after obtaining three additional courses of therapy.[21] In addition, Avril et al showed that PET can predict the early outcome after the first cycle of neoadjuvant chemotherapy. A decrease in SUV > 20% after the first cycle of chemotherapy and > 55% after the third cycle of chemotherapy were specified as criteria for metabolic response. The metabolic responses after the first and third cycles were significantly associated with higher overall survival. A study evaluating the role of FDG PET/CT to assess metabolic response in gynaecological cancers, taking an arbitrary SUV max after treatment of 3.8 as the cut-off for differentiating between responders and non-responders, showed a sensitivity of 90%, a specificity of 63.6%, and an accuracy of 76.2%.[18] Another study revealed a 40% cut-off for the decrease in SUV max as a predictor of histopathological response at the time of interval cytoreductive surgery with sensitivity, specificity, and accuracy of 81.8%, 72.4%, and 72.4%, respectively.[22] PET scan may replace second-look surgery in advanced ovarian cancer because of their similar prognostic values.[23] FDG PET combined with CT might be superior to CT in assessing tumor response and identifying residual viable tumor sites after treatment, since inflammatory lymph nodes or scar tissue may be misinterpreted as sites of viable tumor by CT alone. Presently there is no universal cut-off to predict histopathological response and more research is required on this subject.

Role in Recurrent ovarian cancer

The incidence of tumor recurrence within 2 years is 75–80% in patients with stage III disease and 90–95% in patients with stage IV disease and it is an important prognostic factor (24). Although CA-125 is sensitive in identifying recurrent disease, it has a poor specificity and low negative predictive value. Moreover, the total tumour burden cannot be reliably assessed with CA-125. FDG PET/CT has high sensitivity in detecting recurrent disease especially in the setting of rising CA-125 and macroscopic disease > 1cm.[25] The sensitivity of combined PET and serum CA-125 testing is 97.8% to detect recurrent disease.[26] However, PET has limitations in detecting microscopic disease, lesions < 1cm and subcentimetric peritoneal implants.

A metanalysis of 34 studies analysed the diagnostic accuracy of CA-125, PET alone, PET/CT, CT and MRI to detect recurrent ovarian cancer. They reported a pooled sensitivity of 69% for CA-125, 79% for CT, 75% for MRI and 91% for PET/CT; pooled specificity of 93% for

CA-125, 84% for CT, 78% for MRI and 88 % for PET/CT. They concluded that PET/CT might be a useful supplement to current surveillance techniques, particularly for those patients with an increasing CA- 125 level and negative CT or MR imaging.[27]

PET/CT is a highly sensitive and specific tool to detect early relapses in the setting of normal or rising tumour markers and equivocal conventional imaging. It aids in surgical planning by identifying nodal and extra abdominal extent of disease which is difficult to assess by conventional imaging.

PET/MRI

PET/MRI has a useful role in pelvic malignancies due to its high soft tissue resolution and absence of streak artifact due to pelvic bones in CT. In addition, radiation exposure to the patient is significantly reduced.[28] Although both PET/CT and PET/MRI have a high diagnostic value in detecting ovarian malignancies, PET/MRI may be superior in differentiating benign from malignant adnexal mass and in delineating the primary tumor or T-staging, but offers no advantage in detecting nodal or distant metastases Further studies are required to establish the utility of PET/MRI in ovarian cancer in routine clinical practice.

Non-FDG PET tracers for ovarian cancers

Ga-68 fibroblast activation protein inhibitor (FAPI) is a novel and highly promising radiotracer for PET/CT imaging.[29] High FAPI uptake results in sharp contrasts in primary and metastatic lesions and higher tumor to background ratios than 18F-FDG-PET/CT, thus it can be extremely useful for staging and follow-up of gynecological tumors. The other radiotracers that have been evaluated in preclinical and clinical studies and may play a role in the evaluation of patients with ovarian cancer include F-18 fluorothymidine (FLT) or C-11 methionine (MET).

Role in non-epithelial ovarian cancers

1. Malignant ovarian germ cell tumours (MOGCT):

   Most of the germ cell tumours occur in young adults and are inadvertently managed by incomplete staging surgery by a general gynaecologist. PET/CT is a useful modality for staging after inadequate staging surgery and restaging after adjuvant chemotherapy with a 100% sensitivity, 71% specificity, 54% positive predictive value, 100% negative predictive value and 79% accuracy.[30]

   Post treatment PET/CT imaging can differentiate between residual/progressive GCT and mature teratoma.[31] Persistent mature teratoma presents with low FDG uptake whereas immature teratoma, residual malignant GCT and gliomatosis peritonei present with high uptake.[32,33]

2. Sex cord stromal tumours (SCST):

   Granulosa cells tumours are the most common type of SCST and have a wide spectrum of imaging findings on CT, ranging from predominantly solid to completely cystic tumours. Granulosa cell tumours are considered low-malignant and known to cause false-negative findings on PET/CT imaging.[34]

Current recommendations:

1. **NCCN recommendation:**
   a) PET/CT to be done for initial workup of patients with epithelial ovarian cancer for indeterminate lesions only if the results alter management.[35]
   b) PET/CT can be considered during surveillance of patients with epithelial ovarian cancer as clinically indicated to detect early recurrences with high specificity.
2. **Good clinical practice recommendations for the use of PET/CT in oncology:**
   a) PET/CT is recommended in cases of suspected recurrence of ovarian carcinoma, particularly with elevated serum CA-125.[36]
   b) FDG-PET/CT can be proposed for the local–regional or whole-body extension assessment of advanced ovarian carcinoma (≥ FIGO stage III).

3. European Association of Nuclear Medicine (EANM) guidelines:

Clinical indications for PET/CT in ovarian cancer (37)	**Level of evidence**[a]	**Grade of recommendation**[b]
Initial diagnosis and staging in patients presenting with pelvic mass	III	C
Prognostic value	I	B
Treatment planning	IV	C
Therapy assessment	II	B
Relapse detection	I	A

a-Levels of evidence

- Level I: There are good-quality meta-analyses or good-quality randomized trials with cross-consistent results. New data will most likely not change confidence in the estimated effect.
- Level II: There is good-quality evidence (randomized trials (B1) or prospective or retrospective studies (B2) with overall cross-consistent results. New data may impact confidence in the estimate of effect or may change the estimate.
- Level III: The studies available carry methodological weaknesses, and/or the results of the studies are not always cross-consistent. New data will most likely impact confidence in the estimate of effect and will likely change the estimate.
- Level IV: There are no data or only case series. There is a great deal of uncertainty as to the estimated effect.

b-Grades of recommendation

- A: At least one meta-analysis, systematic review or randomized controlled trials (RCT) directly applicable to the target population and demonstrating overall consistency of results
- B: A body of evidence including high-quality systematic reviews of case–control or cohort studies, directly applicable to the target population, and demonstrating overall consistency of results
- C: A body of evidence including well-conducted case–control or cohort studies with a low risk of confounding or bias, directly applicable to the target population and demonstrating overall consistency of results
- D: Non-analytic studies, e.g. case reports, case series and expert opinion

Conclusion

PET/CT is a useful tool in the gynae-oncologists armamentarium for managing patients with EOC. It has a role in:

1. Evaluating adnexal masses- to differentiate benign and borderline from malignant tumours.
2. To stage the patients, assess extent of disease, diagnose unsuspected extra-abdominal metastasis and synchronous malignancy (N and M staging).
3. To plan treatment based on disease extent.
4. To assess the response to NACT.
5. As a prognostic tool based on metabolic parameters.
6. For early detection of relapse and to plan further management of relapse based on disease extent- secondary cytoreduction or chemotherapy.

The metabolic parameters are useful prognostic markers which have been shown to correlate with patient survival. Future innovations which may reduce the cost of PET/CT and more prospective studies may establish this modality in routine practice for managing patients with ovarian malignancy.

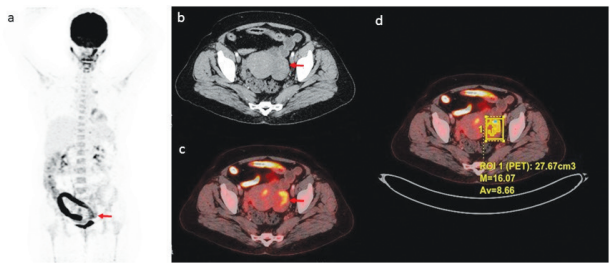


Figure 1: FDG PET/CT in a 59 year old woman with left adnexal mass and normal CA-125 levels; maximum intensity projection (MIP) image shows focal tracer uptake in left adnexal region (red arrow), however it is not well appreciated due to masking by physiological bowel uptake. Axial CT (b) and fused PET/CT (c) images show a left adnexal mass with heterogeneously increased FDG uptake (red arrows). SUVmax of the mass was 16.0 suggesting a high likelihood of malignancy. Histopathology of the mass revealed adult granulosa cell tumor.

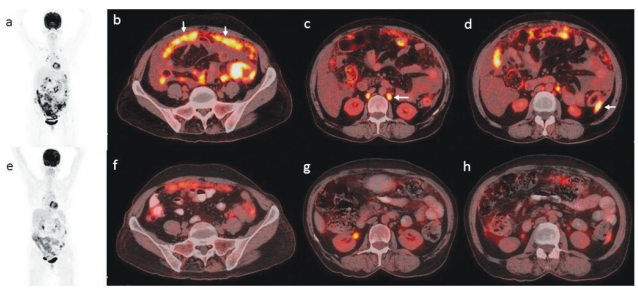


Figure 2: FDG PET/CT in a patient with metastatic ovarian serous adenocarcinoma; baseline maximum intensity projection (MIP) image (a) and fused axial PET/CT images show extensive intra-abdominal disease (a) with omental caking (b), retroperitoneal lymphadenopathy (c) and peritoneal deposits (d) with ascites (findings shown with white arrows). PET/CT done after 3 cycles of neoadjuvant chemotherapy shows decrease in disease burden , with significant reduction in metabolic activity of omental involvement (f), retroperitoneal lymph nodes (g) and peritoneal deposit(h) suggestive of partial response.

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Self Help Group; Need of The Hour

Anupma Gupta
Senior Consultant Gynaecologist and Laparoscopic Surgeon, Santom hospital, Prashant Vihar, Delhi.

Violence can never be justified, least of all against someone

who is ostensibly attempting to save a person's life.

– Sumanth Raman

INTRODUCTION

Medical violence is defined as any act of aggression, physical assault, or threatening behavior that occurs in a health-care setting and causes physical or emotional harm to a health worker. It can range from telephonic threats, intimidation, actual verbal abuse, physical but non-injurious assault, sexual harassment, and physical assault causing injury; simple or grievous, weaponry attacks, and homicide to vandalism and / or arson. Verbal abuse is the most common type of violence encountered but there seems to be some gender bias as well, sexual abuse being nearly exclusive in female workers.[1] A study of risk factors associated with violence against doctors found the following:[2]

- Younger doctors face more physical violence.
- Female doctors are more likely to face violence.
- Department of obstetrics and gynecology reported the highest rates of violence, followed by the medicine department with allied specialties, and surgery with allied specialties.
- Verbal violence was the most common form of violence. In the emergency department, 100% of doctors reported some kind of verbal violence.

WHY A SELF HELP GROUP …WHY NOW ?

Healthcare professionals are at the highest risk of violence in their workplace among all professionals.[3] Healthcare workers are four times more likely to be injured and away from work as compared to other professionals, particularly because a doctor often deals with a person when he/she is in a stressful and emotionally taxing situation.[4]

The Indian Medical Association suggests that up to 75% of doctors have faced some kind of violence at work. Around 83 percent doctors feel stressed out in their profession and 46.3 percent feel violence is the main cause of stress.[5] Much has been said about the importance of communication, documentation, and having professional indemnity. Responsibility to safeguard doctors against violence has often been fixed on the government, the public and the media. But nothing concrete has ever been done. While proper documentation and medical indemnity can save you in the court of law but the actual problem lies elsewhere. Jungle Raaj seems to be the order of the day and it can be a nightmare for a doctor to be surrounded by a belligerent mob ready to physically assault the doctor. The situation is especially grave in stand alone clinics and smaller nursing homes. Implications of such a horrifying experience can be longstanding. The doctor who faces such a violent situation loses whatever shred of dignity he has, loses confidence in himself and his decision making and is forever emotionally and psychologically scathed. A bad impact on the physician's psychology leads to post-traumatic stress syndrome (PTSD) in majority of the physicians, something which is akin to a problem faced by war veterans. This manifests as a physician feeling helpless, becoming irritable, introverted and having thoughts of abandoning medicine or even contemplating suicide. Even more stable personalities might be forced to practice defensive medicine, with intent on saving their own skin rather than considering for the patient.

Actual physical hurt remains a small part of the story. Extrapolated trauma to family is another issue. So many episodes have come to light in recent past alone where in medical professionals

have been assaulted for even minor issues like delayed scans and post operative pain. The final nail in the coffin has been the suicide by a qualified young gynaecologist of Dausa who succumbed to mental, emotional, and psychological abuse that she was subjected to…for a known complication. It is time to take matters in our hands and stop waiting for external help. It's time to let go of our petty differences, super human egos, and stand against this as a fraternity. We have to support each other…not after a violent episode but at the very beginning, so assaults don't happen. And for this physical presence is a must. That's where self help groups come into picture and no better time than today to start one.

HOW WE STARTED A SELF HELP GROUP

Around 350-400 doctors in northwest Delhi have formed a group on Whatsapp. This main group has 256 members. This group is further subdivided into smaller zones with a radius of 2 to 3 kms. Rest of the members are accommodated in respective zonal groups. All zones have their respective admins, 5 to 6 in number who keep changing every three months. Each member has a list of his zone's members with phone numbers. Every member keeps 5 numbers on his speed dial. The same list is advised to be kept with receptionist or hospital staff who are also made aware of the numbers to be dialed in case of emergency. Whenever an untoward event occurs the concerned doctor or his staff raises an alarm by calling any one of the speed dial numbers. It is the duty of that person to call 5 more and so on so forth. A chain reaction is activated. Simultaneously messages are posted on main group and respective zonal group also. Everyone knows that there is a situation and we may need to rush when required. Colleagues from the same zone start rushing to help the affected doctors. Remember to take your staff, OT technician, assistants, and your close non medico friends …whoever is available. The more the merrier. Within 15 minutes around 30 to 40 doctors assemble and form a human barrier between the mob and their colleague. If more strength is required in face of escalating situation, doctors from main group who are already alerted also rush for help. Physical presence of doctors in numbers comparable to or more than miscreants has been found to be a major deterrent to violence. The aim is to deescalate the situation. We are not assembling to aggravate aggression but to abate it. Police is informed simultaneously. The message to the society is clear…we are in this together. No one gets to hit a doctor. If the patient and attendants believe that there is something wrong with treatment, they are welcome to take matters to court where we can also put forth our perspective. BUT NO JUNGLE RAAJ.

This group in northwest Delhi and Rohini has been functional since almost more than two years now. More than 25 episodes of violence have occurred, all tackled well. Not even a single litigation, no doctor assaulted, and an increasing sense of unity and camaraderie. Our inter personal relations have improved considerably. The phone numbers which were saved initially as group members are now friends with name. Message to the society is clear…so repeat episodes in same areas hardly occur. Police is ready to listen to us more compassionately… now that we are a force. Every episode is discussed later in closed group, so we can introspect and improvise. Having a group of colleagues who have your back adds to your confidence and morale and reduces psychological stress considerably. You feel confident and empowered when you know you are not alone and that your colleagues have your back. Medical jousting has reduced considerably as now we are all friends and answerable to an entire zone.

In these help groups we put a message or information regarding patient or attendants who have been aggressive or abusive. So now our colleagues can exercise due caution and discretion when the same patient comes to them for second opinion or further treatment.

HOW EACH ONE OF US CAN HELP

- Local doctors and staff will know a few people amongst the mob. Try to get them on your side.
- Try to divide mob into smaller groups and pacify them.

- Obtain all the documentary evidence of violence. It is a good idea to earmark some hospital staff who will take photographs, audio/video records of the violence.
- Immediately all medical record of the patient should be photocopied because there is a huge possibility that interested person / mob could carry away the original record.
- Call police if you feel situation is going out of hands. Keep a record of such attempts to contact law enforcing agency.
- Lodge a First Information Report with the police.
- While registering a complaint make sure that it is registered under the relevant act i.e. Protection of Medical Personnel.[1]
- A few colleagues are likely to know local SHO, Beat officer, the Sub inspector or the Counsellor. They can help in expediting the process
- Inform the legal counsel / lawyer immediately. Some doctors in same speciality can help with documentation and in completing file. Your colleague may not be in a state of mind to think straight.
- Identify the troublemakers/ community leader / s inciting violence. [1]
- Get written, signed statements from all individuals present (physicians, nurses and other para-medical staff, patients, relatives, and other bystanders) in context of the violence.[1]
- It is very important not to try to 'settle' the issue by paying hush money which seems more as an admission of guilt than otherwise[1]
- Mere physical presence is also important. It adds to number.
- Please be non-judgemental and refrain from loose talks. There are medical boards to decide if at all your colleague was inept.
- Some of our senior elderly colleagues may find it difficult to be always physically present. This is well understood. They can help in calling members of the group and coordinating with the main group. Our senior colleagues are more likely to have influential local contacts over years. We need their wisdom and experience to guide us through it all.
- Help in whatever way is welcome. It's a matter of survival now. Leave your petty differences aside.

PRACTICAL PROBLEMS

- Most of us fail to reach ground zero under one pretext or another. Remember if you don't come today, no one will help you when you need it. This point is driven in very politely but very firmly. There are coordinators and admins in each zone who keep a track of absentees. You can be busy once or twice but not every time. And if you are a perpetual defaulter you are warned.
- Sometimes because of sheer volume of doctors assembling we did not recognise who is who. Now we have closed zonal meetings after the episode to introspect on where we went wrong or what more could have been done and at the same time getting to know each other.
- Some doctors have been carrying out the practice of criticising their own colleagues. Medical jousting if comes to light is addressed and strongly condemned in such meetings. This provides a better cohesiveness amongst colleagues and a better work environment.
- Some colleagues tend to believe they are more important than others because of their status in local medical bodies. Its always possible to remind them in a polite manner that egos will not be entertained and this group can not be used for petty political mileage. Each one of us is important and indispensable.
- Some colleagues tend to pass professional judgements on the treatment given and what more should have been done. These loose talks can have serious repercussions. Everyone was requested not to pass any loose comments. Someone in the crowd is listening. Better to leave such judgements to medical board if things come to that
- A perpetual problem we faced initially was people trying to post good morning messages and happy birthday messages …thereby cluttering the group. Members were asked to delete the same immediately. There are hundreds of groups for such messages. It was ensured that everything posted on the group satisfied the purpose of the group.

- Sometimes important posts on the group used to get missed because of so many messages on WhatsApp. Now each one has this group pinned on top of WhatsApp. And has a different notification tone for messages on this group.
- Some initial hiccups are bound to surface but they can all be tackled with tact and humility. Don't let these scare you. Healthy discussions on forum will always give solutions. Alone I cannot but together we can.

TAKE HOME MESSAGE

No one is immune to violence however senior or qualified. There is no substitute for good communication skills, in depth knowledge, informed consents and written documentation. It is imperative to have a good medical indemnity and a sound legal counsel. But none of the above can replace a good network of supporting colleagues who are ready to physically stand by your side when time comes.

Help others, so when it's your turn someone has your back.

Reminds me of a holocaust poem which can best summarise why we need such groups

First they came for the Jews
and I did not speak out
because I was not a Jew.
Then they came for the Communists
and I did not speak out
because I was not a Communist.
Then they came for the trade unionists
and I did not speak out
because I was not a trade unionist.
Then they came for me
and there was no one left to speak out for me
MARTIN NIEMOLLER

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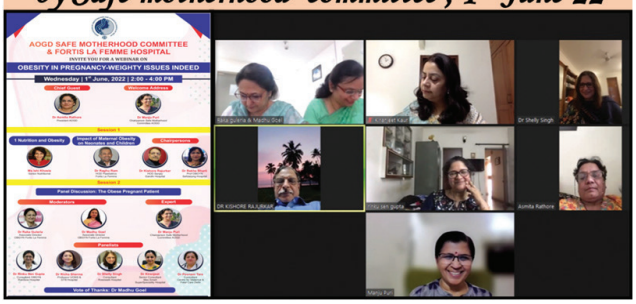
Calendar of Virtual Monthly Clinical Meetings 2022-23

29th July, 2022	Army Hospital (Research & Referral)
26th August, 2022	All India Institute of Medical Sciences
30th September, 2022	DeenDayal Upadhyay Hospital
28th October, 2022	PGIMSR & ESI Hospital
12th & 13th November, 2022	**44th Annual AOGD Conference (Physical)**
25th November, 2022	VMMC & Safdarjung Hospital
30th December, 2022	Sir Ganga Ram Hospital
27th January, 2023	ABVIMS & Dr Ram Manohar Lohia Hospital
24th February, 2023	UCMS & Guru Teg Bahadur Hospital
31st March, 2023	MAMC & Lok Nayak Hospital
28th April, 2023	LHMC & Smt. Sucheta Kriplani Hospital
26th May, 2023	Sitaram Bhartia Hospital

Events held under Aegis of AOGD in June 2022

Obesity in pregnancy – Weighty issues indeed by Safe motherhood committee , 1st June 22



"Diagnosis and Management of Fetal abdominal anomalies" by Genetic & Fetal Medicine Subcommittee, 10th June

AOGD
Genetic & Fetal Medicine Subcommitee

DIAGNOSIS AND MANAGEMENT OF FETAL ABDOMINAL ANOMALIES

10th June, 2022 | 01:00 - 04:30 PM
Venue: Auditorium, Fortis Hospital, Shalimar Bagh

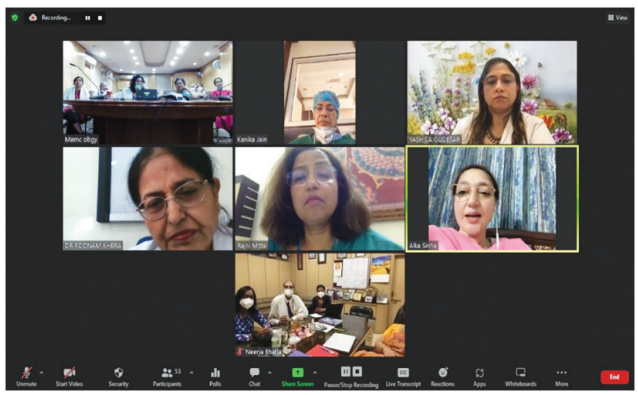
Organizing Chairpersons: Dr. Sangeeta Gupta, Dr. Seema Thakur, Dr. Tanu Gera, Dr. Puneet Jain
Guest of honour: Dr. Asmita Rathore, President, AOGD
Chief Guest: Dr. Sanjivni Khanna, Director, Obs & Gynae, Fortis Hospital, Shalimar Bagh

Time	Topic	Speaker
1:00 - 1:30 PM	Lunch	
1:30 - 1:35 PM	Welcome Address	Dr. Seema Thakur
1:35 - 1:45 PM	Inaugural Speech	Dr. Asmita Rathore
1:50 - 2:00 PM	Chief Guest Speech	Dr. Sanjivni Khanna
	Session 1	
	Chairpersons: Dr. Poonam Lata, Dr. Sonal, Dr. Amit Sethi	
2:05 - 2:20 PM	Embryology of Fetal Abdomen	Dr. Rounak Bagga
	Session 2	
	Chairpersons: Dr. Sunita Varma, Dr. Vandana Gupta, Dr. Netra Singh	
2:25 - 2:50 PM	Fetal Abdominal Wall Defects- Diagnosis and Management	Dr. Alisha Jaggi
	Session 3	
	Chairpersons: Dr. Mamta Mittal, Dr. Jyoti Chugh, Dr. Prabhleen Kaur	
2:55 - 3:20 PM	Congenital Diaphragmatic Hernia	Dr. Tanu Gera
	Session 4	
3:25 - 4:25 PM	**Panel Discussion:** Fetal Abdominal Anomalies **Panelists:** Dr. Puneet Jain, Dr. Arpana Jain, Dr. Ankita Singh, Dr. Anju Gambhir, Dr. Vineet, Dr. Ankita Chandna	**Moderator:** Dr. Seema Thakur
4:25 - 4:30 PM	Vote of Thanks	Dr. Nihar Gupta

FOGSI Conference in collaboration with AOGD & DGF, 11th June

Webinar on "Safety of Gyane Endoscopic Surgeons in the Litigation Era" by Endoscopy committee , 23rd June

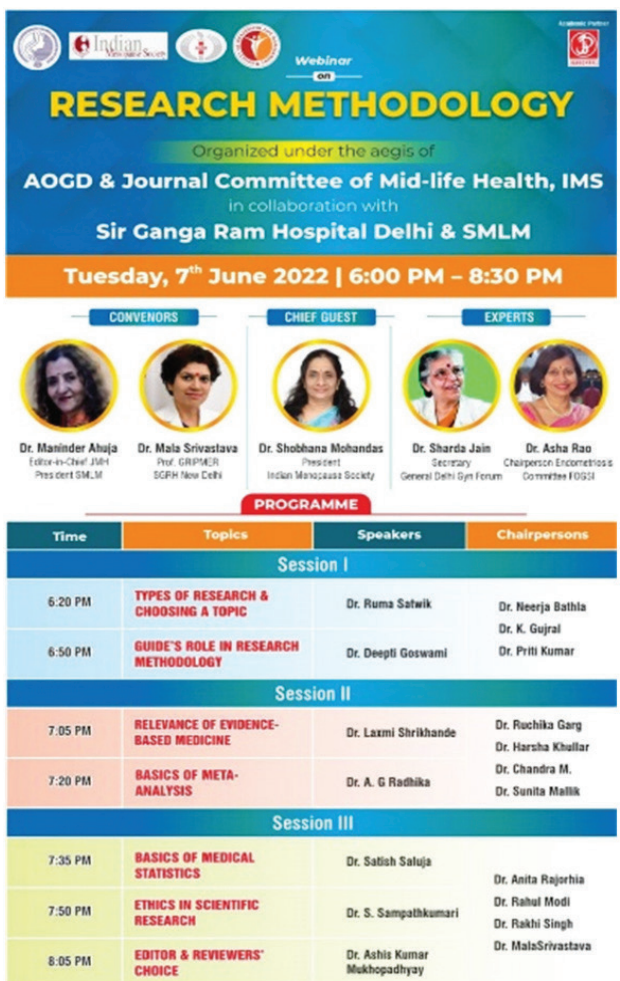
Standardization of PPH management by QI committee, 22nd June



AOGD monthly clinical meeting at B L Kapoor Hospital

Medical abortion: The Newer Horizon-Webinar organised by DGF SOUTHWESTunder the aegis of AOGD and MTP committee- FOGSI

Delhi PG Forum on "Adnexal Mass"



Research Methodology by AOGD & Journal committee of Mid-life Health, IMS in collaboration of SGRH& SMLM

Events held in June 2022

S no	Date	Events
1	01.06.2022	CME on "Obesity in pregnancy – weighty issues" by Safe motherhood sub-committee
2	03.06.2022	"Hyperglycaemia in pregnancy"symposium by DIPSI with AOGD & NARCHI
3	07.06.2022	Research Methodology by AOGD and journal sub-committee of Mid-Life Health, IMS in collaboration with SGGRH, Delhi & SMLM
4	09.06.2022	Public forum on cervical cancer & HPV awareness by Rural health sub-committee in Senior secondary school, Darya Ganj
5	10.06.2022	Online training on "Respectful abortion care (RAC)" By National Master trainers under aegis of AOGD and FOGSI
6	10.06.2022	CME on "Managing women's reproductive health over the past 60 years" under aegis of Breast and cervical cancer prevention sub-committee AOGD and Breast committee FOGSI
7	10.06.2022	"Diagnosis and management of Fetal abdominal anomalies" by Genetics & Fetal Medicine sub-committee
8	11.06.2022	FOGSI Conference in collaboration with AOGD & DGF
9	15.06.2022	Medical Abortion: The Newer horizon – Webinar organized by DGF South-West under aegis of AOGD and MTP sub-committee FOGSI
10	20.06.2022	Delhi PG Forum on "Adnexal Mass"
11	22.06.2022	Standardization of PPH management by QI sub-committee
12	23.06.2022	CME by Endoscopy sub-committee on "Basics of TLH"
13	24.06.2022	AOGD monthly clinical meeting at BLK-Max Super Specialty Hospital

Forthcoming Events

S no	Date	Events
1	01.07.2022	Webinar on Urodynamics for the beginner by Urogynaecology sub-committee
2	01.07.2022	Public form on Doctor's Day by AOGD
3	01.07.2022	Free Women Health Camp on cervical cancer awareness and pap smear by LBC under the aegis of Rural Health sub-committee
4	01.07.2022	CME by Safe motherhood sub-committee
5	02.07.2022	CME on "RPL & Threatened Abortion" by AOGD
6	06.07.2022	Webinar on adenomyosis under aegis of AOGD and ISOPARB in collaboration with SGRH
7	12.07.2022	Diagnosis and management of amenorrhea by Fetal medicine sub-committee
8	15.07.2022	CME on 'Women Health'" by DGFSW & DGF North under aegis of AOGD
9	16.07.2022	Webinar on "Robotics in Gynae-oncology" by oncology sub-committee
10	18.07.2022	PG Forum on "Heart disease in Pregnancy"
11	21.07.2022	CME by Infertility sub-committee
12	23.07.2022	Webinar on cervical cancer by oncology sub-committee
13	24.07.2022	Conference by IFS in association with AOGD
14	28.07.2022	CME by Endoscopy sub-committee
15	29.07.2022	AOGD monthly clinical meeting at Army Hospital (R & R)
16	30.07.2022	Webinar on Critical care by multidisciplinary sub-committee with Safdarjung hospital
17	**12th&13th NOV 2022**	**ANNUAL AOGD CONFERENCE**

AOGD Monthly Clinical Meeting Held on 24th June 2022 at BLK Max Super Speciality Hospital, New Delhi

Cervical Polyps as a Cause of First Trimester Bleeding: New Kid on the Block!

Nidhi Khera[1], Saloni Arora[2], Pravallika Vellanki[3]

[1]Director & Head , Obs And High Risk Pregnancy, [2]Consultant Fetal Medicine, [3]Senior Resident , Obgy Deptt, BLK Max Super Speciality Hospital, New Delhi

- Cervical polyps are benign neoplasms, occurring in 2 to 5% of reproductive-age women but their exact prevalence in pregnancy is unknown. When detected they cause significant anxiety to the patient . Coupled with it the obstetrician is faced with the challenge of dealing with a situation that currently has no definitive guidelines for management and also whether conservative management or polypectomy should be done during pregnancy Although the exact etiology is unknown, they are thought to arise secondary to reactive changes from high circulating hormone levels and from the congestion of blood vessels in the cervix.
- In pregnant patients, these polyps can be asymptomatic or else can cause recurrent vaginal bleeding, discharge, premature labor, infection, chorioamnionitis, or increased bleeding during labor. Cervical polyps in early pregnancy have recently been identified as a risk factor for sLMC/PTD and have been implicated in cervical insufficiency. Polypectomy during pregnancy is equally controversial . Some authors favor it as a strategy for preventing sLMC/PTD .Others have found an increased risk of spontaneous abortion following the procedure. . Ultrasound can aid in creating a treatment plan by assessing the type of polyp and source of symptomatology by helping in tracing the origin and type of the cervical polyps. Furthermore, a polyp size >12 mm, genital bleeding, and polypectomy before 10 weeks of gestation (WG) were identified as significant risk factors for sLMC/PTD.
- We present our series of 15 patients with cervical polyps during pregnancy who had presented with 1 to 8 episodes of first trimester bleeding. 3 of these had a giant polyp measuring > 4cm, and two thirds had presented after 10 weeks of gestation .Almost 50% of our patients ran a stable course and in around half of the patients the polyps had regressed by the third trimester. We followed a conservative approach to management with polypectomy being required in only one patient. 11 patients had a favorable outcome delivering at or after 37 weeks.
- Some cervical polyps can be misdiagnosed in the early weeks of pregnancy as abnormal vaginal bleeding and can lead to the diagnosis of an inevitable miscarriage. A good clinical examination can help prevent over use of progesterone. Giant polyps must be differentiated from other lesion of the cervix such as malignancies including sarcoma botryoides, endocervical carcinoma and other benign lesions such as prolapsing fibroids and retained products of conception. Ultrasound characteristics should be considered for risk stratification and patient counseling prior to formulating a treatment plan. Management depends on factors such as polyp type, symptoms, gestation age, prior history, and the type of operative management. Strict cervical length surveillance with transvaginal ultrasound is necessary in pregnant women with cervical polyps in early pregnancy. In asymptomatic patients with benign-appearing polyps, a conservative approach is usually preferred. In symptomatic patients, instead of proceeding with routine polyp removal , the decision for polypectomy needs to be individualised and a histological examination is mandatory in such cases.

Laparoscopic Pectopexy and High Uterosacral Ligament Suspension for Uterine Conservation in Uterine Prolapse

Dinesh Kansal

HOD & Director at BLK Max Super Speciality Hospital, New Delhi

Pectohysteropexy is a newer technique used for genital prolapse when uterine preservation is required. This is an ideal procedure when uterine prolapse is accompanied by anterior compartment defect. A peritoneal incision is

taken anterior to both round ligaments and midline. Bladder is pushed down . Pectineal ligaments are exposed between internal iliac artery and external iliac vein bilaterally.

Care is taken to avoid injury to accessory obturator veins. A non-absorbable mesh is attached to both pectineal ligaments laterally with the help of non absorbable sutures. Medially, mesh is attached to anterior isthmus of uterus and upper vagina. This takes care of any cystocele if present. The mesh is kept loose so as to decrease chances of mesh erosion. Thus an anterior hammock gets formed in anterior pelvis. Prophylactic native tissue repair for correction of posterior compartment is always performed. Plication and shortening of uterosacral ligaments along with enterocele repair is done. As compared to sacrohysteropexy, this procedure is comparatively less time consuming and technically simpler. Pectopexy can be easily performed in a patient when sacral promontry is not accessible due to various reasons.

High cervical cerclage, a novel vaginal approach for incompetent cervix: A case series

Dr Uma Rani Swain, Dr Laxmi Mantri

BLK Max Super Speciality Hospital, New Delhi

Cervical incompetency is an obstetrical entity characterized by recurrent episodes of 2nd trimester spontaneous abortions. Antenatal or intranatal cervical cerclage remains the viable option to manage these challenging conditions. Different types of cerclage procedure are advocated for both emergency as well as rescue purposes with varied results. According to the level of cerclage, they are classified as low and high type. High cerclage carries higher chance of success as compared to other types. As it effectively maintains the length and competency of cervix, it remains as standard procedure to prolong pregnancy towards term.

Ours is a case series enrolling 9 pregnant patients with previous history of recurrent 2nd and early 3rd trimester pregnancy loss and with corroborating ultrasonography findings for incompetent cervix. Our method is based on the principle of "Shirodkar's cerclage" with few modifications to make it easy for surgeon to achieve better success.

Procedure: both anterior and posterior vagina wall were separated from cx and extended upto internal os keeping the cleavage extraperitoneal. No - 1 prolene suture was selected for this purpose for it's smooth and nontraumatic surface. Suture was passed round the cervix anticlockwise starting point being 5 o'clock and ends 7 o'clock position keeping the level at internal os. The free suture ends are taken out of vagina posteriorly and the knot was placed deep in post fornix corresponds to uterosacral ligaments. Both separated vaginal flaps were reattached to cervix.

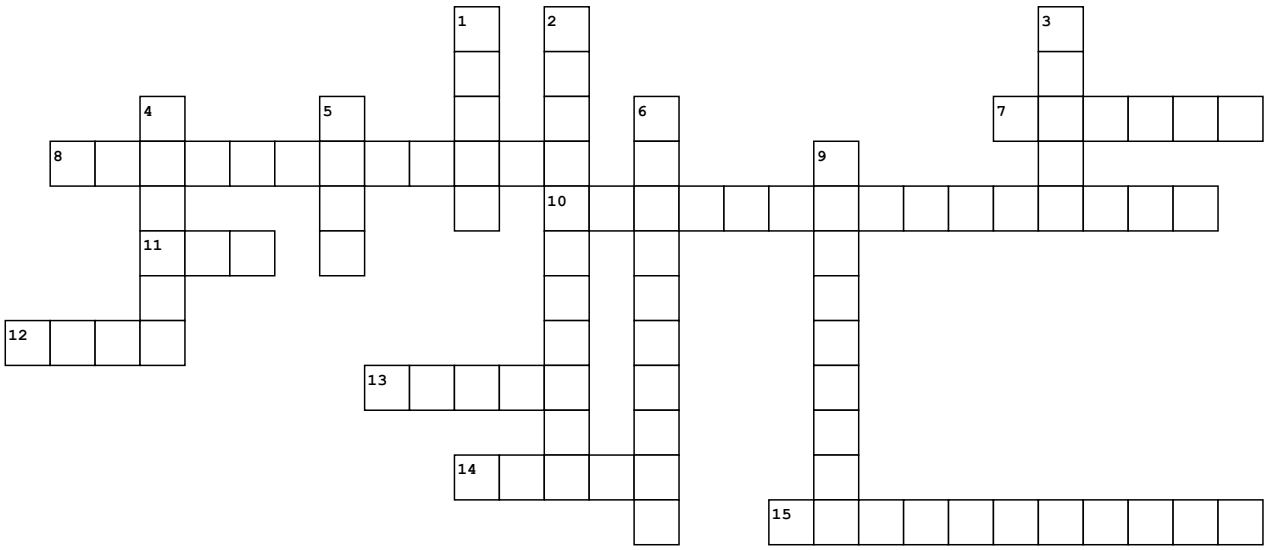
In our series 3 pts are now continuing pregnancy and rest 5 had successful vaginal deliveries at term.

Advantages :

- being extraperitoneal the procedure carries less chance of infection
- monofilament prolene suture is nontraumatic and easy to maneuver.
- cerclage being high in nature claims high success rate comparable with laparoscopic and vaginal intraperitoneal approach.
- whenever needed suture can be easily removed in opd set up.

Cross Word Puzzle

Nalini Bala Pandey*, Sameena Naz**
*Consultant, **Senior Resident, Department of Obstetrics & Gynaecology, MAMC & Lok Nayak Hospital, New Delhi.



Across

7. Ca Ovary Stage 2A include spread to which organ?

8. CA125 is which type of protein?

10. Masculinizing tumour of ovary?

11. How many ultrasound predictors are used by IOTA for assessment of malignant tumour?

12. Name a test to determine risk of malignancy which include 5 analytes?

13. Which stage of ovarian cancer include involvement of retroperitoneal nodes?

14. Most common cancer metastasizes to ovary?

15. Which anti-angiogenic agent is used in advanced recurrent epithelial ovarian cancer?

Down

1. Which model is used by International ovarian tumour analysis (IOTA) group to differentiate between benign and malignant adnexal masses?

2. Histological characteristics of clear cell ovarian carcinoma?

3. Which modality is best for detecting recurrent ovarian cancer?

4. Which antigen-based vaccine is being studied in epithelial ovarian cancer?

5. Which gene mutation is involved in TYPE 1 (low grade) serous epithelial ovarian cancer?

6. Which antiemetic is used for acute and delayed gastrointestinal toxicity of cisplatin?

9. Type of chemotherapy in which paclitaxel is given weekly @ 80mg/m2 with 3 weekly carboplatin?

Mail the answers to aogdeditor22@gmail.com. The correct answers and names of the three winners will be announced in the next issue.

AOGD Sub-Committee Chairpersons 2022-2024

Committee	Chairperson	Contact No	Email.id
Breast and Cervical Cancer Awareness, Screening & Prevention Sub-Committee	Dr Mrinalini Mani	9811835888	drmrinal5@gmail.com
Infertility Sub-Committee	Dr Manju Khemani	9810611598	dr.manjukhemani@gmail.com
Rural Health Sub-Committee	Dr Shivani Agarwal	9868249464	dragarwal.shivani@gmail.com
Multidisciplinary Sub- Committee	Dr Kiran Guleria	9811142329	kiranguleria@yahoo.co.in

AOGD Sub-Committee Chairpersons 2021-2023

Committee	Chairperson & Co- Chairperson	Contact No	Email.id
Endometriosis Sub-Committee	Dr. Anjila Aneja	9810059519	anjilaaneja1966@gmail.com
QI Obst & Gynae Practice Sub-Committee	Dr K Aparna Sharma, Chairperson	9711824415	kaparnsharma@gmail.com
	Dr Jyoti Bhaskar, Co-Chairperson	9711191648	jytbhaskar@yahoo.com
Oncology Sub-Committee	Dr Sunita Malik	9818914579	svmalik@yahoo.com
Urogynaecology Sub-Committee	Dr Geeta Mediratta, Chairperson	9810126985	gmediratta@yahoo.com
Adolescent Health Sub-Committee	Dr Anita Rajouria, Chairperson	9711177891	anitarajorhia716@gmail.com
	Dr Sujata Das, Co- Chairperson	9971946064	drdas_sujata2110@yahoo.co.in
Reproductive Endocrinology Sub-Committee	Dr Surveen Ghumman, Chairperson	9810475476	surveen12@gmail.com
	Dr Deepti Goswami, Co-Chairperason	9968604348	drdeeptigoswami@hotmail.com
Safe Motherhood Sub-Committee	Dr Manju Puri	9313496933	drmanjupuri@gmail.com
Fetal Medicine & Genetics Sub-Committee	Dr Seema Thakur, Chairperson	9818387430	Seematranjan@gmail.com
	Dr Sangeeta Gupta, Co- Chairperson	9968604349	drsangeetamamc@gmail.com
Endoscopy Sub-Committee	Dr Kanika Jain	9811022255	dr.kanika@gmail.com

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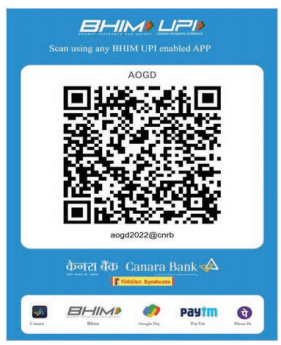

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